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ABSTRACT

Tuberculosis 1

AO001

ASSOCIATION BETWEEN NUTRITIONAL STATUS USING MALNUTRITION SCREENING TOOL AND BACTERIAL LOAD AMONG MDR-TB PATIENTS

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Background and Aims: Malnutrition in MDR-TB patients may increase the risk of treatment failure and death. Therefore, rapid and precise malnutrition detection is essential in the management of MDR-TB. One of the fastest and simplest nutritional screening tools is Malnutrition Screening Tool (MST). The present study aims to determine the association between nutritional status using MST and bacterial load in patients with MDR-TB.

Methods: This cross-sectional study was conducted at RSUP Persahabatan Jakarta in June–October 2017. The study included 81 MDR-TB patients who had not received MDR-TB treatment. GeneXpert was used to diagnose MDR-TB in subjects. To identify nutritional status of subjects, MST questionnaire was used and the result was categorized into at-risk and non-risk group of malnutrition. Meanwhile, classification of sputum bacterial load using *International Union Against Tuberculosis and Lung Disease* (IUATLD) scale. Data were analyzed by SPSS 20.

Results: From 81 subjects, 67% subjects were at risk of malnutrition and 58% subjects have BMI less than 18 kg/m². Bivariate analysis showed that there is no association between MST and bacterial load in patients with MDR-TB ($P = 0.923$). However, the difference in the proportion of positive bacterial loads between the at-risk and non-risk groups of malnutrition is 11.2%. In addition, at risk group of malnutrition, bacterial load tends to be positive

Conclusion: MDR-TB patients who are at risk of malnutrition based on MST have higher bacterial load than non-risk group of malnutrition

AO002

PHARMACOVIGILANCE FOR PUBLIC HEALTH UTILITY: SAFETY MONITORING OF NEW REGIMEN FOR LATENT TUBERCULOSIS INFECTION TREATMENT

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Background and Aims: Postmarketing surveillance is important for drug safety. Once-weekly Rifapentine plus isoniazid (3HP) for latent tuberculosis infection (LTBI) was endorsed in April, 2016 before the Rifapentine was licensed in Taiwan. Severe adverse events (SAEs) could hinder prescription and uptake of such pre-licensed drugs. Our goal is to tighten 3HP pharmacovigilance to raise treatment rates.

Methods: Taiwan's 'LTBI Treatment for All Contacts Program', provides 3HP as an alternative to the 9-month-isoniazid (9H) regimen for LTBI contacts aged 12 years and older. In addition, a pre-licensed, post-marketing 3HP pharmacovigilance project was planned utilizing the discontinuation of prescriptions for the electronic TB case management

system at the Taiwan Centers for Disease Control (TCDC), the spontaneous reporting databases at the Taiwan National Adverse Drug Reaction (ADR) Reporting System, and the drug injury relief database (DIRD) at the Taiwan Drug Relief Foundation (TDRF).

Results: Of the 4721 patients in the TCDC TB case management system prescribed 3HP from April, 2016 to June, 2017, 450 (9.5%) suffered AEs and stopped 3HP permanently. Among 65 SAEs reported, only 34 (0.72%) were associated with 3HP with no mortality or long-term sequelae. According to ADR Reports, only 2 of 31 patients were unidentifiable in TCDC database. Mild rash was noted in one haemodialysis patient at a pilot site and was categorized as non-SAE. The other was a patient who completed treatment smoothly although she encountered dyspnoea and conjunctivitis. As for DIRD, a 74 male hepatitis B carrier patient suffered from hepatotoxicity fitted criteria of SAE, was found to be captured by TCDC case management system, too.

Conclusion: From public health perspective, comprehensive pharmacovigilance projects are crucial to ensure newly-implemented drug regimens are safe. Such programs allow for shorter treatment regimens when drug licensure has not yet been approved. Inter-department information linkage could help to meet safety monitoring goals.

AO003

PUBLIC-PRIVATE MIX ACTIVITIES IN ENHANCING TUBERCULOSIS CASE NOTIFICATIONS IN SURABAYA, INDONESIA

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Background and Aims: WHO estimates more than 1 million cases of TB in Indonesia in 2015. Nevertheless, only approximately 360,000 cases notified. Based on the national basic health survey, East Java has the second highest prevalence of TB among provinces in Indonesia, and Surabaya is the city in east java with the largest number of notified TB cases. However, TB cases in private health providers in this city had not been reported well. Thus, our study was aimed to evaluate the role of Public-Private Mix (PPM) activity in TB case notifications in Surabaya.

Methods: This study trained 26 pulmonologists from 21 private hospitals in Surabaya to participate in PPM activities. Those pulmonologists were encouraged to report their TB cases to the city health department and manage them in accordance with International Standards for Tuberculosis Care (ISTC). Afterward, we evaluated the TB case notifications from October 2014 until 2017.

Results: Our study found that PPM activities contributed notifications of 3455 (20%) out of 17,465 cases. 2738 (79%) were adult, and the rest were children and extrapulmonary cases. 2447 had AFB examinations, and 1044 (42.6%) were AFB positive. 2146 from all of 3455 cases (69.9%) were treated using drugs provided by National TB programme. In the end of treatment, the success rate were 67% (86 out of 128 patients) in 2014, 87% (581 out of 665 patients) in 2015, and 96.8% (1193 out of 1233 patients) in 2016. Loss to follow-up rate were 43%, 26%, and 12% respectively in 2014, 2015, and 2016.

Conclusion: This study showed that PPM activities can increase TB case notifications, thus strengthen the TB management and control

AO004

GENEXPERT MTB/RIF FOR RAPID DIAGNOSIS AND RIFAMPIN RESISTANCE DETECTION OF ENDOBRONCHIAL TUBERCULOSIS

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Background and Aims: Delayed diagnosis and treatment of tuberculosis (TB) contribute to poor outcomes, especially for endobronchial TB (EBTB), which typically leads to tracheobronchial stenosis. Finding rapid and accurate diagnostic tools for EBTB is crucial. GeneXpert Mycobacterium tuberculosis (MTB)/rifampin (RIF) was recommended by the World Health Organization (WHO) as a standard molecular biological diagnostic technique for MTB. The aim of this study was to evaluate the efficacy of GeneXpert MTB/RIF for diagnosing EBTB and for evaluating RIF resistance.

Methods: Biopsy tissue and bronchial brushings from EBTB patients were prospectively assessed with GeneXpert MTB/RIF. The diagnostic yields of auramine O-stained sputum smears and bronchial brush smears were obtained, and the results were compared with the cultures of sputum and biopsy tissues for MTB.

Results: In 61 confirmed cases of EBTB, the sensitivities of sputum smear, bronchial brush smear, sputum culture and tissue culture to diagnose EBTB were 13.1%, 32.8%, 36.1% and 68.9%, respectively. For bronchial brushings and biopsies, our data showed sensitivities of 57.4% and 63.9%, respectively, and a specificity of 100% for GeneXpert MTB/RIF, and these results were superior to those of sputum smears, bronchial brush smears and sputum culture. GeneXpert MTB/RIF for bronchial brushings and biopsies showed complementarity in its diagnostic performance. Resistance to RIF was identified in 17.4% (8/46) of GeneXpert MTB-positive cases.

Conclusion: GeneXpert MTB/RIF may enable more rapid EBTB diagnosis and determination of RIF resistance, which are crucial for timely treatment.

AO005

EFFICACY AND SAFETY OF DELAMANID FOR PULMONARY MULTI-DRUG RESISTANT TUBERCULOSIS

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Background and Aims: Delamanid is a novel drug to treat multidrug-resistant tuberculosis (MDRTB) and was approved by the European Medicine Agency and Japan's Pharmaceuticals and Medical Devices Agency in 2014. Although delamanid has been widely used in Japan, its efficacy and safety in the real world remain uncertain.

Methods: We retrospectively evaluated 10 pulmonary MDRTB patients for whom treatment with regimens including delamanid was started between 2014 and 2017. Treatment outcomes were defined as cure, culture conversion, failure or death.

Results: Mean age of patients was 59.7 years, and 7 patients were male. Six patients had cavitary disease. Drug sensitivity testing showed that two patients had extensively drug-resistant tuberculosis. Two adverse events were reported; QT prolongation requiring discontinuation and mild peripheral neuropathy. Delamanid could be administered as long as 18 months in 3 patients. Overall treatment outcomes were 3 cured, 5 culture conversion and 2 died. Bacteriological success was achieved in 90% (9/10) patients including one patient died of cerebral haemorrhage.

Conclusion: Delamanid has a considerable efficacy for treating pulmonary MDRTB with acceptable safety profile.

AO006

POLY-FUNCTIONAL CD8 T CELLS CAN DISCRIMINATE MAC LUNG DISEASE FROM AIRWAY COLONIZATION IN NON-HIV HOST

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Background and Aims: increases recently in non-HIV host and becomes a clinical concern. Because the clinical relevance (patients with MAC-LD divided those with MAC isolates) is only 30–40 %, it is an important to discriminate true MAC-LD from those with colonization. MAC-specific T cells could be a target to investigate.

Methods: We enrolled patients with MAC-LD (N = 33), MAC airway colonization (N = 22), and the controls (N = 22) for comparing the levels of peripheral blood poly-functional T cells after stimulation by MAC plus CD3 and CD28 antibodies or by phorbol 12-myristate 13-acetate (PMA) and ionomycin. The responses were measured by flow cytometry, and we analyzed the inter-group difference.

Results: The age and sex as well as the average percentages of CD4 and CD8 T cells were similar among the three groups. Between the patients with MAC-LD and the controls, the MAC-related TNF- α cells (with or without other cytokine expression) on CD8+ T cells were higher in the patient with MAC airway colonization than those with MAC-LD (36.2% vs 27.5%, $p = 0.021$ by Mann Whitney U test). In stimulation with PMA plus ionomycin, IL-2 single positive CD8 T cells was higher in MAC-LD than that in MAC airway colonization. comparing with MAC-PD and airway colonization (6.4% vs 3.4%, $P = 0.024$). The percentage of MAC-specific CD8+ all TNF- α and super-antigen induced CD8+ single IL-2+ could have good performance to predict MAC pulmonary infection from airway colonization by ROC curve (the AUC: 0.748, $P = 0.008$).

Conclusion: The MAC-LD had an attenuated CD8 TNF- α T cell response to MAC and might represent the host vulnerability. The MAC-specific CD8+TNF- α T cells and CD8+IL-2+ T cells could be a useful predictor favouring MAC-LD.

AO007

RARE EXTRAPULMONARY TUBERCULOSIS: FOUR CASES REPORT

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Background and Aims: Tuberculosis (TB) is the most common fatal infectious disease worldwide with high rate of incidence, especially in developing countries including Indonesia. Despite of TB mostly found in the lungs, patients with extrapulmonary TB (EPTB) showed significant proportion among all the reported TB cases in different populations. In developing countries, EPTB accounts for about 50% of TB cases.

Methods: Hereby, we will report 4 cases of EPTB.

Results: First, a female teacher, 25 years old with clinical presentation neuropathy, atrophy of right thenar muscles, and scars post neural decompression seen in volar and right dorsal acromion area with histopathological showed caseating necrosis area, with epithelioid histiocytes cells and datia Langhans cells periphery. Thus, the patient was diagnosed as right *n. ulnaris* tuberculoma. Second, a female housewife, 63 years old with clinical presentation nodule in hard and soft palatal, and histopathological revealed chronic granulomatous inflammation. Thus, the patient was diagnosed as palatal TB. Third, a female housewife, 32 year as old with clinical presentation hyperkeratotic plaque, erythematous, and squamatic at region interphalanx of right index finger which histopathological revealed verrucous cutaneous TB. Fourth, a male fisherman, 32 years old with clinical presentation pain and enlargement of right knee joint, which histopathological revealed suppurative chronic granulomatous inflammation. Thus, the patient was diagnosed as right gonitis TB.

Conclusion: The four patients underwent antituberculosis treatment with FDC 2(HRZE)/4(HR)3 and clinical improvement was observed in all cases.

AO008

QUANTIFERON-TB GOLD PLUS IS MORE SENSITIVE THAN QUANTIFERON-TB GOLD IN-TUBE FOR LATENT TUBERCULOSIS INFECTION AMONG RESIDENTS IN LONG-TERM CARE FACILITY

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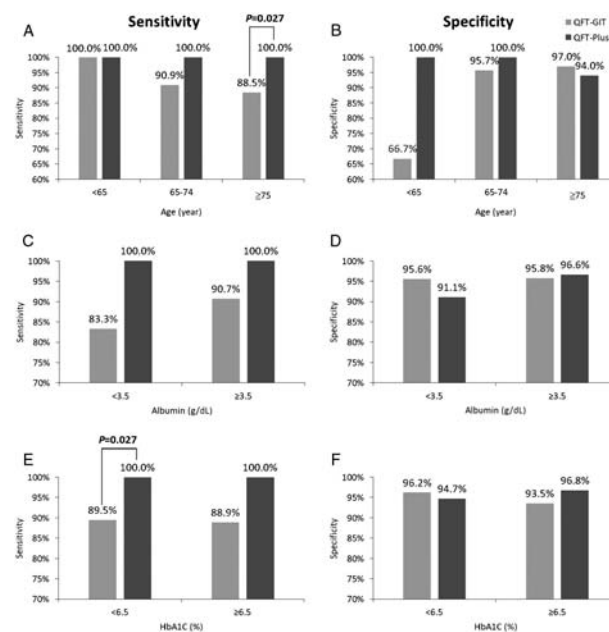
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Background and Aims: We investigated the prevalence of latent tuberculosis infection (LTBI) among the residents in seven long-term care facilities (LTCFs) located in different regions of Taiwan and compared the performance of two interferon-gamma release assays, i.e. QuantiFERON-TB Gold In-Tube (QFT-GIT) and QuantiFERON-TB Gold plus (QFT-Plus) for screening LTBI.

Methods: We assessed the diagnostic performance against a composite reference standard (subjects with persistent-positive, transient-positive and negative results of QFTs during reproducibility analysis were classified as definite, possible and not LTBI, respectively).

Results: Two hundred and forty-four residents were enrolled and 229 subjects were included into analysis. The median age was 80 years (range, 60–102 years old) and 117 (51.1%) were male. Among them, 66 (28.8%) and 74 (32.3%) subjects had positive results of QFT-GIT and QFT-Plus, respectively, and 215 (93.9%) subjects showed agreement results. Using composite reference standard, 66 (28.8%), 11 (4.8%), and 152 (66.4%) were classified as definite, possible and not LTBI, respectively. For definite LTBI, the sensitivity, specificity, positive predictive value, and negative predictive value of QFT-GIT were 89.4%, 95.7%, 89.4%, and 95.7%, respectively, and those for QFT-Plus were 100.0%, 95.1%, 89.2%, and 100.0%. The sensitivity of QFT-GIT decreased gradually with age. Compared to QFT-GIT, QFT-Plus displayed significantly higher sensitivity (100.0% vs 89.4%, $P = 0.013$) and similar specificity (95.1% vs 95.7%).

Conclusion: In conclusion, a high prevalence of LTBI was found among elders in LTCFs in Taiwan. The new QFT-Plus test demonstrated a higher sensitivity than QFT-GIT in the older adults in LTCFs.



Bronchoscopy and Interventional Techniques 1

AO009

CHANGES IN VENTILATION AND PERFUSION FOLLOWING LOWER LOBE ENDOSCOPIC LUNG VOLUME REDUCTION (ELVR) WITH ENDOBRONCHIAL VALVES IN PATIENTS WITH SEVERE COPD

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Background and Aims: We have previously reported changes in ventilation (V) and perfusion (Q) following upper lobe ELVR in patients with severe COPD. There were significant improvements in both V and Q, and V/Q matching in the contralateral lung, especially the non-targeted lower zone. This correlated to significant improvements in gas transfer parameters as measured by KCO at 12 months. The purpose of this study was to investigate V and Q changes following ELVR targeting the lower lobes.

Methods: 7 patients with lower lobe heterogeneous emphysema were recruited and underwent unilateral lower lobe ELVR at Macquarie University Hospital. Complex full lung function tests (PFT), St George's Respiratory Questionnaire (SGRQ), 6-min walk tests (6MWT), and planar ventilation and perfusion (VQ) scans were performed at baseline and at 1, 3 and 12 months post-ELVR.

Results: Compared to baseline, patients showed significant improvements in FEV1, (0.83 ± 0.09 L to 0.97 ± 0.12 L $P < 0.05$), 6MWT (200.33 ± 56.54 m to 274.24 ± 48.03 m $P < 0.05$), and SGRQ (61.13 ± 5.33 to 42.86 ± 6.99 $P < 0.05$) at 3 months after ELVR. This improvement was maintained at 12 months. Targeted atelectasis was achieved in 6 of 7 patients. There was a corresponding significant improvement in the differential ventilation ($30.21 \pm 3.04\%$ to $37.82 \pm 3.76\%$, $P < 0.05$) and perfusion ($31.77 \pm 2.53\%$ to $35.60 \pm 2.58\%$, $P < 0.05$) of the contralateral non-targeted upper zone. There was a trend towards improved KCO which did not reach statistical significance ($57.01 \pm 6.96\%$ to $60.86 \pm 7.67\%$).

Conclusion: In heterogeneous severe COPD patients undergoing ELVR with endobronchial valves targeting the lower lobes, there are clinical and PFT improvements similar to that reported in ELVR targeting upper lobes. There are associated improvements in V/Q matching with the greatest improvement in the contralateral non targeted upper zones. This small initial study needs validation with a larger number of subjects.

AO010

ANALYSIS OF 35 CASES OF BRONCHIAL FISTULA CURED BY IMPLANTATION OF NITINOL DOUBLE DRUM TYPE OCCLUDER

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Background and Aims: Bronchial fistula is a common clinical problem in pulmonary disease and post-surgery operation. We aim to explore the clinical effect of implantation of nitinol double drum type occluder using on bronchial fistulas, and establish a reliable, safe and effective skill in diagnosis and treatment for bronchial fistulas.

Methods: Patients with post-surgery bronchial fistula treated in our department from January 2015 to May 2018 improve the following procedures: chest contrast enhanced CT for understanding of postoperative intrathoracic vascular structure and distribution; bronchoscopy airway exam for understanding the fistula and the bronchus lumen; Interventional Bronchogram by bronchoscope guide contrast agent injection around the fistula and monitoring under X-ray fluoroscopy; determine the fistula about location, diameter, the affiliated bronchial lumen, and the distance to thoracic outlet; Guided by flexible bronchoscopy and wire implant nitinol double drum type occluder. Follow-up by chest X-ray and bronchoscopy after 1, 6, 12 months, and survival period of long-term clinic follow-up.

Results: A total of 35 patients were enrolled, including 25 male and 10 female, mean age 52.2 years; including: 9 cases of left main bronchial fistula, 10 cases of right main bronchial fistula, 4 cases of bronchus fistula, 4 cases of right lower lobe bronchial fistula, 6 cases of right upper lobe bronchial fistula, 2 cases on the left the bronchial fistula, were post-operative fistulas. All patients were successfully implanted nitinol double drum type occluder in the fistula of bronchial stump. The fistula accounted for 4–16 mm of linear distance, the average is 7.83 mm; the implanted occluder device diameter is 10–26 mm, average is 16.62 mm; all cases were performed under conscious sedation and local anaesthesia by flexible bronchoscopy, the follow-up of 6–40 months, all cases of fistula were completely closed, achieved clinical cure, no severe adverse reactions and complications.

Conclusion: Transbronchial implantation of nitinol double drum type occluder for bronchial fistula is a safe and effective, reliable and convenient treatment.

UTILITY AND SAFETY OF COBALT CHROMIUM NEEDLE FOR ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA)

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Background and Aims: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has become one of standard methods for obtaining specimens of mediastinal and hilar lesions. Several types of needles with various sizes and materials are available for EBUS-TBNA, however, there have been no studies to compare the sampling yield and safety of cobalt chromium and stainless steel needles. We aimed to compare the histological specimen yields of EBUS-TBNA performed using stainless steel and cobalt chromium needles.

Methods: A total of 77 patients (88 lesions) who underwent EBUS-TBNA at Kasukabe Municipal Medical Center between July 2016 and December 2017 were retrospectively evaluated. Patients who underwent EBUS-TBNA with a 22G stainless steel needle (Olympus, NA-201SX-4022) (38 patients, 41 lesions) and those who underwent EBUS-TBNA with the use of 22G cobalt chromium needle (Boston Scientific, M00558220) (39 patients, 47 lesions) were classified into the O and B groups, respectively. The differences in the cytological and histological findings were analyzed to compare the diagnostic yield and utility of each needle. In addition, clinical characteristics of the patients, duration of procedure, complications, diagnostic accuracy and sampling yield were compared between these groups.

Results: There were no significant differences between these groups in terms of the baseline characteristics of the patients and punctured lesions. The procedure time of the B group was significantly shorter (B group vs O group, 22 min vs 26 min, $P = 0.007$), while histological specimen yield of the B group was significantly higher (91.5% vs 73.2%, $P = 0.044$). There were no differences between these groups with regard to diagnostic yield or complications.

Conclusion: Cobalt chromium needle for EBUS-TBNA may improve the diagnostic histological specimen yield and reduce the procedure time in comparison to the use of stainless needle.

AO012

USEFULNESS OF TRANSESOPHAGEAL BRONCHOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION IN THE DIAGNOSIS OF MEDIASTINAL LESIONS ADJACENT TO THE OESOPHAGUS

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Background and Aims: In recent years, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is reportedly a feasible and well-tolerated modality for diagnosis mediastinal lesion. However, in cases with severe stage COPD or impending respiratory failure, bronchoscopy itself may cause serious complications. From previous literature, endoscopic ultrasound with bronchoscope-guided fine-needle aspiration (EUS-B-FNA) is reportedly as a feasible and well-tolerated modality. But additional advantages of EUS-B-FNA are yet to be thoroughly investigated. The purpose of this study was to evaluate the ability

of EUS-B-FNA to obtain sufficient tissue specimens for diagnosis of mediastinal lesions adjacent to the oesophagus.

Methods: Between December 2015 and May 2018 in our institute, patients who underwent EUS-B-FNA to diagnose mediastinal lesions adjacent to the oesophagus were enrolled ($n = 31$). EUS-B-FNA was performed when bronchoscopic diagnosis was impossible or difficult to obtain sufficient samples.

Results: EUS-B-FNA was performed on 40 lesions in 31 patients. Among the target lesions, 21 were mediastinal lymph nodes including nodal stations 2 L, and 4 L. The remaining 10 were mediastinal lesions adjacent to the oesophagus. EUS-B-FNAs were completed without complications in all the patients. The diagnostic yield of EUS-B-FNA in diagnosing mediastinal lesions adjacent to the oesophagus was 100%.

Conclusion: EUS-B-FNA is a practical, feasible and well-tolerated method to obtain abundant tumorous tissue samples for diagnosis, especially when the target lesions are inaccessible by other modalities because of their locations or because of the patient's poor physical condition.

AO013

IS BRONCHOSCOPY INDICATED IN PATIENTS WITH HAEMOPTYSIS WHEN THE CT IS NORMAL?

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Background and Aims: There is uncertainty regarding the need for bronchoscopy in patients with haemoptysis when the CT scan is normal. (point-counter point, Chest Feb 2018) Of particular concern is the risk of missing lung cancer if bronchoscopy is omitted. Thus, the aim of this study is to perform a systematic review of the evidence for the diagnostic value of bronchoscopic examination in patients with haemoptysis when lung cancer is not detected on the CT.

Methods: I have performed a critical, qualitative, narrative review leading to a realist synthesis of the literature on this question. This is based upon publications on the investigation of haemoptysis in MEDLINE with search terms limited to 'haemoptysis', 'bronchoscopy', and 'CT'.

Results: The literature search yielded 269 eligible publications from 1990–2018. This report includes data from 2,410 patients described in 16 primary publications. There were 204 patients with lung cancer. The incidence of lung cancer was 0.4% to 35% (1 study only enrolled patients with normal CTs). The diagnosis was missed on CT scan in 4 patients. Thus, in patients presenting with haemoptysis the overall risk of missing lung cancer was 4/2410 [0.17%, 95%CI(0.07% to 0.43%)]. With advances in CT equipment and technique, over the recent 20 years, lung cancer was missed in only 1/1996 patients [0.05%, 95%CI(0.01% to 0.28%)]. Conversely, the risk of missing the diagnosis on CT in patients with lung cancer was 4/204 [2%, 95% CI (0.8% to 4.9%)] overall and 1/164[0.6% 95%CI(0.1% to 3.3%)] in the past 20 years.

Conclusion: In conclusion, missing lung cancer on CT examination is extremely rare in patients presenting with haemoptysis. Thus, in general, bronchoscopy may not be indicated to rule out lung cancer when the CT is normal. However, it might still be indicated for other reasons, in selected patients and exceptional situations.

FEASIBILITY AND CLINICAL IMPACT OF RE-BIOPSY IN ADVANCED LUNG ADENOCARCINOMA AFTER PROGRESSES DURING FIRST-LINE EPIDERMAL GROWTH FACTOR RECEPTOR-TYROSINE KINASE INHIBITORS

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Background and Aims: When advanced adenocarcinoma progresses during first-line epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKI) treatment, re-biopsy may be indicated to detect the mechanisms of acquired resistance, such as secondary EGFR mutations (T790M mutation), mesenchymal-to-epithelial transition factor receptor (MET) amplification, and human epidermal growth factor receptor 2 (HER2) gene amplification. Among these, T790M mutation was observed in nearly half of all cases that were resistant to EGFR-TKIs. The aim of this study was to assess the feasibility and safety of different re-biopsy approaches in advanced adenocarcinoma in a real-world setting.

Methods: We retrospectively reviewed patient characteristics, tumour progression sites and rebiopsy procedures between Jan 2013 and Dec 2017

Results: There were 538 lung adenocarcinoma patients used EGFR-TKI for first line treatment. 410 patients (76.2%) progressed during EGFR-TKI treatment and 102 patients (19%) still use EGFR-TKI for treatment. 26 patients (4.8%) lose follow-up after treatment. Re-biopsy were arranged in 203 patients (49.5%) and was successful in 160 patients (78.8%). Re-biopsy with different approaches and the successful rate were: cytology from pleural effusion: 63.3%, operation: 100%, radial probe endobronchial ultrasound: 83.9%, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): 100%, CT guide biopsy: 76.4%, echo guide biopsy: 70.6%, medical pleuroscopy: 100%. Mutational analysis was possible in almost all technically successful cases. Nine patients (4.4%) had re-biopsy-associated complications, most commonly pneumothorax.

Conclusion: This study conducted in real-world conditions, shows that re-biopsy of lung adenocarcinoma patients after first-line treatment is feasible, acceptable, and useful for therapeutic decision

AO015

THE ROLE OF CT-GUIDED PERCUTANEOUS TRANSTHORACIC NEEDLE BIOPSY WITH VIETNAM BIOPSY CALIBRATOR FOR THE DIAGNOSIS OF PULMONARY NODULES

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Background & Aims: CT guided percutaneous transthoracic needle biopsy is a relatively non-invasive way to obtain tissue for the diagnosis of pulmonary nodules. One barrier to its use is the difficulty of positioning the needle at the right angle and depth. We have developed a three-dimensional positioning angle meter to assist biopsy needle during lung biopsy. To determine the role of the 'Vietnam Biopsy Calibrator' (VBC) and CT-guided percutaneous transthoracic needle biopsy in the diagnosis of lung nodules.

Methods: 85 patients with lung nodules had a CT-guided percutaneous transthoracic needle biopsy done with the assistance of the VBC,

three-dimensional positioning angle. We report the results of this prospective series.

Results: 45.3% had a nodule size < 3 cm. 98.8% of patients were performed in supine and prone position. The average depth of penetration was: 53 mm $\pm$ 18 mm. The percentage of adequate specimens for cytological diagnosis was 97.6%, and adequate specimens for histopathology was 100%. Histopathological diagnosis: 45 patients (52.9%) had cancer, tuberculosis inflammation: 17 (20.0%) patients, and other benign pulmonary lesions. Overall incidence of complications: 22.4%, mostly mild with only 1 patient (1.2%) developed a clinically significant pneumothorax requiring intervention.

Conclusion: Pulmonary CT-guided percutaneous transthoracic biopsy with the assistance of the VBC is an efficient technique in diagnosis lung nodules that has a low incidence of complications.

COPD 1

AO016

LINKING AIRWAY GENE EXPRESSION AND LUNG MICROBIOME IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background and Aims: Bacterial colonisation of the airways frequently complicates chronic obstructive pulmonary disease (COPD). We hypothesised that microbial over-abundance and dysbiosis in airways of patients with COPD would correlate with excessive airway inflammation.

Methods: Patients were recruited during exacerbation or stability from a tertiary referral hospital. Spontaneously-produced sputum was tested using conventional culture, quantitative PCR (qPCR) for 48 bacterial and fungal targets (QIAGEN), 16S rRNA sequencing for the bacterial microbiome, and NanoString gene expression (inflammation array, 249 targets).

Results: 61 patients (37 exacerbation, 24 stable) were recruited (31 male, 30 female, mean age 69 years, FEV1 49% predicted, mean smoking history 42 pack-years). Exacerbation patients had reduced quality of life and more purulent sputum, compared with stable patients. qPCR detected bacterial and fungal species in 95% of sputum samples, versus 43% with culture, with no statistically significant difference in microbial load between exacerbation and stability. NanoString inflammatory gene expression analysis showed decreased HLA-DRB1 (fold change 0.44, $P < 0.001$) mRNA expression in the exacerbation cohort compared to stable. Patients with qPCR-detected *Streptococcus pneumoniae* in sputum (80% of patients) showed increased sputum expression of CXCL1 (fold-change 2.3, $P = 0.006$), whereas presence of *Prevotella oris* (36% of patients) was associated with reduced expression of AREG (fold-change 0.47, $P = 0.003$) and NLRP3 (fold-change 0.55, $P = 0.012$). Sputum microbial richness and diversity, as determined by 16S rRNA sequencing, were not statistically significantly different between exacerbation and stable patients.

Conclusion: COPD patients during exacerbation had similar numbers of bacterial species compared to stable patients, as detected by qPCR or culture. Inflammatory gene expression analysis demonstrated bacterial species-specific patterns of inflammatory mediators in sputum. No difference in microbial richness or diversity was detected in the sputum of exacerbation and stable patients. Identification of bacterial species-specific interactions with airway inflammatory profiles may help better understand the heterogeneity of COPD and to personalise management.

INVESTIGATING MICRORNA-MRNA INTERACTIONS IN THE COPD MICROENVIRONMENT BY NEXT-GENERATION SEQUENCING AND BIOINFORMATICS

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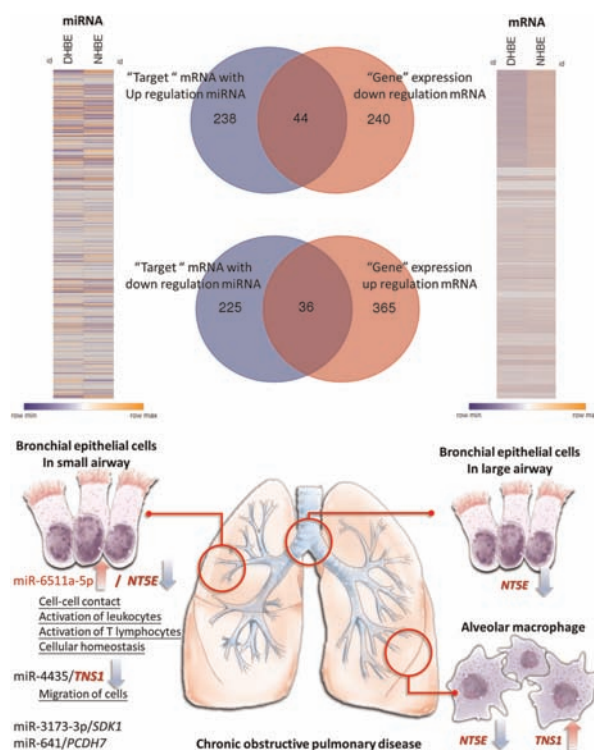
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Background and Aims: Chronic obstructive pulmonary disease (COPD), a chronic inflammatory disease of lungs, affects millions of people in the world. Neutrophils, macrophages, T lymphocytes and bronchial epithelial cells are involved in the inflammatory response in COPD. Finally, COPD would lead to irreversible airflow limitation in the small airway.

Methods: By using next-generation sequencing (NGS), we examined the expression profiles of microRNAs and mRNAs of normal and COPD bronchial epithelial cells. The criteria for microRNAs selection were fold-change >2, and reads per million (RPM) > 1. miRmap database, miRDB database, and TargetScan database were used for predicting the possible miRNA-mRNA interaction. Gene expression omnibus (GEO) database was used to confirm the gene expression in previous studies.

Results: 4 genes with microRNA-mRNA interactions involving in COPD small airway bronchial epithelial cells were identified in this study, including NT5E, SDK1, TNS1, and PCDH7. The significant change of miR-6511a-5p/NT5E interaction was found in small airway bronchial epithelial cells, large airway bronchial epithelial cells, and alveolar macrophage. It implies that miR-6511a-5p/NT5E interaction may be an important factor in COPD. Through bioinformatics, we demonstrated that miR-6511a-5p/NT5E may be associated with the cell-cell contact, activation of leukocytes, activation of T lymphocytes, and cellular homeostasis.

Conclusion: This study offers new information of possible miRNA-mRNA interaction in the COPD microenvironment. miR-6511a-5p/NT5E interaction may have the potential to develop new diagnostic or therapeutic strategies targeting bronchial epithelium for COPD.



AO018

THE EFFECT AND RELATED MECHANISM OF PHOSPHODIESTERASE 4 (PDE4) INHIBITOR ON CD4+ T LYMPHOCYTE PROLIFERATION

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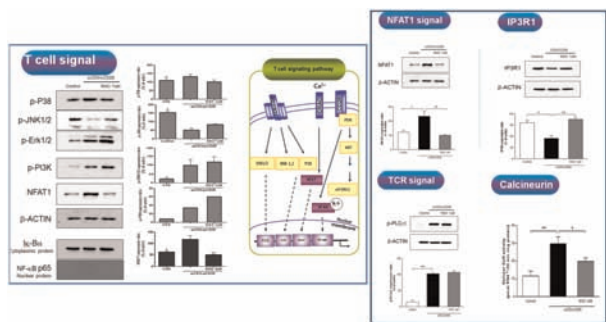
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Background and Aims: PDE4 inhibitors have been attracting attention as new therapeutic agents for chronic airway diseases, it is known to be involved in a wide range of anti-inflammatory and immunomodulatory responses. A pilot study also confirmed that the PDE4 inhibitor inhibited T lymphocyte proliferation. We investigated the PI3K/AKT/mTOR, the MAPK/ERK and the NFAT pathway, which are mainly signaling pathways of T lymphocytes and the mechanism at which stage the PDE4 inhibitor acts.

Methods: After splenocyte isolation of murine cells, CD4 + T cells were isolated and proliferated with anti-CD3/ CD28 antibodies. After treatment with RNO, Western assay was performed with anti-p-P38, anti-p-JNK1/2, anti-p-ERK1/2, anti NFAT1 (NFATc2) and NF-κB (Ik-Bα, NF-κB p65) antibodies. IP3R1, Calcineurin, NFAT1 and p-PLCγ1 were used for the NFAT1 signal pathway.

Results: IL-2 mRNA and IL-2 cytokine were decreased when treated with RNO in proliferated CD4 + cells. RNO inhibited p-P38 and NFAT1 in Western assay. P-JNK1/2, p-Erk1/2, and p-PI3K tend to increase, Ik-Bα and NF-κB p65 were not show significant changes after RNO treatment. In NFAT1 pathway, RNO inhibited NFAT1, Calcineurin synthesis and did not affect IP3R1 and p-PLCγ1(TCR signals).

Conclusion: Phosphodiesterase 4 inhibitor affects the NFAT pathway and affects T lymphocyte proliferation by acting on calcineurin and NFAT1.



AO019

THE ROLE OF MIR-21/SMAD7/TGF-β PATHWAY IN COPD AND THE INFLUENCE ON ACTIVATION OF TH17 CELL

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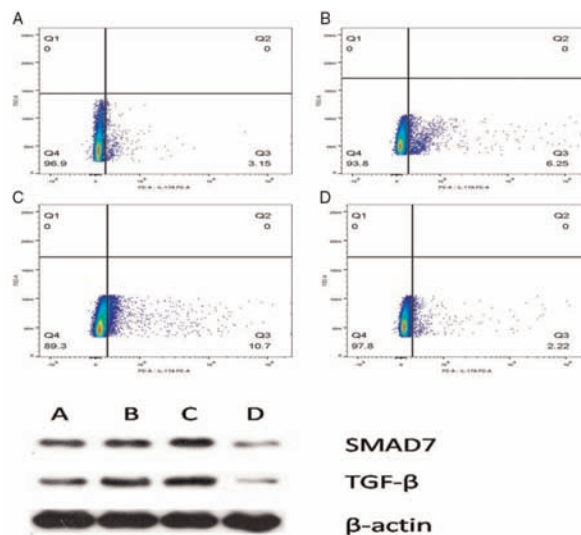
Background and Aims: Chronic obstructive pulmonary disease (COPD) is a multi-pathogenesis disease mainly caused by smoking. The persistent chronic inflammation in lungs result in irreversible damages of lung tissue structure. T-helper cells-17(Th17 cells) promote inflammatory cytokines secretion of other cells, through interleukin-17A(IL-17A), leading

to severer inflammation. However, the mechanisms of Th17 differentiation is inadequately illustrated and we therefore aimed to research the mechanisms behind in COPD.

Methods: The level of miR-21, TGF-β/Smad signals, RORγT and the other Th17 related cytokines were detected in lungs of COPD patients and healthy people. Mice COPD models were built with both wild-type and miR-21-/- mice. Inflammatory cells in mice lungs were observed by immunohistochemical staining (IHS). The proportion of Th17 cells in mice spleen lymphocytes were detected by flow cytometry. The primary CD4+ T cells were isolated from mice by magnetic activated cell sorting and treated with cigarette smoke extract, miR-21 mimics or inhibitors respectively, after which, the change of Th17 proportion were observed, along with TGF-β/Smad signals and RORγT.

Results: The level of miR-21, Smad7, p-Smad2, p-Smad3, TGF-β and Th17 related cytokines were increased in lungs of COPD patients. The lung function of model mice were deteriorated along with increased number of RORγT, CD3+, CD4+, and CD68+ cells in lung tissue. And miR-21-/- mice were between the model and the control. The ratio of Th17 cells were increased in model mice spleen lymphocytes. Moreover, the primary CD4 + lymphocytes tended to differentiate into Th17 cells by CSE and miR-21 mimics, and the protein level of RORγT, Smad7, p-Smad2, p-Smad3 and TGF-β were all increased. MiR-21 inhibitors played a reversed role.

Conclusion: These findings demonstrate that Th17 cells were increased in COPD and it might be partly caused by the enhance of miR-21 through the Smad /TGF-β pathway.



The ratio of Th17 cells and WB of SMAD7/TGFβ

Note: Lanes A,B,C,D: A: control group B: 2.5%CSE group C: miR-21 mimics group D: miR-21 inhibitor group

AO020

DECREASED LEVELS OF PTEN, A NEGATIVE REGULATOR OF PHOSPHOINOSITIDE 3-KINASE (PI3K)/AKT PATHWAY, ARE CORRELATED WITH OBSTRUCTIVE IMPAIRMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Cigarette smoking causes persistent airway inflammation and is considered to be a major cause of chronic obstructive pulmonary disease (COPD). The activation of Phosphoinositide 3-kinase (PI3K)/Akt pathway is known to be important in COPD pathogenesis. Phosphatase and Tensin Homolog Deleted from Chromosome 10 (PTEN) is a negative regulator of PI3K/Akt pathway and reported to be associated with COPD. However, the level and the role of PTEN in COPD subjects remain unclear.

Methods: We acquired bronchial epithelial cells by bronchial brushing from COPD, healthy smokers and healthy non-smokers. PTEN and PI3Kdelta expression in bronchial epithelial cells were measured by real-time PCR and Western blotting. Moreover, we examined the correlation of PTEN and PI3Kdelta with pulmonary functions.

Results: Forty-nine COPD, thirty-one healthy smokers, and twenty-two healthy non-smokers were enrolled in this study. In COPD subjects, PTEN expression was significantly decreased in bronchial epithelial cells and negatively correlated with pack year ($r = -.4$, $P < 0.001$). PTEN mRNA expression was significantly correlated with the parameters of obstructive impairment, such as %FEV1 ($r = 0.26$, $P < 0.01$), FEV1/FVC ($r = 0.2$, $P = 0.04$), and %DLco ($r = 0.34$, $P = 0.0011$). There was no significant difference in PI3Kdelta mRNA levels between each group.

Conclusion: The decrease of PTEN expression was correlated with obstructive impairment of COPD. PTEN might be a possible therapeutic target for COPD.

AO021

OBSERVATION OF THE EFFECT OF METERED DOSE INHALERS AND ELECTRICAL IMPEDANCE TOMOGRAPHY PATTERNS ON MECHANICALLY VENTILATED PATIENTS WITH ACUTE EXACERBATION OF OBSTRUCTIVE PULMONARY DISEASES

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Background and Aims: There is limited information on immediate effect of ICS/LABA therapy on mechanically ventilated patients with acute exacerbation of obstructive pulmonary diseases management in the intensive care unit (ICU).

Methods: We prospectively enrolled acute exacerbation (AE) of chronic obstructive pulmonary disease (COPD) and severe asthma that required invasive mechanical ventilation in 2016–2017. Patients randomly received Foster[®] or Seretide[®] evohaler metered dose inhaler (MDI). The values of dynamic airway resistance and compliance and electrical impedance tomography (EIT) patterns were recorded at baseline, 30, 60, and 100 min post MDIs inhalation.

Results: In total, 17 patients (12 COPD, 5 asthma) received Foster[®] MDI and 15 patients (11 COPD, 4 asthma) treated with Seretide[®] MDI. There were no differences between two groups in baseline demographics, PaO₂/FIO₂ ratio, comorbidity, and APACHE II scores. Patients with AECOPD and severe asthma showed significant improvement of airway resistance after Foster[®] inhalation (-2.48 ± 3.40 cmH₂O/L•S-1, $P = 0.009$). This improvement was not observed in patients with Seretide[®] (-0.40 ± 1.94 cmH₂O/L•S-1, $P = 0.426$). There was no significant change in compliance after treatment in both groups. Clinically, there were no differences between two groups in steroid use, ventilator days, ICU days, and in hospital survival. For EIT patterns, there were no differences in regularity and specific patterns regarding delta-EELI and spatial or temporal differences of ventilation distribution between two groups. We further examined the level of end-expiratory flow (EEF), which related to air trapping and intrinsic PEEP in mechanical ventilated patients. We observed a significant correlation between global

EEF and the sum of regional EEF (correlation coefficient $r = 0.65$, $P < 0.00001$). However, the improvement of regional EEF after ICS/LABA inhalation was significant in asthma ($P < 0.005$) but not in COPD patients.

Conclusion: These findings indicate that Foster[®] had better immediate effect on reducing airway resistance. Regional EEF could provide diagnostic information to monitor the disease progress during treatment.

AO022

SMALL MOLECULE C ENHANCES CELLULAR METABOLISM VIA CREB SIGNALLING IN EXPERIMENTAL MODELS OF COPD

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is inflammatory respiratory disease. The cigarette smoke (CS)-induced alveolar epithelial injury and energy metabolic disorders are known as cause of pathophysiologic changes with COPD. Indeed, CS also increase inflammatory response, reactive oxygen species (ROS) and nitric oxide (NO) and activates MAPKs pathway in alveolar epithelial cells. Here, we founded small molecule C that is able to reduce CS- and PPE-mediated inflammation, ROS or apoptosis through cAMP-related pathway. We would like to show the therapeutic effect of the small molecule C in COPD experimental model in vivo and in vitro.

Methods: For animal models of COPD, mice were injected PPE (5 U/100 g) for 2 weeks, and then small molecule C (0.5 mg/kg) was administered to mice by daily i.p. injection. The murine alveolar type II epithelial cells (MLE-12) were exposed by 0.6% cigarette smoke extract (CSE) for 24 h, and 0.1–3 μ M small molecule C was pre-treated for 24 h before the exposure with CSE in vitro.

Results: Small molecule C inhibited CSE-mediated apoptosis, inflammation and oxidative stress. CSE increased MAPKs pathway signalling in MLE-12 cells, while small molecule C attenuated activation of MAPKs signalling. In mice, PPE-induced emphysematous pathology was reduced by treatment of small molecule C. Moreover, small molecule C increased cAMP activity in the lung tissues.

Conclusion: We have shown the therapeutic ability of small molecule C in COPD experimental models in vivo and in vitro.

AO023

CHANGES OF NEW EPIGENETIC MODIFICATIONS IN THE LUNGS OF CIGARETTE SMOKE EXTRACT-INDUCED MURINE EMPHYSEMA MODEL

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Background and Aims: To investigate whether there are a variety of changes in epigenetic modifications in lung tissue of cigarette smoke extract-induced murine emphysema model in order to provide a new target for the treatment of chronic obstructive pulmonary disease (COPD).

Methods: 12 BALB/c mice were randomly divided into 2 groups: CONTROL group, CSE group, with 6 mice in each group. CONTROL group was injected intraperitoneally with 0.3 mL PBS at days 0, 11, and 22. The other group was injected intraperitoneally with 0.3 mL CSE at days 0, 11, and 22. The lung function and morphometry were measured. The acetylation, ubiquitination, malonylation, succinylation, crotonylation changes were measured by Western blotting.

Results: 1. Compared with the CONTROL group, the airway resistance (RAW) of the CSE group was significantly increased and the lung compliance (Cdyn) was significantly decreased.

2. Compared with the CONTROL group, the MLI and DI of the lung tissue of CSE group were significantly increased.

3. Compared with CONTROL group, acetylation, ubiquitination, succinylation and crotonylation of histone in CSE group were significantly higher than those in control group, and there was no significant difference in malonylation.

Conclusion: There are a variety of new epigenetic changes in the lungs of lung emphysema induced by CSE, but the specific role and mechanism need to be further verified and explored.

Clinical Respiratory Medicine 1

AO024

PATTERN OF SPUTUM CULTURE IN ADULT PATIENTS WITH BRONCHIECTASIS IN THE TOP END OF AUSTRALIA

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Background and Aims: Bronchiectasis is a condition of irreversible bronchial dilatation and distortion, leading to pooling of airway secretions. Bronchiectasis is associated with bacterial colonization, which results in ongoing inflammation and recurrent infections that has impact on natural history and prognosis. There is, resulting in clinical sequelae of symptoms. The purpose of the study was to access sputum culture results in patients identified to have bronchiectasis in the Top End of Australia.

Methods: This was a retrospective observational study of sputum cultures of 388 adults (>18 years old) who were referred to specialist respiratory inpatient, outpatient, and outreach services at the Royal Darwin Hospital, and had a radiological diagnosis of bronchiectasis on HRCT. Patient characteristics studied include age, gender, indigenous status, BMI, residence location and sputum cultures.

Results: The mean patient age was 57.5 + 15.5 (range: 18 – 92 years), and mean BMI was 24.1 + 6.3 (range: 12.9 to 48.5). There were 227 males and 161 females. In terms of Indigenous status, there were 64.8% of Aboriginal; 0.5% of Torres Strait Islanders, and 33.3% of neither descent. The most common micro-organism in sputum culture was *Haemophilus* (37.4%), followed by *Pseudomonas* (25.8%), *Streptococcus* (19.8%), *Candida* (18.3%), *Moraxella* (12.9%), *Aspergillus* (11.6%), *Staphylococcus* (9%), *Burkholderia* (4.9%). Within the population with a positive *Haemophilus* culture, the micro-organisms that are found concurrently in their sputum are *Streptococcus* (38.6%), *Pseudomonas* (36.6%), *Moraxella* (24.1%), *Staphylococcus* (13.1%), *Burkholderia* (4.1%). There is an association between *Haemophilus* infection and residence location ($X^2(3) = 12.079$, $P = 0.007$), but no association with gender ($X^2(1) = 2.118$, $P = 0.146$).

Conclusion: The most common sputum culture in patients with bronchiectasis was *Haemophilus* (37.4%), and most common concurrent infection with it was *Streptococcus* (38.6%). There is an association between *Haemophilus* infection and residence location.

AO025

ENDOTHELIN-1 INDUCES MESOTHELIAL MESENCHYMAL TRANSITION AND CORRELATES WITH PLEURAL FIBROSIS IN TUBERCULOUS PLEURAL EFFUSIONS

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Background and Aims: Endothelin (ET)-1 is involved in various inflammatory and fibrotic diseases. However, the pathogenic role of ET-1 in inflammatory pleural effusions has never been investigated. We aimed to determine the implication of ET-1 in tuberculous pleural effusion (TBPE).

Methods: Sixty-eight consecutive patients were enrolled, including transudative pleural effusion (TPE, $n = 12$), parapneumonic pleural effusion (PPE, $n = 20$) and tuberculous pleural effusion (TBPE, $n = 36$) groups and the effusion ET-1 levels were measured. Treatment outcome and pleural fibrosis, defined as radiological residual pleural thickening (RPT), were assessed at 12-month follow-up. Additionally, in human pleural mesothelial cells (PMCs) treated with or without ET-1 (10 nM), the phenotypic changes, the expression of mesothelial mesenchymal transition markers, and the production of extracellular matrix proteins were assessed serially for 4 days.

Results: The median levels of ET-1 in TBPE were significantly higher than those in TPE (3.3 vs 1.8 pg/ml, $P < 0.001$) and PPE (3.3 vs 1.4 pg/ml, $P < 0.001$), and markedly higher in TBPE patients with RPT > 10mm than those with RPT ≤ 10mm (4.9 vs 2.3 pg/ml, $P < 0.0001$). Moreover, ET-1 levels correlated significantly with residual pleural shadowing of TBPE ($r = 0.47$, $P = 0.004$) at the end of 12-month follow-up. In vitro, ET-1 time- and concentration-dependently upregulated α -smooth muscle actin and downregulated E-cadherin expression, and substantially induced mesothelial mesenchymal transition and collagen production in human PMCs.

Conclusion: ET-1 is significantly raised in TBPE and is implicated in and correlates with tuberculous pleural fibrosis. The profibrotic effect of ET-1 on PMCs confers a novel insight into the pathogenesis and potential therapies for fibrotic pleural diseases.

AO026

THE CORRELATION BETWEEN SMOKING STATUS AND URINARY COTININE LEVEL WITH FEF_{25-75%} IN HIGH SCHOOL STUDENTS

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Background and Aims: Cigarette smoke has been widely demonstrated as a risk factor for respiratory problems. The estimation of newer smokers among teenagers all the world is 82–99 thousand teenagers every day. Cotinine, the primary metabolite of nicotine, has been used as a biological marker of tobacco smoke exposure. Cigarette smoke particles with an average size of 0.1–0.5 mm can reach small airways which are the primary site of airways resistance resulting from cigarette smoke exposure. FEF_{25-75%} measurement is a test to evaluate the function of small airways.

This study aims to determine the correlation between smoking status and urinary nicotine level with FEF_{25-75%} in High School students.

Methods: This observational analytical study using cross sectional design with a simple random sampling was conducted at Vocational High School in Surabaya Indonesia in 2016. The subjects were active and passive-smoker students who meet the inclusion and exclusion criteria. The variables consisted of smoker status (active and passive-smoker), level of urinary cotinine, and FEF_{25-75%}.

Results: The subjects were 40 active-smoking and 40 passive-smoking students with the average age of 17-year old.

The mean levels of urinary cotinine in active-smokers and passive-smokers were 13.02 pg/ml and 7 pg/ml, respectively. The mean value of FEF_{25-75%} in the active-smokers was 80.15%, while in the passive-smokers it was 102.2%. This study showed that there was a significant difference between smoking status and the mean value of FEF_{25-75%},

and a strong correlation between urinary cotinine level and FEF_{25-75%} with a correlation coefficient – 0.512.

Conclusion: This study showed that the smoking status and urinary cotinine level were associated with the impairment of FEF_{25-75%} although the mean value of FEF_{25-75%} were in the normal range (>60% predicted)

AO027

IMPLEMENTATION OF COLLABORATIVE NURSING INTERVENTIONS AND POINTING AND CALLING FOR CHECKING AND DELIVERING VENTILATION PARAMETERS OF INVASIVE MECHANICAL VENTILATOR

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Background and Aims: The ventilator requires precise setting of parameters to achieve the therapeutic effect, however, the prescription of settings is so complex that difficult for nursing staff to set. To improve the safety and quality of nursing service, pointing and calling (P&C) for checking parameters was introduced to designated area of respiratory ward of M&G of UCH.

- Enhance quality of patient care by delivering prescribed parameters to patient on IMV and reducing human error.
- Ensure precise prescription of parameters by P&C and early identifying of problem.
- Enhance nursing staff's confidence in setting the parameters correctly by P&C.

Aims

Methods:

- Set parameters by two nurses with at least one senior nurse following P&C whenever any parameters are modified by doctor.
- Check and record the parameters by two nurses with at least one senior nurse following P&C every shift on specified nursing care report.
- Check and record the parameters by nurse during charting the ventilator chart whenever patient is on IMV support.
- Encourage junior nurse to seek advice from senior nurse whenever in doubt with the prescribed parameters.
- Clarify with doctor when in physician with the prescribed parameters if necessary.
- Senior coverage by specialty nurse to junior on IMV patient care.

Results: Specified nursing care report and ventilator chart were recorded, indicating that prescribed parameters were delivered accordingly. Nursing staff reported that the use of P&C enhanced alertness and accuracy of setting parameters. Moreover, doubtful prescribed parameters were clarified with physician. No case of belated clarification of prescribed parameters with physician was reported. Junior nurse reported that enhanced confidence in setting parameters IMV.

Conclusion: No incidence related to discrepancy between prescribed IMV parameters and actual parameters given was reported, which indicating that the implementation of collaborative nursing interventions and P&C improved patient safety. In addition, competency in caring complex IMV patient case of junior nurse was enhanced.

AO028

ADDITIONAL ROLE OF BRONCHIAL MUCOSAL BIOPSY FOR CILIARY STRUCTURAL ABNORMALITY IN DIAGNOSIS OF PRIMARY CILIARY DYSKINESIA

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Background and Aims: Primary ciliary dyskinesia (PCD) is diagnosed by identifying ultrastructural abnormalities of cilia with transmission electron microscopy (TEM). The mucosal samples obtained for cilia examination are generally procured from the nasal turbinate, but these specimens often yield inadequate results. The bronchial mucosa is recognized as an alternative sample, but no study has examined the utility of bronchial mucosa compared with nasal mucosa in the diagnosis of PCD.

Methods: The medical records of 96 patients who underwent TEM for suspected PCD between April 1997 and June 2017 were retrospectively reviewed. Patients were divided into three groups based on the site of mucosal biopsy: Nasal biopsy group (NB group) with nasal mucosal biopsy only; Bronchial biopsy group (BB group) with bronchial mucosal biopsy only; and Nasal and bronchial biopsy group (NBB group) with a combination of nasal and bronchial mucosal biopsies.

Results: The rate of PCD diagnosis was 28.8% (17/59) in the NB group, 41.2% (7/17) in the BB group, and 60.0% (12/20) in the NBB group. The yield of PCD diagnosis significantly increased in the NBB group compared with the NB group ($P = 0.012$). In the NBB group, 25% (5/20) of patients were diagnosed with PCD by nasal mucosal biopsy, and 35% (7/20) of patients were additionally diagnosed with PCD by bronchial mucosal biopsy. The presence of radiologic findings for sinusitis or bronchiectasis was not associated with prediction of PCD diagnosis from nasal or bronchial mucosal biopsy.

Conclusion: The combination of nasal and bronchial mucosal biopsy for TEM showed higher yields of PCD diagnosis than nasal mucosal biopsy alone.

AO029

EFFECT OF ORAL CHLORHEXIDINE IN PREVENTING HOSPITAL-ACQUIRED PNEUMONIA AMONG NON-INTUBATED PATIENTS IN THE PHILIPPINES

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Background and Aims: Hospital-acquired pneumonia (HAP) is one of the most common nosocomial infections but no recommendation has been established to effectively prevent it among non-intubated patients. Oral chlorhexidine is part of the standard of care among intubated patients in preventing ventilator-associated pneumonia (VAP) but limited studies are available on its benefit among non-intubated patients in preventing HAP. In this study, we performed a randomized controlled trial to investigate the effect of oral chlorhexidine in preventing HAP among non-intubated patients.

Methods: A prospective randomized open-labeled parallel group controlled trial design was used. 0.12% oral chlorhexidine was given in the treatment group while none was given in the control group. 160 patients were randomized to either treatment ($n = 80$) or control ($n = 80$) group. Occurrence of HAP was based on the Centre for Disease Control and Prevention (CDC) criteria.

Results: Overall incidence of HAP is lower among patients with oral chlorhexidine (6.25% vs 12.5%). The duration of hospital stay in the treatment group was shorter than the control group (mean 5.5 days vs mean 6.5 days). The onset of HAP was earlier among patients not receiving oral chlorhexidine (mean 4 days vs mean 9 days). Patients with end stage renal disease, chronic kidney disease, known malignancy, chronic obstructive pulmonary disease, and bronchial asthma are more likely to develop HAP.

Conclusion: Oral chlorhexidine has decreased the incidence of HAP among non-intubated patients. It has also decreased the duration of hospital stay. The use of oral chlorhexidine among non-intubated patient is strongly recommended to prevent HAP.

AO030

THE USE OF MEDICAL RESEARCH COUNCIL (MRC) DYSPNOEA GRADE IN PREDICTING PEAK OXYGEN UPTAKE AND WORK RATE IN UNDIFFERENTIATED DYSPNOEA.

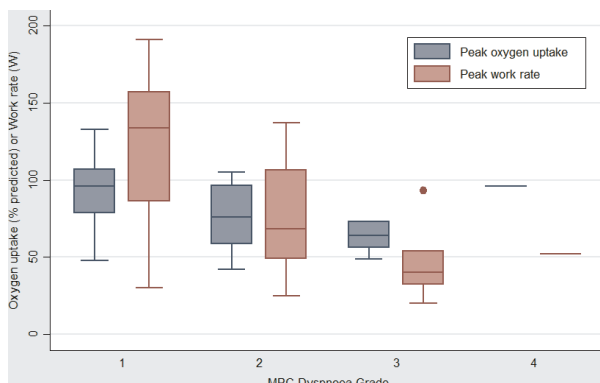
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Background and Aims: Undifferentiated dyspnoea is not uncommon in clinical practice. Cardiopulmonary exercise test (CPET) is an established investigation modality but it requires trained personnel and specialised equipment. The predictive value of self-reported dyspnoea grade for exercise tolerance is unclear. We aim to study the association between MRC dyspnoea grade and peak oxygen uptake (VO₂) and work rate (WR).

Methods: We analysed prospectively collected clinical data of all individuals who underwent incremental symptom-limited CPET for undifferentiated dyspnoea from 31-03-2017 to 31-03-2018. MRC grade was recorded as part of the pre-exercise evaluation.

Results: Thirty-two consecutive individuals, mostly male (71%) and ever smokers (56%) with median (interquartile range, IQR) age of 61 (54–69) years and body mass index (BMI) of 23.1 (19.3–26.8) kg/m² were included. Median (IQR) MRC score was 2 (1–2). Mean (standard deviation, SD) pre-exercise forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were 85 (23) and 87 (20) %predicted respectively. Mean (SD) peak VO₂ was 1.23 (0.48) L or 84 (22) %predicted. Twenty-two individuals had an abnormal CPET pattern; the most common limitation was circulatory impairment (73%). Median peak VO₂ and WR were higher in MRC grade 1 than grade 2–4. A quarter (25%) of individuals with MRC grade 1 had peak VO₂ < 80% predicted (see Figure). One-way ANOVA analysis demonstrated significant difference in peak VO₂ and work rate between different MRC grades ($P = 0.03$ and < 0.01 respectively). However, pair-wise comparison only showed significant difference between MRC grade 1 versus 2 or 3 but not among grade 2–4. Higher MRC grades were associated with older age ($P < 0.01$). There was no association between BMI, FEV₁ or FVC and worsening MRC dyspnoea grades.



Conclusion: In individuals with undifferentiated dyspnoea, lower self-reported MRC dyspnoea grade was associated with higher peak oxygen uptake and work rate but the association is less clear at higher MRC grades.

AO031

PULMONARY REHABILITATION IN JAPAN: A POSITION STATEMENT FROM THE JSRCR/JSRPT/JRS

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Background and Aims: The aims of this statement are to update the 2001 statement, including proposals on new definitions of pulmonary rehabilitation and self-management education, and to highlight new concepts, benefits, and future directions in this field.

Methods: Fifteen experts from the Japan Society for Respiratory Care and Rehabilitation, the Japanese Society of Respiratory Physical Therapy, and the Japanese Respiratory Society participated.

Results: The updated definition agreed by all experts was 'Pulmonary rehabilitation is a comprehensive intervention tailor-made for people suffering from health problems related to respiratory system. It provides those individuals with support over the course of their life, enabling them to manage their condition on their own and live as independently as possible. It is developed based on a collaborative partnership with health care professionals with the aim of the individuals being able to do as much as possible to prevent their ailment from progressing and to restore and maintain their health'. And self-management education was defined for the first time in Japan by 3 academic pulmonary societies as 'Self-management education is comprehensive support tailor-made to produce behavior modification that will improve and maintain the health of those persons suffering from health problems. It is more than simply acquiring knowledge about their condition. Such education is accomplished by the individuals working collaboratively with healthcare professionals to create action plans with achievable goals based on diverse perspectives, enhancing their problem-solving skills, and boosting their self-confidence'.

Conclusion: Pulmonary rehabilitation is a seamless continuum, from the maintenance to the terminal phase, and includes the acute, recovery phase and perioperative, postoperative phase. After the health care insurance was indicated in 2006, pulmonary rehabilitation is gradually becoming widespread in Japan. There are remaining challenges to the field in delivering the program and in optimizing the outcome of pulmonary rehabilitation in real practice in Japan.

Respiratory Structure and Function

AO033

AO032

CHRONIC INHALATION OF UNFLAVORED NICOTINE AND NO-NICOTINE CONTAINING ELECTRONIC CIGARETTE VAPOR LEADS TO IMPAIRED LUNG FUNCTION

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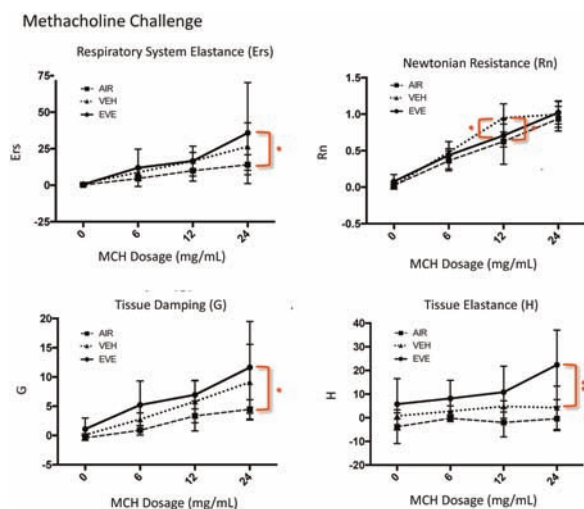
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Background and Aims: Modern electronic (e)-cigarettes have only been available since 2003. Nothing is known of the long-term health consequences of inhaling e-cigarette vapor (EV). We hypothesized that daily inhalation of heated and aerosolized propylene glycol, glycerin and nicotine would lead to repetitive injury to lung airways and parenchyma and culminate in increased airway resistance and decreased lung compliance.

Methods: Male C57BL/6 mice, 6–8 weeks old, were exposed for 1 h daily to: 1. EV containing nicotine, 2. vehicle no-nicotine EV (VEH), or 3. room air only (AIR). After six months of exposure via the InExpose system (SciReq), mice were sedated, trachea and attached to the flexiVent mouse ventilator (SciReq). Lung mechanics scans were conducted, and airway responsiveness assessed with inhaled methacholine (MCH) challenge at 0, 6, 12, and 24 mg/mL.

Results: There were no significant differences between baseline lung parameters in the three groups. There were significant differences between EV and AIR for Respiratory System Elastance (Ers), Tissue Damping (G), and Tissue Elastance (H) at 24 mg/mL of MCH. EV vs VEH was also significantly different for Tissue Elastance (H) at 24 MCH. There was a significant difference between AIR vs VEH and VEH vs EV for Newtonian Resistance (Rn), a measure of central airway resistance, at 12 MCH but not at higher doses of MCH.

Conclusion: Our data suggest that airway resistance and lung compliance changes occur with chronic exposure to key components of e-cigarettes - nicotine, propylene glycol and glycerin. This indicates that e-liquid flavors are unlikely to be the sole causes of lung toxicity, especially in the setting of long-term daily e-cigarette use.



ASTROCYTIC ACTIVATION IS NECESSARY FOR HYPOXIC RESPIRATORY FACILITATION

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Background and Aims: Hypoxia increases ventilation, often transiently, via excitation of peripheral chemoreceptors, such as the carotid body. However, peripheral chemoreceptor-denervated animals increase ventilation in response to hypoxia when unanesthetized and awake, indicating the existence of unidentified central respiratory hypoxia-sensing mechanisms. Recently, it has been clarified that astrocytes play active roles in various brain functions, and we have hypothesized that astrocytes are involved in the central mechanism of hypoxic respiratory regulation. To validate our hypothesis, we aimed to analyze the effects of astrocytic activation blockade on hypoxic respiratory responses.

Methods: We conducted experiments using arundic acid, a blocker of astrocytic activation, in the isolated medulla-spinal cord preparation of newborn rats, which is ideal for the study of the purely central mechanism of respiratory control. Neural respiratory output was recorded from ventral roots of the 4th cervical cord. Firstly, we compared neural respiratory frequency while superfusing preparations with normoxic (95% O₂, 5% CO₂) artificial cerebrospinal fluid before and after administration of arundic acid (100 and 500 μM). Secondly, hypoxic responses were tested without and with two doses of arundic acid, by replacing the superfusates that were saturated with hypoxic (95% N₂, 5% CO₂) gas mixture to briefly load hypoxia.

Results: Without arundic acid, hypoxia increased respiratory frequency. A low concentration (100 μM) arundic acid did not appreciably affect either respiratory output in a normoxic condition or a hypoxic respiratory response. However, a high concentration (500 μM) arundic acid decreased respiratory frequency in a normoxic condition, and suppressed a hypoxia-induced increase in respiratory frequency.

Conclusion: We conclude that astrocytes play an active role in a respiratory facilitating response to hypoxia.

AO034

RETROSPECTIVE ANALYSIS OF FIVE YEARS ON SINGLE CENTER PULMONARY FUNCTION TEST

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Background and Aims: Through the analysis of the data of pulmonary function tests over the past 5 years in our hospital, we hope that this paper can provide some reference value for the popularity of pulmonary function tests.

Methods: We retrospectively analysed the age, sex, annual cases, patient department source, pulmonary function test results, pulmonary function test results, failure rate of pulmonary function tests, and pulmonary function test adverse reactions in patients who performed pulmonary function tests in the past five years.

Results: 1) There were 5754 cases, 5929 cases, 7128 cases, 8775 cases and 10659 cases of pulmonary function test cases in the past 5 years, showing an increasing trend year by year. 2) The outpatient departments that require patients for pulmonary function tests mainly include Department of pulmonary and critical care medicine, department of cardiology, and department of hematology. The top three departments of the inpatient department were the department of thoracic surgery, department of general surgery, and department of urology. The patients who performed pulmonary function tests in these three departments accounted for 65.1%, 64.4%, 62.1%, 63.5%, and 62.4% of the same period. 3) The failure rate of pulmonary function tests in the past 5 years were 2.17%, 2.83%, 2.19%, 1.87%, and 1.48%, respectively. 4) The adverse reactions of pulmonary ventilation function tests in the past 5 years were mainly dizziness, vertigo, numbness of the extremities, tingling of the lips, and falling. The incidence rates of the adverse reactions respectively were 0.49%, 0.42%, 0.41%, 0.39%, and 0.44%.

Conclusion: The clinical demand for pulmonary function examination is increasing year by year, and only deploys staff and equipment rationally can meet the needs of clinical work. Because the failure rate of pulmonary function test is low and the incidence of adverse events is very low, it is relatively safe.

AO035

COMPARATIVE ANALYSIS OF PFT AND 3D LOW DOSE CHEST CT BASED LUNG VOLUME ASSESSMENTS IN SCOLIOSIS PATIENTS BEFORE AND AFTER SURGICAL CORRECTION

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Background and Aims: Pulmonary function test (PFT) is a mainstay in the monitoring of lung-function deterioration associated with scoliosis patients, as well as the prognosis after surgical correction of the deformity. Computed tomography (CT)-based lung volume assessments have proven efficacy and some advantages in measuring lung volumes of scoliosis patients before and after surgery. Herein, we compared the results of PFT and CT-based lung volume assessment in scoliosis patients before and after surgical correction.

Methods: Ninety-eight adolescent idiopathic scoliosis (AIS) patients who received surgical correction were divided into two groups: group I (N = 21), patients with increased lung volume and group D (N = 77), patients with decreased lung volume based on CT-based lung volume assessment at approximately 21-months post-surgical correction of scoliosis. Subsequently, various statistical tests were conducted to determine the relationship of various perioperative parameters between the groups and also among the CT-based lung volume changes and other PFT parameters.

Results: Patients with poor pre-operative lung functions had a significant positive relationship with CT-based lung volume changes. Lung volumes were significantly increased in patients with poor pre-operative lung functions; moreover, the lung volumes showed a significant correlation with vital capacity (VC)% changes and a good agreement with FEV1% and FVC% in our patients. These results suggested that CT-based lung volume changes could be a good indicator for postoperative lung function assessment.

Conclusion: CT-based lung volume assessments can be used to measure lung function in a certain group (co-morbidity and non-cooperative patients) of scoliosis patients, who cannot perform PFT.

INTER-OPERATOR VARIABILITIES OF AIRWAY INDICES IN MDCT IMAGES OF COPD PATIENTS

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Background and Aims: Airway indices, such as Pi10 (the square root of airway wall area of a hypothetical airway with an internal perimeter of 10 mm), are calculated using a segmented airway tree out of MDCT images to characterize the airflow limitation in COPD patients. Although this airway segmentation procedure is semi-automated in specifically designed software, the resulting airway tree requires manual correction because of errors such as leakage of pixels and unrecognized airway branches. This may introduce some fluctuations in the segmented tree, leading to variabilities in airway indices. Recently, we have developed a novel airway index; D of airway inner cross-sectional area (D_{ICSA}). We assessed the inter-operator variabilities of Pi10 and D_{ICSA} in MDCT images of COPD patients.

Methods: COPD patients and non-COPD smokers were recruited at our outpatient clinic. Chest MDCT images were obtained in those who gave informed consents to participate in our COPD cohort. We picked up 30 MDCT images randomly for this study. Airway trees were segmented using the Apollo software (VIDA diagnostics, IA) by two different operators after randomizing the order of the images. Pi10 and D_{ICSA} were calculated to observe inter-operator variabilities. They were also calculated at each processing stage, i.e. before correction, deletion of leakage, and extension of airway branches, to see which caused variability.

Results: Both Pi10 and D_{ICSA} showed significant correlations between two operators (adjusted R² were 0.94 and 0.87, and slopes were 0.996 and 1.004, respectively). The indices did not change much at each processing stage, although some of the variabilities stemmed from difference in recognition of airway branches.

Conclusion: Manual correction of a segmented airway tree needs consistency to minimize variabilities of airway indices.

AO037

SPIROMETER VALIDATION USING A FLOW/VOLUME SIMULATOR

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Background and Aims: Quality control of spirometers is the most important factor affecting measurements. The aim of this study is to validate the accuracy and repeatability of spirometers using a flow/volume simulator, which is recommended to produce flow-volume waveforms by a mechanical pump.

Methods: Hans-Rudolph flow-volume simulator (model 1120) was used to discharge defined test profiles C1 to C13 to spirometers and measure FVC, FEV1 and PEF three times for each defined test profile. Two spirometers were test: Jaeger (model: Masterscreen-pneumo, Germany), Cosmed (model: MicroQuark, Italy). C1 to C13 test profiles were defined according to ISO 26782:2009(E).

Results: The accuracy of FVC, FEV1, PEF was shown in Table 1. The accuracy of FVC for Jaeger spirometer is better than Cosmed spirometer

($-0.025L \pm 0.067L$ VS $-0.137L \pm 0.086L$, $P < 0.01$). There was no significant difference between the two spirometers for the accuracy of FEV1 and PEF, and the repeatability of FVC, FEV1 and PEF.

Conclusion: According to ATS spirometry standardization and ISO 26782:2009(E) criteria, the accuracy and repeatability of FVC and FEV1 should be $\pm 3\%$ or $\pm 0.050L$, whichever is greater. The accuracy and repeatability of PEF should be $\pm 10\%$ or $\pm 0.400L$, $\pm 5\%$ or $\pm 0.200L$, respectively. This study indicated that the repeatability of the three parameters and the accuracy of FEV1 and PEF for the two spirometers was acceptable. However, the accuracy of FVC for Cosmed spirometer was not achieve performance requirement. Cosmed spirometer is a kind of turbine flowmeter, while Jaeger is differential pressure flowmeter. The Cosmed spirometer in the study has been used in pulmonary function laboratory for eight years, while the Jaeger spirometer was a newly one. We considered that the turbine did not detect the flow signal when the simulator blowing at low flow, so that the measurement of FVC might be lower than actual level. In conclusion, validation of accuracy is important and necessary for the quality control of spirometer.

Table 1 The spirometer accuracy of FVC,FEV1,PEF

Defined profile	FVC(L)		FEV1(L)		PEF(L/s)	
	Jaeger	Cosmed	Jaeger	Cosmed	Jaeger	Cosmed
C1	0.036	-0.021	-0.033	-0.043	-0.134	-0.030
C2	0.007	-0.117	-0.016	-0.023	-0.054	-0.026
C3	-0.030	-0.200	-0.024	-0.028	-0.125	-0.059
C4	0.017	-0.166	0.011	-0.044	-0.038	-0.032
C5	0.052	-0.128	0.021	-0.050	-0.008	0.005
C6	-0.020	-0.090	-0.026	-0.046	-0.053	-0.111
C7	-0.007	-0.020	-0.035	-0.015	-0.086	-0.068
C8	-0.053	-0.173	-0.041	-0.054	-0.095	-0.140
C9	-0.063	-0.199	-0.031	-0.039	-0.091	-0.103
C10	-0.119	-0.236	0.022	-0.009	-0.077	0.029
C11	0.040	-0.100	0.028	-0.049	-0.074	-0.065
C12	-0.184	-0.300	-0.033	-0.031	-0.063	0.000
C13	-0.003	-0.033	-0.037	-0.021	-0.075	-0.080
mean	-0.025	-0.137	-0.015	-0.035	-0.075	-0.052
SD	0.067	0.086	0.026	-0.015	0.034	0.049
P	0.004		0.286		0.509	

AO038

QUANTITATIVE ASSESSMENT OF AIRWAY STRUCTURE USING ULTRA-HIGH RESOLUTION COMPUTED TOMOGRAPHY

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Background and Aims: Accurate evaluation of airway structure is important for better understanding of the pathogenesis of airway disease such as COPD and asthma. This study examines whether a recently introduced ultra-high resolution computed tomography (CT) scan allows for more accurate quantitative measurements of airway dimensions than the conventional CT scan.

Methods: Measurement errors of wall thickness and lumen areas of phantom tubes were compared between the conventional (512×512 matrix, 0.5 mm slice thickness) and ultra-high resolution (1024×1024 and

2048×2048 matrixes, 0.25 mm slice thickness) scans. In addition, the airway dimensions were measured in 11 subjects with COPD and 3 control subjects using the 1024×1024 and 512×512 scans reconstructed by a forward-projected model-based iterative reconstruction solution (FIRST) algorithm.

Results: In a phantom study using a tube 2 mm diameter and 0.5 mm wall thickness, the measurement errors for the lumen area were substantially smaller in the ultra-high resolution scans than the conventional 512×512 scan. Further analysis using 6 phantom tubes at 3 mm diameter with different wall thickness (0.5, 0.6, 0.7, 0.8, 0.9, and 1.0 mm) showed that the ultra-high resolution scans resolved ≥ 0.6 mm wall thicknesses of the tube with $< 11\%$ error, whereas the conventional scans over-estimated the wall thickness of these tubes. In human study, the measured wall thickness was consistently higher in the 512×512 scans than the 1024×1024 scans for all examined airways including segmental (3rd), sub-segmental (4th), and sub-sub-segmental (5th) generations of right apical upper lobe (RB1) and posterior lower lobe (RB10) bronchus in both COPD and controls.

Conclusion: The ultra-high resolution scan enables more accurate measurements of smaller airway dimensions with less over-estimation of the wall thickness than the conventional scans.

AO039

THE VALUE OF RESPIRATORY BIPHASIC PULSE OSCILLATION INDEX IN DIFFERENTIAL DIAGNOSIS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASTHMA AND THE DIAGNOSIS OF EMPHYSEMA

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Background and Aims: The main pathological changes of asthma are the lesions of airway. Nevertheless, there are both airway lesions and emphysema in COPD. Because of emphysema, patients with COPD have decreased elastic recoil force of lung tissue and loss of small airway traction, compared with asthma patients. Therefore, the small airway closes prematurely during the exhalation period, resulting in more significant increase in airway resistance on exhalation than on inhalation. We intend to preliminarily explore the value of respiratory biphasic pulse oscillation index in differential diagnosis of COPD and asthma and the diagnosis of emphysema.

Methods: Inspiratory-expiratory impulse oscillometry was assessed in 37 patients with asthma, 19 with COPD and 23 normal subjects.

Results: 1. Z5, R5, X5 and R20 in the asthma group and COPD were significantly higher than those in the normal group. 2. Z5, X5, R5 were not significantly different in patients with asthma or COPD. Nevertheless, The difference of R5 in exhalation and inhalation phase in patients with COPD (1.6 ± 2.1 vs 0.8 ± 0.96 , $P < 0.05$) and the ratio (1.33 ± 0.42 vs 1.11 ± 0.14 , $P < 0.05$) was significantly higher than in asthma. Similarly, The difference of R5-R20 in exhalation and inhalation phase in patients with COPD (2.57 ± 2.93 vs 1.26 ± 0.35 , $P < 0.05$) and the ratio (1.67 ± 2.0 vs 0.78 ± 1.0 , $P < 0.05$) was significantly higher than in asthma. 3. A total of 43 patients with COPD or asthma had received chest CT examination. The difference of X5 in exhalation and inhalation phase in patients with high EI was significantly greater than that low EI (-2.9 ± 3.3 vs -0.3 ± 1.8 , $P < 0.05$).

Conclusion: 1. Compared with asthma, patients with COPD have higher respiratory impedance in exhalation than inhalation. 2. Increased emphysema severity may result in increased changes in respiratory biphasic impedance indicators. 3. The respiratory biphasic IOS index may contribute to the differential diagnosis of COPD and asthma and the diagnosis of emphysema, but a larger sample of studies is needed to verify this.

Lung Cancer 1

AO040

FUNCTIONAL ANALYSIS OF MOB1 IN RESECTABLE LUNG ADENOCARCINOMA

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Background and Aims: Mps One Binder Kinase Activator(MOB) 1A/1B, core components of the Hippo pathway, have been recognized in various human tumors. However, the roles of MOB1 in lung adenocarcinoma are largely unknown. We investigated the relationship between MOB1 expression and prognosis of lung adenocarcinoma patients.

Methods: MOB1 expression was immunohistochemically studied in 208 surgically resected lung adenocarcinoma. The association between expression of MOB1 and clinicopathological parameters was evaluated.

Results: MOB1 expression was significantly associated with vascular invasion ($P = 0.0005$). However, P -TNM stage was not significantly associated with MOB1 expression ($P = 0.3151$). In MOB1 high expression group, the disease-free survival was significantly shortened compared to the MOB1 low group ($P = 0.0161$), but no significant difference was observed in the overall survival.

Conclusion: This study suggests that MOB1 expression in lung adenocarcinoma is a risk factor for early recurrence, and further studies are required on the effect of MOB1 on tumor growth or vascular invasion.

AO041

FROM IMMUNOSURVEILLANCE TO IMMUNOEDITING: THE ROLE OF IMMUNOBIOLOGY IN EARLY LUNG CANCER DETECTION

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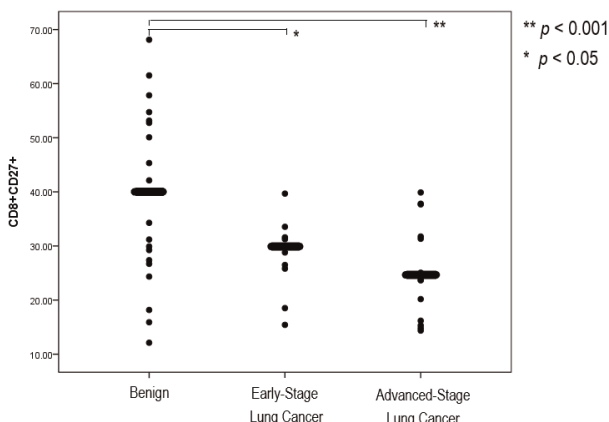
Background and Aims: Using chest computed tomographic (CT) images showed an improved detection rate and survival of early-stage lung cancers. Although chest CT scan suffers from high cost also lack of sensitivity and specificity. Biomarkers for lung cancer have the potential to improve early detection beyond the use of CT scans. This study investigated the process of cancer immunoediting involved in lung cancer diagnosis.

Methods: Patients with pulmonary nodules detected by chest CT scan was selected to enroll the study. Peripheral blood samples were collected for analysis of T cell population. T cells subtypes including CD3, CD4, CD8, CD27, CD28, CD45, CD45RA, CD57, CCR7 and PD1 were counted by cytometer flow cytometer (Beckman Coulter) before surgical resection or biopsy. Definite diagnosis was made based on pathological examination of surgical specimens. Patients' basic data were retrieved from electronic medical records and analyzed for age, gender, histology type and cancer staging.

Results: The differences between lung cancer patients ($n = 27$) and benign lesions ($n = 26$), and the changes in the frequency of T-cell subpopulations among lung cancer patients corresponded to those seen in immunosenescence: lower proportions of CD8+CD27+ cells consisting of naive and central memory cells according to lung cancer clinical stage compared to patients without malignancy. In addition, higher proportion of CD8+PD1+ cells among the advanced stage lung cancer patients was

detected. Also observed was a tendency of higher CD8+PD1+ expression cells in squamous cell lung cancer.

Conclusion: Immunosenescence was present at the development of lung cancer. It appeared to be pronounced in patients with advanced stage of lung cancer. Cancer immunoediting will provide early-stage cancer detection and further therapeutic strategies.



AO042

GENETIC VARIANTS IN THE C-MYB SIGNALING PATHWAY GENES PREDICT SURVIVAL OF NON-SMALL CELL LUNG CANCER PATIENTS IN THE PLCO CANCER SCREENING TRIAL

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Background and Aims: Genetic variants in biological pathways are likely to influence survival of non-small cell lung cancer (NSCLC) patients. C-Myb pathway plays a key role in regulating expression of target genes involved in differentiation, proliferation of cells. We hypothesized that single nucleotide polymorphisms (SNPs) in the c-Myb pathway are associated with NSCLC survival.

Methods: Study populations included 1,185 NSCLC patients in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial and 984 NSCLC patients in the Harvard Lung Cancer Study as the discovery and validation datasets, respectively. We selected 8587 SNPs in 83 genes in the signaling and extracted genotyping data from the PLCO. We performed Cox proportional hazards regression analysis to evaluate associations between the SNPs and survival and validated the significant SNPs, and analyzed their functional relevance.

Results: rs11606640 *ETS1* GA+AA and rs62053220 *ZFHX3* CG+GG genotypes of two validated SNPs predicted a better overall survival (OS) ($P = 0.004$ and 0.001 , respectively). The number of their combined genotypes predicted a better OS in a multivariable Cox model. Stratified analysis showed that patients with a high-score protective genotypes exhibited significantly favorable survival in subgroups of current smoker, adenocarcinoma, IIIB-IV tumor stage, and without surgery (all $P < 0.05$). *ETS1* and *ZFHX3* mRNA expression levels were significantly lower in lung cancer tissues than in normal tissues ($P < 0.05$). The TCGA-based expression quantitative trait loci analysis showed that *ETS1* rs11606640 genotypes were significantly associated with their corresponding mRNA expression levels in lung cancer tissues in an additive model and a recessive model ($P = 0.045$ and 0.042 , respectively). *ZFHX3*

rs62053220 genotypes were significantly associated with their corresponding mRNA expression levels in lung cancer tissues in a dominant model ($P = 0.048$).

Conclusion: In a pathway-based analysis of genetic variants in PLCO and Harvard GWAS datasets, we identified *ETS1* rs11606640 G>A and *ZFX3* rs62053220 C>G to be associated with survival in NSCLC patients.

Genotype	OS Univariate analysis				OS Multivariate analysis *			
	Frequency	Death(%)	HR (95%CI)	P	Frequency	Death(%)	HR (95%CI)	P
ETS1 rs11606640 G>A								
GG	n=1177				n=1167			
GA	942	569 (57.6)	1.00		835	562 (67.3)	1.00	
AA	307	332 (65.8)	0.94 (0.80-1.11)	0.480	394	200 (50.8)	0.78 (0.66-0.92)	0.004
GA+AA	28	21 (75.0)	1.07 (0.69-1.66)	0.753	28	21 (75.0)	0.87 (0.56-1.35)	0.530
Trend	335	223 (66.6)	0.96 (0.82-1.12)	0.089	332	221 (66.6)	0.79 (0.68-0.93)	0.004
Genotype missing *	8				8			0.008
Phenotype missing *	NA				10			
ZFX3 rs62053220 C>G								
CC	n=1181				n=1171			
CG	1002	685 (68.4)	1.00		992	676 (68.2)	1.00	
GG	173	109 (63.0)	0.84 (0.69-1.03)	0.095	173	109 (63.0)	0.75 (0.61-0.92)	0.006
CG+GG	6	2 (33.3)	0.36 (0.10-1.52)	0.170	6	2 (33.3)	0.20 (0.05-0.81)	0.025
Trend	179	111 (62.0)	0.82 (0.67-1.01)	0.058	179	111 (62.0)	0.72 (0.59-0.88)	0.001
Genotype missing *	4			0.039	4			<0.001
Phenotype missing *	NA				10			

NSCLC = Non-small cell lung cancer; OS = Overall survival; SNPs = Single nucleotide polymorphisms; HR = Hazard ratio; 95%CI = 95%Confidence interval; * Adjusted for age, sex, smoking status, histology, tumor stage, chemotherapy, radiotherapy, surgery, and top four principal components; † Eight observations missing of *ETS1* rs11606640; ‡ Four observations missing of *ZFX3* rs62053220; § Two observations missing of tumour stage and 8 observations missing of chemotherapy/radiotherapy/surgery in PLCO dataset.

AO043

NSCLC PATIENTS WITH BOTH WILDTYPE EGFR AND HIGH CD151 EXPRESSION HAVE POORER DISEASE OUTCOME

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Background and Aims: Lung cancer ranks highest amongst cancer mortalities worldwide, with non-small cell lung cancer (NSCLC) comprising of 85% all reported cases. Most advanced stage patients are largely reliant on targeted therapies. However, EGFR-targeted therapies are only effective in patients harboring an EGFR mutation, leaving the remaining 70–90% wildtype EGFR patients with an urgently unmet medical need. The tetraspanin, CD151, is associated with poor prognosis in NSCLC, but the clinical significance of its expression and relationship with EGFR mutation status is unknown. We investigated the association between CD151 expression with EGFR mutation status in NSCLC and determined the prognostic biomarker value of this relationship.

Methods: 157 adenocarcinoma patient lung biopsy sections (from 1989–2011, in Singapore), were evaluated by immunostaining for CD151 expression and then compared with patient clinicopathological parameters and survival outcome. Gene expression and clinical data from 199 wildtype EGFR patients in the TCGA lung adenocarcinoma (LUAD) cohort were analysed for further validation.

Results: There is a strong association between CD151 expression and wildtype EGFR patients ($P = 0.005$). CD151 expression was also associated with Chinese ethnicity and TNM (tumor, node and metastasis) stage, respectively. Importantly, higher cumulative incidence of death due to disease was observed in patients with both wildtype EGFR and high CD151 expression when compared against the other subgroups ($P = 0.011$). In support of this, higher rate of disease-specific death was observed in the high CD151 subgroup from the TCGA LUAD cohort compared to the remaining low CD151 subgroup.

Conclusion: Expression of both wildtype EGFR and high CD151 is strongly associated with poorer disease outcome compared to other NSCLC subgroups, suggesting that (1) CD151 is a prognostic biomarker

which may help to further stratify wildtype EGFR subsets, and (2) CD151 as a therapeutic target in the development of novel alternative and/or complementary agents for the treatment of wildtype EGFR-NSCLC subgroups.

AO044

FACTORS PREDICTING THE EFFICACY OF OSIMERTINIB IN T790M-MUTATED METASTATIC LUNG ADENOCARCINOMA

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Background and Aims: T790M mutation accounts for half of the resistance mechanisms to the first and second generation (1G & 2G) epidermal growth factor receptor (EGFR) tyrosin kinase inhibitors (TKI) for the treatment of EGFR-mutated adenocarcinoma. Although the 3G EGFR-TKI osimertinib is an effective agent for T790M mutation, the efficacy varies and whether the front line treatment using the 1G or 2G EGFR-TKI affects the efficacy of osimertinib is not wellunderstood.

Methods: 56 patients of metastatic EGFR-mutated lung adenocarcinoma failing 1G or 2G EGFR-TKI with documented tissue or plasma T790M mutation received osimertinib treatment. Patients were grouped based on 1G or 2G EGFR-TKI use in first-line (1L) treatment; namely the 1L1G or 1L2G group, and the clinical factors and survival outcome were analyzed.

Results: Among the 56 patients, 36 (64.2%) have their original driving mutation as exon 19 deletion, 17 (30.4%) as L858R mutation and 3 (6.4%) as uncommon mutation (G719X or L861Q). Patients of 1L1G group have a significantly higher proportion of exon 19 deletion (60.0% vs 40.0%, $P = 0.023$) and a longer progression free survival of osimertinib treatment (20.3 vs 11.4 months, $P = 0.022$) compared to the 1L2G group. In the univariate Cox regression analysis, 1L1G group (HR: 0.424, 95% CI: 0.20–0.90, $P = 0.027$), ECOG PS < 2 (HR: 0.457, 95% CI: 0.22–0.95, $P = 0.035$) were the positive predictors of the osimertinib efficacy, whereas a trend for smoking as the negative predictor (HR: 1.87, 95% CI: 0.92–3.84, $P = 0.086$) was also noted. In multivariate analysis, 1L1G group (HR 0.38, 95% CI: 0.18–0.82, $P = 0.013$), ECOG PS < 2 (HR: 0.39, 95% CI: 0.19–0.84, $P = 0.015$), and smoking (HR: 2.73, 95% CI: 1.26–5.91, $P = 0.011$) remained the significant predictors for the osimertinib efficacy.

Conclusion: Generation of the first-line EGFR-TKI used, ECOG PS and smoking played an important role in predicting the efficacy of osimertinib.

AO045

THE CLINICAL ANALYSIS OF PULMONARY LYMPHOEPITHELIOMA-LIKE CARCINOMA WITH EPITHELIOID GRANULOMA: FOURTEEN CASES AND LITERATURE REVIEW

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Background and Aims: Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare subtype of non-small cell lung cancer associated with Epstein-bar virus (EBV) infection, with which accompanied epithelioid granuloma (EG) was less reported and easily misdiagnosed.

Methods: We collected 14 patients with EG from 105 patients diagnosed with PLELC from January 2013 to December 2018, and their clinicopathological characteristics and treatment was analyzed.

Results: The 14 patients with EG (13.3%) in our group were followed-up 15 months (10–31 months). The median age was 48.5 year-old (38–67 year-old) and 85.7% of them were under the age of 60, meanwhile females had a slightly higher proportion than males (1.8:1). Most patients were at early stage (71.4%) with nonspecific manifestations such as cough, expectoration and lack of rich-lewis phenomenon. EG was often located in tumor or beside the tumor (71.4%), which was all negative in specific stain of pathology. In situ hybridization of EBV-encoded RNA (EBER) was all positive. In our group, there were 2 patients received palliative chemotherapy (the duration of progression-free survival were 8 and 10 months, respectively). Twelve of them underwent surgical resection including 10 with adjuvant or neoadjuvant chemotherapy, of which two had disease relapsed in 8 and 25 months after surgery. None of them had tuberculosis occur, progression or relapse, even if antituberculosis therapy were not taken.

Conclusion: PLELC with EG was lack of specific clinical characteristic compared with the patients without EG. It is important for us to make an exact pathological diagnosis, and attentions should be paid to obtain samples by biopsy and make differential diagnosis. PLELC with EG could receive multimodality therapy such as chemotherapy, and anti-tuberculosis therapy was not necessary. The formation of EG may be caused by immunological hypersensitivity to tumor cell or EBV infection instead of tuberculosis.

AO046

GEMCITABINE ENHANCES ANTI-TUMOR ACTIVITY OF PACLITAXEL BY MODULATING TUBULIN ACETYLATION

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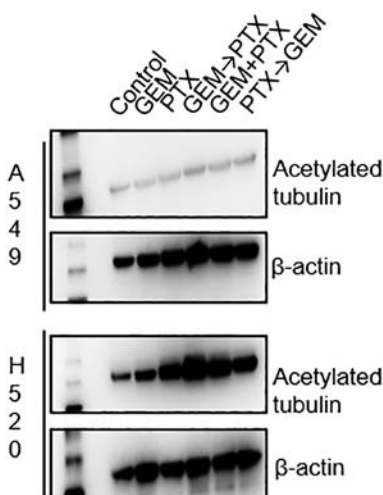
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Background and Aims: The combination of Gemcitabine (GEM) and Paclitaxel (PTX) was appealing for basic and clinical exploration due to a distinct mechanism of action and non-overlapping toxicities. This study aims to elucidate a potential effect of GEM in combination with PTX.

Methods: To determine half inhibition concentration (IC₅₀), two non-small cell lung cancer (NSCLC) cell lines, A549 and H520 were treated with GEM and PTX for 48 h. With a constant ratio of IC₅₀, simultaneous exposure of cell lines to drugs by the sequence as follows: GEM→PTX, vice versa PTX→GEM, or GEM and PTX simultaneously (GEM+PTX) to analysis combination Index (CI). Western blot in determining GEM's effect on acetylation of tubulin

Results: IC₅₀ of GEM in A549 and H520 were 6.6nM and 46.1nM, respectively. IC₅₀ of PTX in A549 and H520 were 1.35nM and 7.59nM, respectively. The sequence of GEM→PTX in A549 and H520 resulted in slight synergism and strong synergism, respectively. Immunoblotting showed intense expressions band of acetylated tubulin protein in both cell lines in the sequence GEM→PTX.

Conclusion: GEM enhances anti-tumor activity of PTX via modulating tubulin acetylation. GEM→PTX sequence may be a promising candidate regimen against NSCLC.



AO047

THE REAL-WORLD EFFICACY OF FIRST-LINE TYROSINE KINASE INHIBITORS IN ASIAN PATIENTS WITH EGFR MUTATION NON-SMALL CELL LUNG CANCER

VINCENT YI-FONG SU^{1*}, KUANG-YAO YANG², YUH-MIN CHEN²

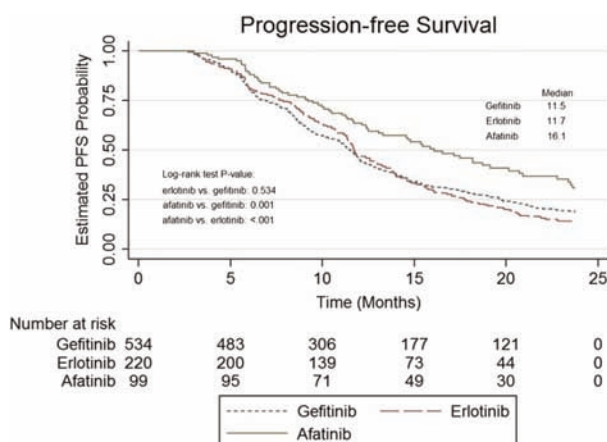
¹Taipei city hospital, Taiwan, and ²Taipei Veterans General Hospital, Taiwan

Background and Aims: Tyrosine kinase inhibitors (TKIs) including gefitinib, erlotinib, and afatinib are recommended as first-line therapy for patients with advanced non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR)-activating mutations. However, few studies compared these three TKIs together.

Methods: We conducted a retrospective cohort study using database from the claims database of Taipei Veterans General Hospital, a medical center in Taiwan. New or recurrent stage IIIB and IV NSCLC patients with EGFR mutations receiving more than 3 months as first-line treatment from 2011 to 2016 were enrolled. Primary endpoint was progression-free survival and observation period was 2 years. Secondary endpoint was all-cause mortality. Patients using co-medications at least 28 defined daily dose in first three months of TKIs therapy were assigned to co-medications groups.

Results: A total of 853 subjects (gefitinib: 534, erlotinib: 220, afatinib: 99) were enrolled in the study. The median duration of progression-free survival was 11.5 months in the gefitinib arm, 11.7 months in the erlotinib arm, and 16.1 months in the afatinib arm (log-rank test, $P < 0.001$). After adjusting for age, sex, EGFR mutation status, lung cancer stage, ECOG performance status, smoking status, radiotherapy, baseline brain-metastases, Charlson Comorbidity Index, co-medications, afatinib showed lower progression risk compared with gefitinib (hazard ratio [HR] = 0.54, 95%CI = 0.41–0.71) and erlotinib (HR = 0.62, 95%CI = 0.46–0.83). HR of progression for TKI users received systemic steroids were higher than TKI alone users (HR = 1.47, 95%CI = 1.08–2.01). Overall survival was significantly longer in the patients who received afatinib or erlotinib compared to those who received gefitinib. In the section of brain metastases, there was no significant difference among three TKIs.

Conclusion: Afatinib use was associated with a lower risk of progression in patients with NSCLC harboring EGFR mutations compared to gefitinib and erlotinib use. Concurrent use of systemic glucocorticoid showed higher progression risk.



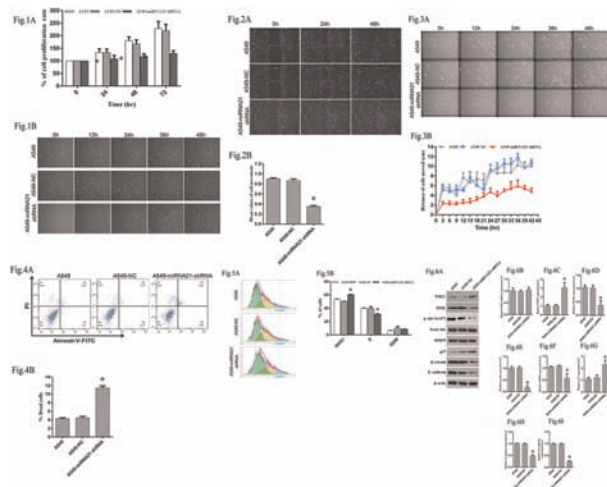
AO048

MICRO RNA-21 TARGETING PI3K/PTEN/AKT SIGNALING AXIS REGULATES MULTIPLE BIOLOGICAL FUNCTIONS IN HUMAN LUNG CANCER

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Background and Aims: The aim of this study is to investigate whether miR-21 regulates multiple biological functions in A549 human lung cancer cells via PI3K/PTEN/Akt signaling axis.



Methods: A549 cells were transduced with miR-21 shRNA and control shRNA. Cell proliferation, motility, cell cycle and apoptosis of transduced A549 cells were evaluated by CCK-8 assay, Cell-IQ live cell imaging analysis, scratch wound healing and flow cytometry, respectively.

The relative expression of miR-21 and PTEN mRNA was detected by RT-PCR. The expression levels of PTEN, phosphorylated Akt, PI3K and the downstream targets were detected by Western blotting.

Results: Down-regulation of miR-21 significantly reduced cell proliferation (Fig.1), migration (Fig.2) and movement (Fig.3) in A549 cells. In addition, down-regulation of miR-21 dramatically increased cell apoptosis (Fig.4) and blocked cell cycle at the G0/G1 and S phase (Fig.5). The expression of PTEN protein was increased when miR-21 was down-regulated, while the expression of PTEN mRNA did not change. The expression levels of phosphorylated Akt, PI3K and the related downstream targets were marked reduced or increased when miR-21 was down-regulated (Fig.6).

Conclusion: MiR-21 targeted PTEN at the post-transcriptional level and regulated cell proliferation, motility, cell cycle and apoptosis in A549 cells. MiR-21 may serve as a novel therapeutic target in human lung cancer.

Critical Care Medicine 1

AO049

INTENSIVE CARE UNIT ADMISSION AND SURVIVAL IN STAGE IV CANCER PATIENTS WITH SEPTIC SHOCK: A POPULATION-BASED COHORT STUDY

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Background and Aims: The impact of intensive care unit (ICU) admission during life-threatening critical illness on survival of patients with advanced cancer remains unknown.

Methods: We identified incident stage IV cancer patients from Taiwan Cancer Registry during 2009–2013 and ascertained the first episode of septic shock after cancer diagnosis. Patient was classified as ICU admission and no ICU admission during the index hospitalization. Primary outcome of interest was overall survival. Propensity score (PS) and proportional hazards regression were used to control potential confounders.

Results: A total of 11,825 stage IV cancer patients with septic shock were identified. Among them, 6,089 (51.5%) patients were admitted to ICU during the index hospitalization and 3,626 (30.7%) patients survived the index hospitalization. A 1:1 propensity score (PS)-matched cohort of 7,186 patients were created for patients with/without ICU admission among the total study population. Both the PS-stratified analysis among the overall population (pooled hazard ratio [HR]: 0.78, 95% confidence interval [CI]: 0.74–0.81) and analysis among the PS-matched population (HR: 0.76, 95% CI: 0.72–0.79) showed association between ICU admission and better overall survival. ICU admission was also associated with a lower risk of in-hospital mortality in both PS-stratified analysis (pooled odds ratio [OR]: 0.69, 95% CI: 0.63–0.75) and PS-matched analysis (OR: 0.61, 95% CI: 0.55–0.68). In PS-stratified analysis for long-term survival after discharge among hospital survivors, ICU admission was associated with improved long-term survival after discharge (pooled HR: 0.73, 95% CI: 0.68–0.80). Also ICU admission was associated with better long-term survival after discharge (HR: 0.77, 95% CI: 0.70–0.85) in PS-matched analysis.

Conclusion: Though ICU admission with aggressive treatment may be associated with improved survival, the majority (70%) of stage IV cancer patients with septic shock were unable to survive until hospital discharge.

AO050

NETS PROMOTES ALI/ARDS INFLAMMATION BY REGULATING ALVEOLAR MACROPHAGES POLARIZATION

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Background and Aims: Neutrophils activated in acute lung injury form neutrophil extracellular traps (NETs) allow neutrophils to capture pathogens. However, excessive production of NETs can lead to severe inflammatory reactions and tissue damage. Macrophages are classified into M1 and M2. In inflammation reaction, M1 has pro-inflammatory effects and M2 has anti-inflammatory effects. In the acute phase of acute lung injury, alveolar macrophages polarize to M1, which causes the release of a large number of inflammatory factors and aggravates tissue damage. The aim of this study was to investigate the effect of NETs on macrophages polarization and the damage mechanism of NETs on lung tissue in acute lung injury.

Methods: In this study, we investigated the relationship of NETs and macrophages polarization during the early inflammatory reaction of lipopolysaccharide (LPS)-mediated acute lung injury (ALI) animal model and assessed the use of NE inhibitor, for the macrophages polarization in ALI. Additionally, we observed close interactions between macrophages and nets in vitro. Numerous techniques were used to evaluate the outcome of the present study, including HE staining, flow cytometry, immunostaining, Immunofluorescence, qRT-PCR, ELISA and western blot.

Results: NETs formation was detected in murine ALI tissue and was associated with increased M1 markers, as well as the decreased M2 markers in BALF and lung tissue. Treatment with the NE inhibitor significantly degraded NETs and down regulated M1 markers as well as up-regulated M2 markers. Regardless of whether there is LPS pre-stimulation, significant secretion of the IL-6, TNF- α were detected from bone marrow-derived macrophages (M0 and M2) cocultured with PMA-activated NETs. NETs were able to trigger cytokine release from macrophages, and the M1 markers were upregulated, conversely, the expression level of M2 markers were downregulated.

Conclusion: NETs can promote ARDS Inflammation in acute phase by promoting the polarization of macrophages to M1. We propose that NETs plays an important role in the interaction between neutrophils and macrophages during the early acute phase of ALI.

AO051

A PREDICTIVE VALUE OF TRYPTOPHANYL-TRNA SYNTHETASE ON THE MORTALITY IN INTENSIVE CARE UNIT PATIENTS

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Background and Aims: Sepsis is associated with a high mortality, the activation of innate immune system and prognostic factors are not fully understood. In this study, we statistically determine the value of tryptophanyl-tRNA synthetase (WRS), induced by inflammatory stimuli, to predict the mortality of medical intensive care unit.

Methods: We retrospectively reviewed the medical records of medical ICU patients at Yonsei University College of Medicine from March to December 2015. The 28-day all-cause mortality prediction of WRS were compared with Acute Physiology and Chronic Health Evaluation II

(APACHE II), APACHE IV, Sequential Organ Failure Assessment (SOFA) and Lactate using Cox proportional-hazards analysis, receiver operating characteristic analysis and Kaplan-Meier survival analysis.

Results: The 156 patients were enrolled in this study; on the 28th day of medical ICU admission, mortality rate was 30.1% ($n = 47$). Non-survivors had higher APACHE II, APACHE IV and SOFA scores, Lactate and WRS. The area under the curve (AUC) was 0.667, 0.719, 0.720, 0.661 and 0.722 for APACHE II, APACHE IV, SOFA, Lactate and WRS. The cut-off value of WRS in evaluating 28-day mortality were 96.9 and cumulative mortality rate by Kaplan-Meier analysis was significantly higher in WRS > 96.9 compared WRS < 96.9. (Log rank $P < 0.001$)

Conclusion: WRS secreted early in sepsis, may be useful not only for early detection of sepsis but also for mortality prediction in critically ill patients.

AO052

ADD ON AZITHROMYCIN: REDUCE NOSOCOMIAL INFECTIONS AND VENTILATOR ASSOCIATED PNEUMONIA IN CRITICAL PEDIATRIC CARDIOVASCULAR SURGERY PATIENTS

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Background and Aims: Ventilator associated pneumonia (VAP) is a frequent cause of nosocomial infection (NI) after cardiac surgery in pediatric patients, and results in a significantly longer stay in the intensive care unit. VAP caused by potentially drug-resistant bacteria. Azithromycin has been shown to retard *Pseudomonas aeruginosa* biofilm formation. *Staphylococcus epidermidis* and *Staphylococcus aureus* are the most frequent causes of nosocomial infections and infections on indwelling medical devices, which characteristically involve biofilms. This study was to determine whether an anti-biofilm antibiotic (azithromycin) reduced NI and VAP for patients undergoing critical pediatric cardiac surgery.

Methods: We enrolled 207 patients (< 20 years) who underwent cardiovascular surgery for congenital heart disease. Data on postoperative courses were compared between children with and without intravenous azithromycin treatment. We administered perioperative conventional antimicrobial prophylaxis (cefazolin and gentamicin) for 3 days, with (AZI group) and without (previous group) intravenous azithromycin for 3 days. Furthermore, 78 patients from the medical record retrieval system of Kaohsiung Veterans General Hospital, Kaohsiung from 2012 to 2015 were recorded (NOW group).

Results: The previous group had higher rates of VAP infection, longer periods of ventilator dependence and length of post-operative stay in hospital than AZI Group. There was a significantly higher rate of NI in the previous group compared to the AZI group ($P < 0.05$). We also found the same trend with higher rate of NI in NOW group compared with AZI group ($P < 0.05$).

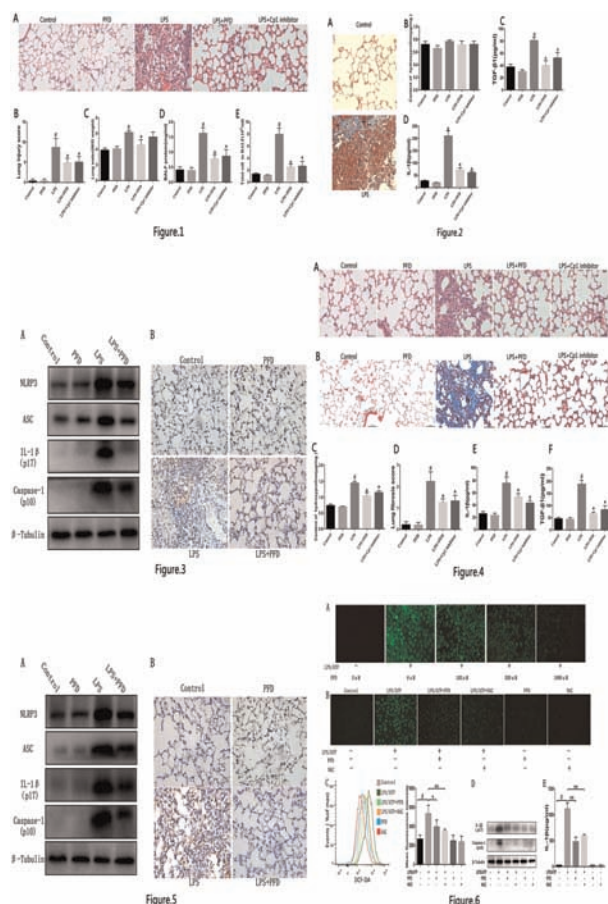
Conclusion: We suggest that patients only receiving conventional antimicrobial prophylaxis are more likely to have NI than those receiving additional azithromycin treatment. We use azithromycin to reduce antibiotic usage and hospital stay.

AO053

PIRFENIDONE AMELIORATES LIPOPOLYSACCHARIDE-INDUCED PULMONARY INFLAMMATION AND FIBROSIS BY BLOCKING NLRP3 INFLAMMASOME ACTIVATION

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Background and Aims: Acute lung injury (ALI) can trigger persistent lung inflammation and fibrosis through activation of the NLRP3 inflammasome and subsequent secretion of mature IL-1 β , suggesting that the NLRP3 inflammasome is a potential therapeutic target for ALI, for which new therapeutic approaches are needed. Our present study aims to assess whether pirfenidone, with anti-fibrotic and anti-inflammatory properties, can improve LPS-induced inflammation and fibrosis by inhibiting NLRP3 inflammasome activation.



Methods: Male C57BL/6 J mice were intratracheally injected with LPS to induce ALI. Mice were administered pirfenidone by oral gavage throughout the entire experimental course. The mouse macrophage cell line (J774 A.1) was incubated with LPS and ATP, with or without PFD pre-treatment.

Results: We demonstrated that PFD remarkably ameliorated LPS-induced pulmonary inflammation and fibrosis and reduced IL-1 β and TGF- β 1 levels in bronchoalveolar lavage fluid (BALF). Pirfenidone substantially reduced NLRP3 and ASC expression and inhibited caspase-1 activation and IL-1 β maturation in lung tissues. In vitro, the experiments revealed that PFD significantly suppressed LPS/ATP-induced production of reactive oxygen species (ROS) and decreased caspase-1 activation and the level of IL-1 β in J774 A.1 cells.

Conclusion: Taken together, the administration of PFD reduced LPS-induced lung inflammation and fibrosis by blocking NLRP3 inflammasome activation and subsequent IL-1 β secretion. These findings indicated that PFD can down-regulate NLRP3 inflammasome activation and that it may offer a promising therapeutic approach for ARDS patients.

AO054

INDUCED PLURIPOTENT STEM CELLS ATTENUATE ENDOTOXIN-INDUCED ACUTE LUNG INJURY VIA TREM-1 EXPRESSION TO REDUCE P38/I κ B PATHWAY ACTIVITY

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Background and Aims: Induced pluripotent stem cells (iPSCs) can attenuate the pathological severity and neutrophil migration of LPS-induced ALI. However, interactions between iPSCs and the triggering receptor expressed on myeloid cells (TREM) family of protein receptors remain unclear.

Methods: Murine iPSCs (miPSCs) were delivered via tail vein injection to male, 8–12 week old wild-type, TREM-1 knock-out (KO), and TREM-2 KO C57BL/6 mice 4 h after intratracheal delivery of LPS. Twenty-four hours later, bronchoalveolar lavage fluid and lungs were collected to perform histology, immunohistochemistry, Western blot, and enzyme-linked immunosorbent assays. Neutrophils were also isolated from bone marrow and subjected to Transwell migration assays.

Results: Relative to wild-type control mice, LPS was found to induce overexpression of TREM-1 and TREM-2 in lung tissue. The TREM-2 KO mice induced TREM-1 hyperexpression, and vice versa. In the TREM-2 KO mice (with hyperexpression of TREM-1), increased severity of LPS-induced ALI, increased neutrophil migration, a greater number of neutrophils in BALF, increased expression of Ly6G (a neutrophil marker) in lung, and a higher ratio of P-p38/p38 in neutrophils were observed. However, following the administration of miPSCs, TREM-1 expression was reduced and both histological signs and neutrophil infiltration in the lungs of ALI mice were attenuated. The ratio of P-p38/p38 and expression of VCAM-1 were higher in whole lung extracts following LPS-induced ALI, and these levels were even higher in LPS-treated TREM-2 KO mice. Conversely, the level of I κ B in lung tissue decreased in LPS-induced ALI mice and was restored in TREM-2 KO mice with ALI. ELISAs performed with whole lung extracts detected lower levels of pro-inflammatory cytokines (MIP-2 and TNF- α) following the administration of iPSCs, although this reduction was inhibited in LPS-treated TREM-2 KO mice.

Conclusion: In LPS-induced ALI, iPSCs attenuate the infiltration of neutrophils via a mechanism involving TREM-1 expression and the p38/I κ B signaling pathway.

AO055

POINT-OF-CARE ULTRASOUND: A NEW CHOICE OF EARLY QUANTITATIVE DIAGNOSE OF PULMONARY EDEMA

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Background and Aims: To figure out the value and provide possible methods for improving the accuracy of point-of-care ultrasound in assessing the severity of pulmonary edema by analyzing the relationship between the lung ultrasonographic features and the severity of pulmonary edema.

Methods: ①Oleic acid (OA) induced pulmonary edema model was used. 24 New Zealand rabbits were randomly divided into control group (Physiological saline), mild group (OA 0.04 ml/kg), moderate group (OA 0.08 ml/kg) and severe group (OA 0.12 ml/kg). The number and appearance time of B-line, pH, PaO₂, PaCO₂, lung coefficient, wet/dry lung ratio and pathological changes of lung tissue were measured. The ultrasound features scale and severity scale were designed, thus, ultrasound features and severity of pulmonary edema were scored. The correlation between the two scales was analyzed. ②Another six severe group

pulmonary edema rabbits were examined by point-of-care ultrasound. Lung tissues of each rabbit were divided into B-line free area, B-line less clustered area and B-line much clustered area and marked with different color dyes by percutaneous lung puncture. Lung tissues pathological test was performed. The correlation between the number of B-line and lung tissue pathological changes were analyzed.

Results: ①The number of B-line, lung coefficient and wet/dry lung ratio were all increased ($P < 0.05$), lung pathological changes were aggravated ($P < 0.05$) while the appearance time of B-line, pH, PaO_2 and PaCO_2 were all decreased ($P < 0.05$) in pulmonary edema groups compared with control group. The number of B-line, lung coefficient and wet/dry lung ratio were all increased, lung pathological changes were aggravated while pH, PaO_2 and PaCO_2 were decreased with increasing dose of OA ($P < 0.05$). There is a positive correlation between ultrasound features score and severity score of pulmonary edema ($r = 0.879$, $P < 0.05$). ④ There is a positive correlation between the number of B-line and the degree of pathological changes ($r = 0.814$, $P < 0.05$).

Conclusion: Point-of-care ultrasound could be used to quantitative assess the severity of pulmonary edema early and reflect lung pathological changes accurately.

Scale 1: Ultrasound features of pulmonary edema

Score	The number of B-line	The appearance time of B-line (min)
0	<5	∞
1	<15	>6
2	<30	>3
3	>30	<3

Scale 2: Severity of pulmonary edema

Score	Blood gas analysis			Wet/Dry	Pathology
	pH	$\text{PaO}_2(\text{mmHg})$	$\text{PaCO}_2(\text{mmHg})$		
0	Normal	Normal	Normal	<4.9	Normal
1	<7.35	<90	<40	<5.7	Mild
2	<7.25	<82	<34	<6.5	Moderate
3	<7.20	<75	<30	>6.5	Severe

AO056

EFFECTS OF ACID FIBROBLAST GROWTH FACTOR ON LIPOPOLYSACCHARIDES-INDUCED ACUTE LUNG INJURY IN RAT

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Background and Aims: To investigate the effect of acid fibroblast growth factor(aFGF) on lipopolysaccharides(LPS)-induced acute lung injury (ALI) in rat.

Methods: Sixty healthy adult Sprague-Dawley male rats were randomly divided into negative control group,ALI group and aFGF treated group.LPS was used to induced ALI.The pathological changes and the SP-C expression in lung tissue were analyzed, alveolar permeability and alveolar fluid clearance(AFC) were observed,TNF- α were assessed in bronchoalveolar lavage fluid (BALF), the expression of p-p38 MAPK were measured.

Results: Analyses across three groups, compared with LPS group, the rat treated with aFGF group demonstrates decreases of lung injury scores, the level of TNF- α in BALF(11 ± 0.37 vs 5.71 ± 0.37)($P < 0.01$), and increases of AFC(15.59 ± 0.64 vs 27.41 ± 1.05)($P < 0.01$), the expression of SP-C in lung tissue is elevated. The protein expressions of p-p38MAPK increased compared to LPS group.

Conclusion: Acid fibroblast growth factor plays a protective role in acute lung injury process.It can decrease the apoptosis of injured lung cells,

alleviating the inflammatory response, improving the ability of liquid reabsorption in alveoli, and p38 MAPK pathway maybe involve in this progress.

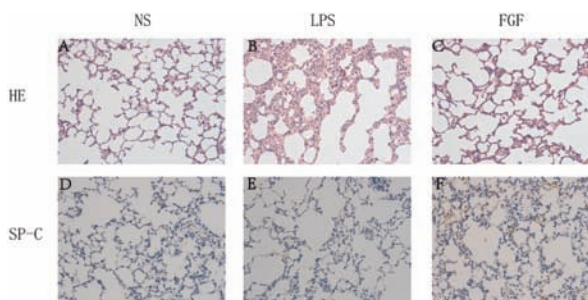


Fig.1 The expression of SP-C in lung tissue(200 $\times$).

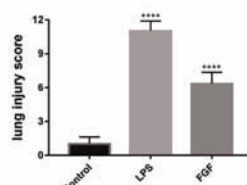


Fig.2 Lung injury score

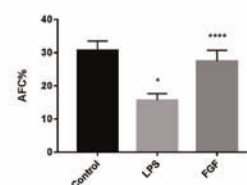


Fig.3 Alveolar fluid clearance

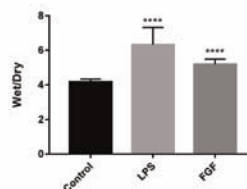


Fig.4 Ratio of wet to dry in lung

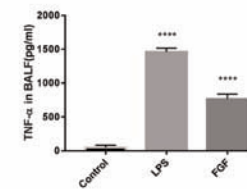


Fig.5 The level of TNF-α in BALF

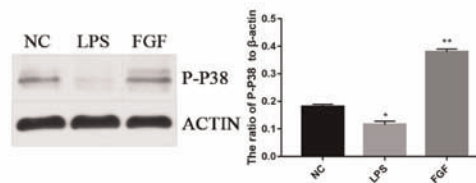


Fig.6 Expression of p-p38MAPK protein in three groups.

(* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, compare with control group)

Respiratory Infections (Non-Tuberculous) 1

AO057

EMPIRIC VANCOMYCIN TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA (CAP): INCREASING USE IN USA FROM 2007 TO 2015 AND POSSIBLE STRATEGY FOR DEESCALATION

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Background and Aims: Initial treatment of community-acquired pneumonia (CAP) is often empiric. IDSA/ATS CAP guidelines from 2007 advised vancomycin use when methicillin-resistant *Staphylococcus aureus* (MRSA) was suspected. Subsequent definition of 'health care-associated pneumonia' (HCAP) increased awareness of multidrug-

resistant (MDR) respiratory pathogens but also led to vancomycin over-use when treating patients with recent hospital stays, nursing home residency or immunocompromise. This study documents increased vancomycin use treating CAP between 2007 and 2015 and seeks ways to limit this.

Methods: Bryn Mawr Hospital is a 250-bed community teaching hospital in the USA. An active antimicrobial stewardship program (ASP) since 2010 increased awareness of MDR pathogens during a sepsis management campaign and later promoted short course antibiotic therapy for UTIs and pneumonias. Review of infectious diseases consultations from Sept-Dec 2007 and Oct-Dec 2015 identified over 100 consecutive pneumonia cases from each period. Hospital-acquired pneumonias were excluded as were cases with initial therapy based on known pathogens. CAP cases were entered into a database and sorted by initial antibiotic therapy and eventual duration.

Results:

Year	Cases	No vanco	Vanco used:	< 24h	48–72 h	> 4 days	pen allergy
2007	101	55 (54%)	Yes -->	5 (5%)	7 (7%)	34 (34%)	20 pts
2015	101	29 (29%)	Yes -->	21 (21%)	20 (20%)	31 (31%)	23 pts

Conclusion: Empiric vancomycin use in CAP increased from 45% of cases in 2007 to 71% in 2015. Penicillin allergy frequency was comparable in both periods and did not drive vancomycin use. Rapid nasal MRSA probes were available in 2015 but not commonly used. During 2015, vancomycin was often stopped within 1 to 3 days based on cultures and clinical response. Previous acceptance of ASP recommendations for shorter course CAP therapy suggests that education about more rigorous definition of MDR-risks may reverse the trend for increased empiric vancomycin use.

AO058

PREDICTORS OF DEVELOPING MYCOBACTERIUM KANSASII PULMONARY INFECTION WITHIN 1 YEAR AMONG PATIENTS WITH SINGLE ISOLATION IN MULTIPLE SPUTUM SAMPLES

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Background and Aims: *Mycobacterium kansasii* (MK) is one of the most virulent nontuberculosis mycobacteria (NTM) species, yet single MK isolate in multiple sputum samples is still unable to establish the diagnosis of pulmonary disease (PD) based on current guidelines. This study aimed to evaluate the predictors of developing MK-PI within 1 year for subjects with single MK isolate, with a special emphasis on concomitant presence of other NTM species in sputum.

Methods: Patients with a single MK isolate from at least three sputum samples collected within three months from 2008 to 2016 were retrieved from six hospitals in Taiwan. Those with ≥ 2 follow-up sputum samples and chest radiography in the subsequent 9 months were included for final analysis. The primary outcome was development of MK-PI during follow-up, and the secondary outcome was radiographic progression. Independent outcome predictors were investigated by multivariate logistic regression analysis.

Results: A total of 84 episodes of single MK isolate at the initial 3 months from 83 cases were analyzed. The mean age was 69.4 ± 19.0 , with a male/female ratio of 1.9. Within one year, 17 (20%) episodes progressed to MK-PD; risk factors included high acid-fast smear (AFS) grade (≥ 3), elementary occupation workers, and initial radiographic score >

6, whereas coexistence with other NTM species was protective. Among patients who developed MK-PD, all experienced radiographic progression, and 41% died within 1 year.

Conclusion: Although a single MK isolation does not fulfil the diagnostic criteria of MK-PD, this disease may develop if the initial sputum AFS grade is high, initial radiographic score >6, patient has elementary occupations, and no concomitant NTM species other than MK are present. Early anti-MK treatment should be considered for high-risk patients.

Table: Univariate and multivariate logistic regression analysis for predictors of progression to *Mycobacterium kansasii* pulmonary disease

Variables	Univariate (n=84)		Multivariate (n=66)*	
	OR (95% CI)	p value	OR (95% CI)	p value
Age > 65	2.44 (0.84-9.36)	0.164		
Male sex	0.70 (0.23-2.08)	0.518		
Body-mass index < 18.5	4.20 (1.32-13.37)	0.010	1.19 (0.14 - 10.15)	0.876
Elementary occupations [†]	17.70 (4.93-63.54)	<0.001	14.65 (2.05 - 104.57)	0.007
Chronic obstructive pulmonary disease	3.89 (1.29-11.76)	0.013	1.50 (0.15 - 15.09)	0.731
History of pulmonary tuberculosis	0.50 (0.13-1.95)	0.314		
Bronchiectasis	0.84 (0.24-2.91)	0.780		
Diabetes mellitus	0.21 (0.04-0.99)	0.044	0.34 (0.04 - 3.04)	0.332
Congestive heart failure	1.58 (0.37-6.73)	0.533		
Steroid use	4.85 (1.07-21.91)	0.049	3.22 (0.30 - 36.20)	0.388
Hemoptysis	3.99 (1.23-12.94)	0.016	3.29 (0.30 - 36.20)	0.331
Cough	2.19 (0.65-7.45)	0.201		
Sputum	1.81 (0.37-8.90)	0.463		
Dyspnea	1.77 (0.59-5.33)	0.307		
Leukocyte > 9000 /uL	6.36 (2.02-20.05)	0.001	1.12 (0.14 - 8.77)	0.917
Hemoglobin < 12 g/dL	3.34 (1.06-10.57)	0.034	4.05 (0.56 - 29.22)	0.166
Initial radiographic scores > 6	6.36 (2.02-20.05)	0.001	10.54 (1.16 - 95.90)	0.037
Anti-MK treatment: intent to treat [‡]	2.69 (0.76-9.44)	0.114		
Anti-MK treatment: per-protocol [‡]	4.33 (0.56-33.29)	0.129		
High-grade (Gr 3 or 4) positive for AFS [§]	32.59 (1.60-665.77)	0.007		
Co-existence of NTM species other than MK [¶]	0.78 (0.65-0.88)	0.034		

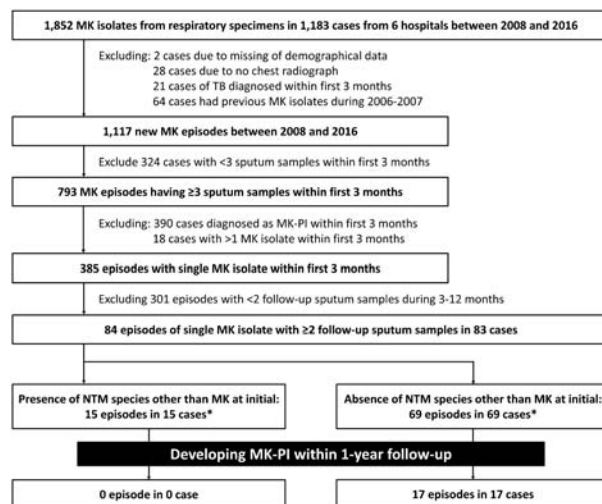
Abbreviation: AFS, acid-fast smear; NTM, nontuberculous mycobacteria.

* Among the 15 episodes with coexistence of other NTM species, none progressed to MK-PD during 1-year follow-up, whereas 17 (25%) of the 69 without concomitant NTM species did ($p = 0.034$). Of the 69 episodes, 3 had high-grade positivity (grades 3 and 4) in sputum AFS, and all developed MK-PD, whereas 14 (21%) of the 66 episodes without high AFS grade did ($p = 0.013$). Thus, we conclude that coexistence with other NTM was a significant protector against MK-PD and that high AFS grade was a significant predictor for MK-PD. We excluded 18 episodes from the data in fitting the multivariate logistic model.

[†] The category of occupation was noted according to the International Standard Classification of Occupations, 2008 (ISCO-08).

[‡] Patients who had ever received any drugs against MK, regardless of duration.

[§] Patients who had ever received combination chemotherapy against MK for more than 2 months in the first 3 months.



AO059

THE FIRST CASE OF COMMUNITY-ACQUIRED PRIMARY AND MULTIPLE LUNG ABSCESS DUE TO SEROTYPE K2 HYPERVIRULENT *KLEBSIELLA PNEUMONIAE* IN ADULT; AN EXTREMELY RARE CLINICAL COURSE

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Background and Aims: Hypervirulent *Klebsiella pneumoniae* (HVKP) is typically associated with community acquired invasive infections such as pyogenic liver abscess, bacteremia, and meningitis;

however, primary lung abscess caused by HVKP is not common. Herein we present a case of primary and multiple lung abscess due to HVKP with capsule genotype K2 in slow-progressive clinical course.

Methods: A 69-year-old male with hypertension, chronic kidney failure on dialysis treatment, and diabetes mellitus was admitted to our hospital complaining of seven months history of bloody sputum with weight loss of 5 kg during this time. Physical examination revealed only lack of breath sounds over the thorax on auscultation. Computed tomography of the chest showed multiple lung abscess particularly in upper lobes (chest X-ray film which conducted 6-month ago also revealed nodular lesion in right upper lobe in retrospective evaluation). No liver and kidney abscess was found in the CT series. Both sputum and bronchoalveolar lavage fluid confirmed capsulated gram-negative rods on Gram-stain, and that cultures yielded only *K. pneumoniae*. Isolate was positive for the HVKP phenotype (positive string test >5 mm). Genetic analysis identified this strain as K2 serotype and having *rmpA*, *mrkD*, *entB*, and *iutA* genes. Ampicillin/sulbactam (ABPC/STB) was immediately started and the patients is still being treated.

Results: It is noted that this case had a prolonged clinical course (more than 6 months) although HVKP was isolated. There was only one report regarding community-acquired lung abscess due to HVKP in Taiwan. Difference between the previous and present case are summarized in Table 1, and characteristics of those strains are completely different. In addition, the association between lung abscess and HVKP serotype is still unknown.

Conclusion: To be our knowledge, this is the first identified case of community-acquired primary lung abscess due to serotype K2 HVKP. Further investigation regarding the relationship between HVKP and lung abscess is needed.

Characteristics of the Present and Previous Case

	Present case	Reported case
Age, sex	69, male	80, female
Country	Japan	Taiwan
Underlying disease	Hypertension Diabetes mellitus Chronic kidney failure	Diabetes mellitus
String test	Positive	Positive
Serotype	K2	K1
<i>rmpA</i>	Positive	Positive
<i>iutA</i>	Positive	Unknown
<i>entB</i>	Positive	Unknown
<i>mrkD</i>	Positive	Unknown
MLST	Under survey	ST 23

Cheng KC, et al. J Formos Med Assoc; 114: 379-80, 2015

AO060

ANTIBIOTICS SUSCEPTIBILITY AND TREATMENT OUTCOMES OF MYCOBACTERIUM CHIMAERA PULMONARY DISEASE – A RETROSPECTIVE STUDY

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Background and Aims: *Mycobacterium chimaera* is a new species discover under *Mycobacterium avium* complex (MAC) using modern gene sequencing. Unlike *Mycobacterium avium* and *Mycobacterium intracellulare*, little is known about the clinical features and treatment response of *Mycobacterium chimaera* pulmonary disease.

Methods: This retrospective study was conducted in a medical center from December 2012 to July 2015. Patients who fulfilled the 2006 ATS/IDSA diagnostic criteria for nontuberculous mycobacterial lung disease were enrolled, and categorized by whether they received anti-MAC treatment (e.g. combination of macrolides, rifamycins, ethambutol, fluoroquinolones or aminoglycosides) or not. Minimal inhibitory concentration (MIC) for each antibiotic was tested for all *Mycobacterium chimaera* isolates from their pulmonary specimens, and the susceptibility was defined according to the epidemiologic cutoff value by CLSI. Favorable clinical outcome was defined as patient survival, with culture conversion and radiographic resolution 1 year after diagnosis or treatment. Logistic regression was used to identify the independent factors associated with favorable clinical outcome.

Results: Among 28 patients, 17 (60.7%) of them were female. The mean age was 72.0 ± 13.5 years old. All of the *Mycobacterium chimaera* isolates were susceptible to clarithromycin and rifabutin, 10 (35.7%) were susceptible to amikacin. Under chest radiography and computed tomography follow-up, 6 (60%) of the 10 patients in the treatment group and 3 (16.7%) of the 18 patients in the non-treatment group had radiographic resolution ($P = 0.035$). The odds ratio of favorable outcome was 10.8 (95% CI, 1.1–106.7, $P = 0.042$) in patient with anti-MAC treatment in the multivariable analysis.

Conclusion: According to our study results, treatment with macrolides and rifamycins based regimen for pulmonary *Mycobacterium chimaera* disease led to improved clinical outcomes.

AO061

NEXT GENERATION SEQUENCING ASSISTED PATHOGENIC DETECTION CAN IMPROVE OUTCOMES IN IMMUNOCOMPROMISED HOST WITH PULMONARY INFECTION

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Background and Aims: The number of immunocompromised patients keeps increasing and many of them will suffer from pulmonary infection. This study was undertaken to assess the impact of next generation sequencing assisted pathogenic detection in immunocompromised host with pulmonary infection.

Methods: A total of 72 immunocompromised patients diagnosed of pulmonary infection was admitted in this study. The intervention group consisted of 33 patients who received next generation sequencing assisted pathogenic detection and the rest 39 patients made up the non-intervention group who only received microscopic examination and microbial culture test. Outcomes accessed included significance positive rate, turn around time of results, hospital and intensive care unit length of stay, all-cause 28-day and 90-day mortality, and total hospital expenditures.

Results: Next Generation Sequencing Assisted Pathogenic Detection improved turn around time (74.09 h in the non-intervention group versus 60.14h in the intervention group, $P < 0.01$), significance positive rate (23.08% vs 63.64%, $P < 0.001$), 90-day mortality (41.03% vs 18.18%, $P < 0.05$). The intervention of this detection method remains a significant predictor of survival (OR, 0.176; 95% confidence interval [CI], 0.036–0.874) after multivariate logistic regression. There wasn't significant difference of mean hospital costs in the two groups.

Conclusion: Next Generation Sequencing Assisted Pathogenic Detection resulted in significant improvements of clinical outcome in immunocompromised patients diagnosed of pulmonary infection. The intervention decreased turn around time of results increased the significance positive rate, decreased mortality risk while not increased mean hospital costs.

AO062

PROGNOSTIC VALUES OF CURB-65, EXPANDED-CURB-65, AND CURB-65 PLUS ALBUMIN AND PLATELET IN COMMUNITY ACQUIRED PNEUMONIA IN CIPTO MANGUNKUSUMO NATIONAL GENERAL HOSPITAL, JAKARTA

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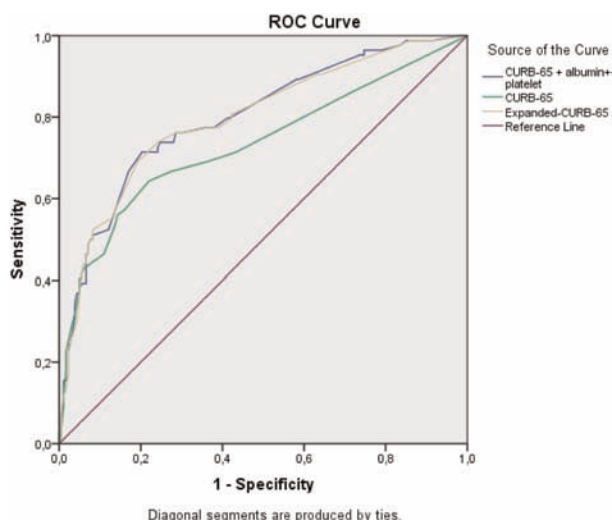
¹University of Indonesia, Indonesia, ²Division of Respiriology and Critical Care Medicine, Department of Internal Medicine, Faculty of Medicine University of Indonesia - dr.Cipto Mangunkusumo National General Hospital, Indonesia, and ³Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine University of Indonesia - Dr.Cipto Mangunkusumo National General Hospital, Indonesia

Background and Aims: Community acquired pneumonia is a major health problem, especially in Indonesia. The CURB-65 score is a widely used scoring system, but has some drawbacks to predict mortality of community pneumonia in our hospital. Recently promising new scoring system such as expanded-CURB-65 also known. This study aims to assess the CURB-65, expanded-CURB-65 and CURB-65 with addition low albumin and low platelet as a predictor of 30-days mortality of CAP patients in dr.Cipto Mangunkusumo National General Hospital.

Methods: This prospective cohort study involved 267 CAP patients who came to the Emergency Room (ER), pulmonary clinics or hospitalized in Dr. Cipto Mangunkusumo National General Hospital, Jakarta. The assessed outcome was patient mortality within 30 days. Performance of the CURB-65, expanded-CURB-65, and CURB-65 with addition low albumin and low platelet assessed using the area under the curve (AUC).

Results: During the 30-day period, there were 84 deaths (31.5%). The AUC CURB-65, expanded-CURB-65 and CURB-65 with addition low albumin and low platelet, respectively were as follows: 0,733 (*P* value 0,0001), 0,796 (*P* value 0,0001), and 0,799 (*P* value 0,0001). Additional result from our study using bivariate analysis is Lactate Dehydrogenase (LDH) from the expanded-CURB-65 score does not predict 30 day mortality of CAP patients in our hospital.

Conclusion: CURB-65 score with addition low albumin and low platelet is simple, objective and more accurate scoring system for predicting the mortality in CAP patients, better than CURB-65 score and expanded-CURB-65. It also more cost effective than expanded-CURB-65.



Asthma 1

AO065

DEVELOPMENT OF THE SEVERE ASTHMA TOOLKIT: A CLINICAL WEBSITE RESOURCE FOR THE MANAGEMENT OF SEVERE TREATMENT-REFRACTORY ASTHMA

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Background and Aims: Providing clinicians from a range of disciplines with resources to implement new treatments for severe asthma into practice is a priority. The Severe Asthma Toolkit was developed to address this.

Methods: Roundtable discussions and a needs assessment survey were carried out to identify clinician preferences, format and content. A reference group consisting of peak and consumer-bodies and experts was convened to provide advice and feedback. A multidisciplinary team of international experts was engaged to develop content. Written content was extensively referenced to literature. Peer and editorial review were performed to finalise content and inform the web-design strategy.

Results: Roundtable discussions identified a need for dedicated severe asthma management resources and skills training (McDonald *et al* 2017 *Respirology*). This was confirmed by 24/24 respondents to the needs assessment survey, and 88% suggested it be web-based. The end product (toolkit.severeasthma.org.au) launched March 2018, includes modules covering an overview of severe asthma, diagnosis, assessment, management, medications, co-morbidities, living with severe asthma, establishing a clinic, paediatrics and adolescents and clinical resources. In the first 8-weeks, 1,291 users accessed the site from 39 countries. A user survey (*n* = 76) shows that most (88%) are health professionals. Respondents agreed that the Toolkit increased their knowledge (71%) and confidence in managing severe asthma (64%), and 82% are likely to use the resource in clinic.

Conclusion: The Severe Asthma Toolkit is a comprehensive, accessible and independent resource developed by leading severe asthma experts to improve clinician knowledge and skills in severe asthma management.

The authors thank the Severe Asthma Toolkit contributors (<https://toolkit.severeasthma.org.au/contributors/>). Funding was provided through the NHMRC Centres of Research Excellence programme.

AO066

ESTABLISHMENT OF EOSINOPHILIC BRONCHITIS MOUSE MODEL WITH NONINVASIVE LUNG FUNCTION TEST

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Background and Aims: Eosinophilic bronchitis (EB) is a disease characterized by chronic cough and airway eosinophil infiltration, responsive to hormone therapy but without airway hyperreactivity (AHR). To date, there is no mouse model established with those whole features of EB.

Methods: 28 mice were divided into the normal saline (NS), asthma (AS), EB, and dexamethasone (DXM) groups. The AS group received 200 µg/50 µL while the EB and DXM groups received 10 µg/50 µL OVA intranasal stimulation, while the NS group with normal saline. The DXM group received intraperitoneal injection of 5 mg/kg of DXM 1 h before stimulation. After model establishment, the cough sensitivity of the mice was evaluated. Airway reactivity with noninvasive lung function test was assessed 6h later. The percentages of eosinophils (EOS%) in the bronchoalveolar lavage fluid (BALF) and the pathological changes of the lung tissues were observed in all groups.

Results: The cough sensitivity was significantly increased in the AS, EB, and DXM groups compared to the NS group ($P < 0.05$). After DXM treatment, the cough sensitivity was significantly decreased compared to the AS and EB groups ($P < 0.05$). After stimulation with methacholine (Mch; 12.5, 25 and 50 mg/mL), the Penh was significantly higher in the AS group than in the other 3 groups ($P < 0.05$). No significant difference was found among the other 3 groups at any Mch concentration. The BALF and pathological results showed that the mice in the AS and EB groups had obvious airway eosinophilic inflammation and that DXM attenuated the airway inflammatory infiltration in the EB mice.

Conclusion: Small OVA dose (10 µg) via intranasal stimulation successfully established a mouse EB model with following 4 features: increase in the number of coughs, airway eosinophilic inflammation, no AHR, and responsiveness to hormone treatment. EB mouse model established with noninvasive lung function test is in favor of studies needing repeated detection.

AO067

IMPACT OF FRACTIONAL EXHALED NITRIC OXIDE MEASUREMENT ON MANAGEMENT OF PATIENTS WITH SUSPECTED ASTHMA

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Background and Aims: Fractional exhaled nitric oxide (FENO) is an airway inflammation biomarker, but its role in clinical practice remains controversial. We therefore assessed the real-world impact of FENO in the diagnosis, treatment and 1-year outcomes of patients with suspected asthma.

Methods: Patients with suspected asthma and who had FENO done at an adult respiratory medicine clinic in 2016 were studied. Patients with pre-existing physician-diagnosed asthma were excluded. Each patient was evaluated for diagnostic and therapeutic changes and 1-year outcomes (any severe asthma exacerbation, defined as one resulting in an emergency department visit, hospitalization or death). Analyses were done using two definitions of elevated FENO: moderate (≥ 25 parts per billion [ppb]) or high (≥ 50 ppb).

Results: 171 patients (age 44.7 ± 18.0 years; 85/49.7% female; 142/83.0% never-smokers; forced vital capacity $99 \pm 19\%$ predicted; 1st-

second forced expiratory volume $102 \pm 20\%$ predicted) were studied. Median FENO was 25 ppb, interquartile range 16–48 ppb. 89 (52.1%) patients had moderate FENO elevation: they had increased asthma diagnosis (OR 10.1, 95% CI 4.1–24.8, $P < 0.001$), inhaled corticosteroids (OR 8.6, 95% CI 3.7–19.7, $P < 0.001$) and inhaled long-acting beta-agonist (OR 12.7, 95% CI 3.4–48.3, $P < 0.001$). 41 (24.0%) patients had high FENO elevation: they had increased asthma diagnosis (OR 11.9, 95% CI 4.5–31.3, $P < 0.001$), inhaled corticosteroids (OR 9.3, 95% CI 3.7–23.5, $P < 0.001$) and inhaled long-acting beta-agonist (OR 7.8, 95% CI 3.1–19.5, $P < 0.001$). No patient had any severe asthma exacerbation at 1-year of follow-up.

Conclusion: Among patients suspected to have asthma, FENO elevation was associated with increased asthma diagnosis, inhaled corticosteroid use and long-acting beta-agonist use.

AO068

REDUCED NUCLEAR FACTOR- κ B REPRESSING FACTOR AND INCREASED INTERLEUKIN-8 IN BRONCHIAL EPITHELIAL CELLS IN ASTHMA

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Background and Aims: Asthma is mediated by type 2 CD4+ T-helper cell (TH2) cytokines such as IL-4 and neutrophilic inflammation represents a distinct form of severe asthma. Rhinovirus infection promotes the release of interleukin (IL)-8, a potent chemokine recruiting neutrophils, from bronchial epithelium, and aggravates the symptoms of asthmatic patients. Nuclear factor- κ B repressing factor (NKRF) reduces the basal expression of IL-8. We hypothesised that the NKRF-negative regulatory mechanism is defective in asthmatic bronchial epithelium cells, resulting in exaggerated IL-8 production upon rhinoviral infection.

Methods: Primary bronchial epithelial cells were obtained from patients with non-severe or severe asthma and non-asthmatic subjects by bronchoscopic brushing. The effect of IL-4 on the expression of NKRF, and the effect of synthetic double-strain RNA polyinosinic:polycytidylic acid (poly I:C), which activates toll-like receptor 3 resembling rhinovirus infection, on IL-8 production were evaluated by immortalised human bronchial epithelial BEAS2B cell line model. mRNA of IL-8 and NKRF in primary bronchial epithelial cells and BEAS2B cells was determined by RT-qPCR. The effect of IL-4 on NKRF protein production was determined by western blotting.

Results: Primary epithelium cells from severe asthma patients expressed less NKRF mRNA and more IL-8 mRNA compared to those from non-severe asthma patients and non-asthmatic subjects. IL-4 increased NKRF in BEAS2B cells at protein level. Poly I:C attenuated the expression of NKRF mRNA but increased the expression of IL-8 in BEAS2B cells.

Conclusion: Bronchial epithelial cells from severe asthma patients exhibited reduced NKRF, which may be down-regulated by TH2 cytokines and further suppressed during respiratory virus infection, leading to uncontrolled IL-8 production and subsequent neutrophilic inflammation during asthmatic exacerbation.

AO069

THE EFFECTIVENESS OF MEPOLIZUMAB IN 19 PATIENTS WITH SEVERE ASTHMA IN JAPAN

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Background and Aims: Mepolizumab, a humanized monoclonal antibody against interleukin-5 (IL-5), showed efficacy in previous clinical trials in terms of reduction of exacerbations and the oral corticosteroid-sparing effect in severe eosinophilic asthma. An understanding of the effectiveness and safety of mepolizumab in real world setting is needed.

Methods: The analysis includes patients with severe asthma who received mepolizumab at least twice at our institution from July 2016 to May 2018. We reviewed blood eosinophil counts, the number of exacerbations, the corticosteroid dose, and safety data during the follow-up. We also analyzed the asthma control scores of Asthma Control Test (ACT), Asthma Control Questionnaire (ACQ), and the QOL scores of Asthma Quality of Life Questionnaire (AQLQ) and Asthma Health Questionnaire (AHQ).

Results: Subjects are 19 patients with median age of 65 (39–81). All of them had received asthma treatment equivalent to GINA step 4/5, 12 with oral corticosteroid, 7 with a history of anti-IgE antibody, and 3 with completion of bronchial thermoplasty. At follow up, the rate of exacerbation decreased in 15 (80%) patients and all of the patients (100%) showed the decrease of eosinophil counts. Seven (37%) patients reduced oral prednisone more than 50%. Of 6 patients followed up with questionnaires, asthma control scores improved in both two questionnaires; ACQ from 2.3 (1.6–4.6) to 1.6 (0.6–2.8), ACT from 13 (9–21) to 18.5 (13–20). Regarding QOL scores, AQLQ improved from 3.5 (2.9–4.5) to 2.2 (3.5–5.7) and AHQ from 52.5 (42–75) to 30 (16–65), indicating better control and QOL. Eight patients had discontinued the treatment, 5 switched to another anti-IL-5 antibody, 1 due to achieving good control, 2 due to adverse events (1 with liver injury and 1 with decreased vision).

Conclusion: Mepolizumab is effective in reducing asthma exacerbation and the oral corticosteroid dose, and improving asthma control and health-related QOL in real world setting.

AO070

METABONOMICS OF ALLERGIC ASTHMA: POTENTIAL BIOMARKERS HETES AND THEIR METABOLIC KEY ENZYME GPX

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Background and Aims: Allergic asthma is a chronic airway inflammatory disease, and its pathophysiological mechanism has not yet been fully elucidated. Metabolomics happens to be a powerful tool for discovering new biomarkers and resolving disease pathophysiology. Therefore, our aim was to use UHPLC-Q-TOF-MS to investigate the serum lipid metabolomic differences between patients and healthy people. Then, the changes of eicosanoid metabolism in patients with allergic asthma before and after routine drug treatment were analyzed.

Methods: Thirty patients with allergic asthma were enrolled in the asthma group, and another 30 healthy individuals were recruited as the

healthy group. Serum was collected, sample pretreated and derivatized, and used for non-targeted lipid metabolomics detection and analysis. Then, based on eicosanoid-targeted metabolomics, the changes of serum target metabolites in 25 children with allergic asthma before and after routine drug treatment were retrospectively analyzed.

Results: We detected 278 lipid metabolites using the +ESI and found a suitable OPLS-DA model for distinguishing asthma group from healthy group (R² = 0.556, Q² = 0.953). Differential metabolite analysis showed that eicosanoid levels in the asthma group were significantly higher than those in the healthy group (*P* < 0.05), especially HETEs. From the ROC curve, it can be concluded that the differential metabolite with the largest AUC is 12(S)-HETE (AUC = 0.983, 95% CI = 0.941–1.000). Metabolic pathway enrichment analysis showed that differential metabolites are concentrated in arachidonic acid metabolic pathways, and this pathway is mostly associated with inflammatory reactions and oxidative stress. After routine drug treatment, the target metabolites were significantly decreased (*P* < 0.05), and the LOX-mediated arachidonic acid metabolism pathway was significantly downregulated.

Conclusion: The results of this study suggest that HETEs are potential biomarkers for allergic asthma. GPx may be a key enzyme that links the inflammatory response and oxidative stress of allergic asthma, and it may be a new target for anti-inflammatory and anti-oxidative therapy for allergic asthma.

Table 1. Statistical parameters characterizing the discriminant properties of the selected putative biomarkers

Markers	P-value t test	ROC curve analysis AUC	95% CI
AA	<0.0001	0.966	0.894-1.000
5(S)-HETE	0.0014	0.849	0.691-1.000
8(S)-HETE	0.0017	0.899	0.763-1.000
11(S)-HETE	0.0023	0.731	0.506-0.956
12(S)-HETE	0.0009	0.983	0.941-1.000
15(S)-HETE	0.0005	0.798	0.691-1.000

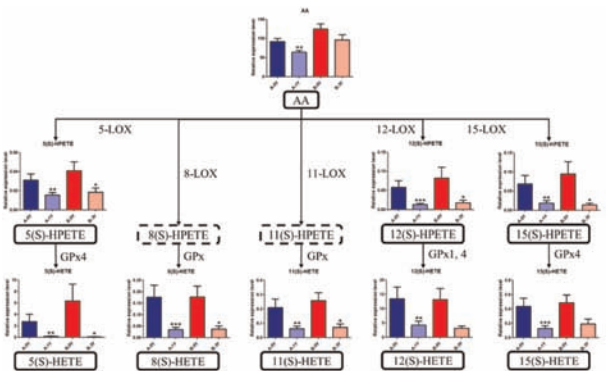


Figure 5. Comparison of the intensities of metabolites in arachidonic acid metabolism pathway mediated by LOX.

AO071

ANTI-REMODELLING FEATURES OF ARTESUNATE AS A POTENTIAL NOVEL DRUG FOR THE TREATMENT OF ASTHMA

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Background and Aims: Airway wall remodelling (AWR) is one of the major features of asthma pathophysiology. AWR features include, but are not limited to, increased airway smooth muscle (ASM) mass due to ASM hypertrophy and hyperplasia, mucus hypersecretion, extracellular matrix deposition and angiogenesis. Current anti-asthma therapy have limited efficacy on AWR features. Hence, new treatment options targeting AWR features in asthma are needed. Artesunate is a semi-synthetic artemisinin derivative recommended by the World Health Organisation for malarial treatment. We previously showed that artesunate attenuates airway inflammation with accompanied reductions in ASM mass via the PI3K/Akt pathway in an ovalbumin-induced acute mouse model of inflammation. We now examine the anti-AWR properties of artesunate in a house dust mite (HDM)-induced chronic mouse model of asthma, where AWR is a prominent feature.

Methods: 6–8 weeks old female C57BL/6 mice were sensitized with 20 µg HDM in Al(OH)₃ on days 0 and 14, then challenged with 10 µg HDM (intranasal instillation, weeks 3–8). From weeks 7–8, mice were treated with artesunate 30 mg/kg/day (or equivalent sodium bicarbonate as vehicle control). Mouse lung lobes were harvested 24 h after the last HDM challenge for immunohistochemistry, mRNA or protein analysis.

Results: Artesunate significantly attenuated HDM-induced ASM mass, as measured by sm-α actin expression. The reduction in ASM mass was not due to artesunate-induced toxicity or reduction in inflammatory cytokine levels. Artesunate also reduced HDM-induced mucus hypersecretion. However, it had limited effect on MMP9 and VEGF expressions, markers for collagen remodelling and angiogenesis respectively. Mechanistically, pre-treatment with artesunate attenuated HDM-induced cyclin D1 and p-Akt protein abundance, suggesting an involvement of the PI3K/Akt pathway in the anti-proliferative activity of artesunate in ASM cells.

Conclusion: Whilst further studies are required to assess the effects of artesunate on other AWR features, current studies support its potential as a novel anti-AWR therapy for asthma.

AO072

THE PREVALENCE AND CLINICAL CHARACTERISTICS OF T2-LOW AND T2-HIGH ENDOTYPE OF SEVERE UNCONTROLLED ASTHMA DISTINGUISHED BY COMBINING TYPE-2 BIOMARKERS

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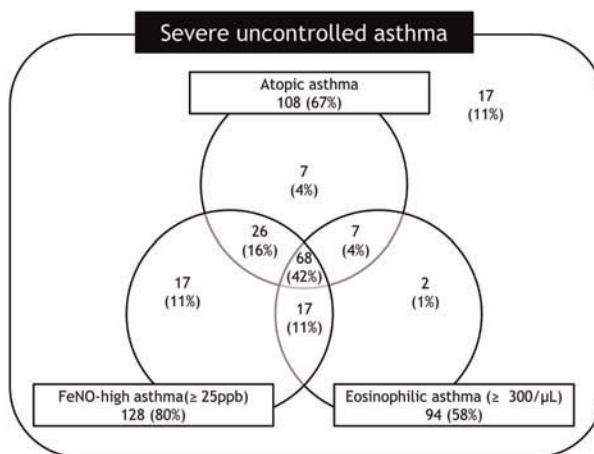
Background and Aims: Currently, two major endotypes of asthma have been distinguished: T2-low and T2-high asthma. In patients with

severe uncontrolled asthma, it is important to identify an endotype and stratify the treatment approach. In clinical practice, the designation of the T2-high endotype is commonly used to the presence of atopy and/or eosinophilic inflammation, identified on the basis of blood eosinophil counts (B-Eos) and fraction of exhaled nitric oxide (FeNO). However, the prevalence and clinical characteristics of T2-low and T2-high endotype of severe asthma distinguished by combining type-2 biomarkers have not been well examined.

Methods: This retrospective study examined clinical data of 161 patients with severe uncontrolled asthma defined by ERS/ATS guidelines. T2-high asthma was determined by the presence of atopy (RAST +) and/or FeNO > 25 ppb and/or B-Eos > 300 µL⁻¹, while T2-low asthma was distinguished by the absence of these characteristics.

Results: The prevalence of patients with severe uncontrolled asthma was classified into the T2-high (*n* = 144, 89%) and T2-low asthma (*n* = 17, 11%). The majority (*n* = 68, 47%) of patients with T2-high severe asthma showed all of atopy, blood eosinophilia, and High FeNO. Compared to the T2-low asthma patients, T2-high patients showed a significantly lower pulmonary function; FVC of predicted (median 94.5% vs 103.2%; *P* < 0.05), and FEV1 of predicted (median 77.5% vs 92.7%; *P* < 0.005). The prevalence of chronic sinusitis was higher in the T2-high than in T2-low patients (*P* < 0.005). There was no significant difference in the number of exacerbations during the last 12 months and ACQ score between T2-high and T2-low patients.

Conclusion: The majority of patients with severe uncontrolled asthma was classified into the T2-high endotype by measuring the multiple type-2 biomarkers. T2-high endotype group was associated with lower lung function.



AO072

THE PREVALENCE AND CLINICAL CHARACTERISTICS OF T2-LOW AND T2-HIGH ENDOTYPE OF SEVERE UNCONTROLLED ASTHMA DISTINGUISHED BY COMBINING TYPE-2 BIOMARKERS

KEIJI OISHI^{1*}, TSUNAHICO HIRANO², KAZUKI MATSUDA², KAZUKI HAMADA², SHO UEHARA², RYO SUETAKE², YOSHIKAZU YAMAJI², MAKI ASAMI-NOYAMA², NOBUTAKA EDAKUNI², KAZUTO MATSUNAGA²

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Background and Aims: Currently, two major endotypes of asthma have been distinguished: T2-low and T2-high asthma. In patients with

MULTIDIMENSIONAL GAPS IN HEALTH CARE FACILITIES FOR ASTHMA PATIENTS IN INDONESIA; A FORMATIVE RESEARCH

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Background and Aims: Indonesia runs National Health Insurance (JKN) and nearly 70% population are covered. JKN recognizes tiering system, Primary Health Centers (*Puskesmas*) is a first gate prior referring to hospitals. National survey in 2013 revealed that the prevalence of asthma was 4.5%. The study is intended to understand

AOL001

the readiness and gaps of health care system tackling asthma diseases.

Methods: The study used a mixed method convergent design using quantitative and qualitative data collected simultaneously. Quantitative survey was conducted to 32 health care providers and 160 patients in 25 *Puskesmas* and 7 hospitals in 3 selected districts. Qualitative survey was performed to 25 health care providers, 8 patients, 3 program managers at District Health Office through in depth interview and focused group discussion.

Results: (a) Availability of drugs and infrastructures; only 30–50% of drugs in the national guideline is available in *Puskesmas*. Reliever and controller drugs are limited. (b) Health staff; Health staffs lack of capacity to recognize the sign and symptoms of asthma, and the use of asthma devices especially in *Puskesmas*. (c) Implementation of SOP; All health care facilities in this study have SOP for asthma services but the adherence is not as expected. (d) Patient Care; Education, Information and Consultation (EIC) has been conducted focusing on asthma triggers. Majority of patients did not comply to medications. (e) Clinical Leadership; The relevant Medical Associations have not been consistently collaborate with District Health Office or Provincial Health Office in asthma.

Conclusion: Multidimensional gaps in health care facilities for asthma patient need to be addressed. The Ministry of Health of Indonesia sets a program to prioritize tackling asthma disease; 1) Encourage collaborations to uplift health staffs capacity, 2) Provision of drugs, especially controllers and nebulizer devices in *Puskesmas*, and 3) Include counseling as a standard service for patients in current guidelines for asthma.

Environmental & Occupational Health and Epidemiology

AO073

MESENCHYMAL STEM CELL-BASED THERAPY ATTENUATES SILICA-INDUCED MACROPHAGE ACTIVATION VIA CIRCZC3H4/ZC3H4 PATHWAY

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Background and Aims: Silicosis, a chronic pulmonary disease caused by inhalation of silica dust, is one the most common occupational diseases. After silicon dioxide (SiO₂) exposure, a series of inflammatory cascades occurs in alveolar macrophages which results in fibroblast proliferation and migration, followed by pulmonary fibrosis, while no valid therapeutics are available. Mesenchymal stem cell (MSC)-based therapy is a novel approach with great potential for the treatment of fibrotic diseases. However the therapeutic mechanism of MSC in silicosis remains unclear. Previous data from our laboratory suggested that the circZC3H4/ZC3H4 pathway involved in SiO₂-induced macrophage activation. Whether protective effects of MSC targeting ZC3H4 pathway deserve to be elucidated.

Methods: Murine bone marrow-derived macrophages and human macrophages were exposed to SiO₂. Protein level change was detected by Western Blot and immunocytochemistry. CRISPR/Cas9 system was applied to specific knock-in/down of protein in macrophages, combined with Hoechst staining and the scratch assay to explore the functional change. Co-IP was used to detect the protein interaction. The conditioned mediums collected from human and mouse bone marrow-derived MSCs were used to investigate the anti-inflammatory effect of MSC. To validate the in vitro finding, mouse silicosis model was established. After intratracheal instillation of MSC or saline, both CT imaging and immunohistochemistry staining were applied to detect the change of pulmonary inflammation and fibrosis.

Results: The experiments demonstrated that 1) SiO₂ induced increase of ZC3H4, HMGB1 protein expression, as well as interaction between them; 2) ZC3H4 promoted macrophage activation, followed by fibroblast proliferation and migration indicated by conditioned medium experiments; 3) MSC prevented SiO₂-induced macrophage activation by targeting ZC3H4 pathway in both in vitro and in vivo experiments.

Conclusion: Current study elucidated the mechanism of MSC-based therapy for silicosis, which provide novel insight into the potential targeting of ZC3H4 in the development of potential stem cell therapeutic strategies for pulmonary disease.

AO074

LONG-TERM EXPOSURES TO AIR POLLUTANTS AND RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACEs), A NATIONWIDE 10-YEAR OPEN COHORT STUDY IN TAIWAN MING-SHUN HSIEH^{1*}, PAU-CHUNG CHEN¹, CHORNG-KUANG HOW², CHEN-JUNE SEAK³, VIVIAN CHIA-RONG HSIEH⁴

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Background and Aims: To evaluate the long-term exposure to air pollution (PM_{2.5}, CO, and NO₂) and the risk of major adverse cardiovascular events (MACEs) (including acute myocardial infarction, congestive heart failure, ischemic stroke, intracranial hemorrhage, and malignant dysrhythmia) in Taiwan.

Table 2 Cox model with hazard ratio and 95% confidence interval for MACEs in the patients exposed to various daily average concentrations of air pollutants

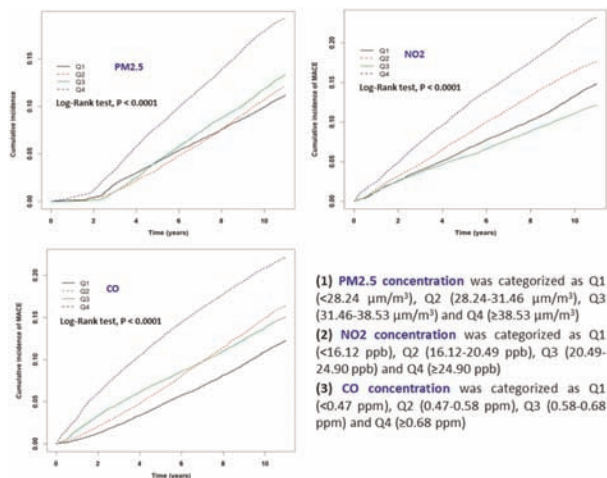
Variables	Crude		Adjusted model 1		Adjusted model 2		Adjusted model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
PM _{2.5} (µm/m ³), daily average	1.029(1.027-1.031)	<.0001	1.086(1.081-1.091)	<.0001	-	-	-	-
NO ₂ (ppb), daily average	1.034(1.012-1.057)	<.0001	-	-	1.021(1.018-1.024)	<.0001	-	-
CO (ppm), daily average	1.912(1.810-2.019)	<.0001	-	-	-	-	2.071(1.946-2.204)	<.0001
Gender								
Female	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Male	1.287(1.247-1.329)	<.0001	1.127(1.088-1.168)	<.0001	1.083(1.049-1.118)	<.0001	1.083(1.049-1.118)	<.0001
Age group								
40-49	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
50-59	2.292(2.189-2.401)	<.0001	1.471(1.397-1.549)	<.0001	1.535(1.463-1.611)	<.0001	1.532(1.46-1.607)	<.0001
60-69	5.024(4.802-5.258)	<.0001	1.919(1.818-2.021)	<.0001	2.071(1.975-2.176)	<.0001	2.081(1.99-2.182)	<.0001
70-80	9.225(8.797-9.674)	<.0001	2.465(2.325-2.614)	<.0001	2.592(2.458-2.734)	<.0001	2.602(2.468-2.745)	<.0001
Residential area								
Northern	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Taipei	0.878(0.838-0.921)	<.0001	1.28(1.206-1.358)	<.0001	0.959(0.911-1.011)	0.1304	0.941(0.894-0.992)	0.023
Central	0.962(0.909-1.018)	0.1782	0.534(0.497-0.575)	<.0001	0.929(0.877-0.983)	0.0136	0.977(0.916-1.03)	0.3305
Southern	1.123(1.055-1.196)	0.0005	0.413(0.378-0.451)	<.0001	1.085(0.997-1.177)	0.0617	1.125(1.053-1.202)	0.0005
Comorbidities (reference)								
HTN	2.968(2.889-3.069)	<.0001	1.283(1.228-1.344)	<.0001	1.463(1.402-1.526)	<.0001	1.461(1.4-1.524)	<.0001
DM	2.939(2.815-3.068)	<.0001	1.384(1.312-1.46)	<.0001	1.416(1.35-1.485)	<.0001	1.419(1.353-1.488)	<.0001
Chronic kidney disease	2.348(2.154-2.561)	<.0001	1.299(1.179-1.437)	<.0001	1.344(1.231-1.468)	<.0001	1.342(1.229-1.466)	<.0001
Cancer	1.549(1.424-1.728)	<.0001	1.115(0.996-1.248)	0.0593	1.154(1.048-1.276)	0.0037	1.174(1.061-1.295)	0.0013

Methods: We linked two nation-scale databases, that is, the national health insurance claims database and the air quality-monitoring database to conduct this open cohort study between 2003 and 2013. Cox proportional regression with time-dependent model was used to evaluate the HR of varied air pollutants to the MACEs development. The residential areas were divided into four groups according to the daily average concentration of air pollutants, Q1 to Q4 (Q4 = the worst). The cumulative incidence of MACEs was examined by the Kaplan-Meier analysis with log-rank test.

Results: A total of 15,415 new onset of MACEs cases (16.07%, 15,415/95,916) were identified during the follow-up period with 100,410 non-MACEs cases (83.93%, 80,501/95,916). The patients in the MACEs group had an older age than the patients in the non-MACEs group (mean ± SD, 60.55 ± 10.71 and 51.72 ± 9.27 years, respectively) and also had more comorbidities, such as hypertension, diabetes, chronic kidney disease, and previous cerebrovascular diseases. In the multivariate analysis, after adjusting for age, gender, urbanization level, residential area, baseline comorbidities, and drug use, the adjusted HRs were that PM_{2.5} =

1.09, 95% CI 1.08–1.09, $\text{NO}_2 = 1.02$, 95% CI 1.018–1.024, and $\text{CO} = 2.07$, 95% CI 1.95–2.20, respectively, all $P < 0.0001$ (Table). The Kaplan-Meier analyses with log-rank tests showed that $\text{PM}_{2.5}$, NO_2 , and CO concentration were all obviously associated with the increased cumulative incidence rate of MACEs during the follow-up period (Figure).

Conclusion: Long-term exposure to air pollutants ($\text{PM}_{2.5}$, CO , and NO_2) was associated with an increased risk of new-onset of MACEs, especially in the susceptible populations of older age and with chronic diseases.



AO075

THE ROLE OF SIRTUIN1 IN THE MACROPHAGE

POLARIZATION INDUCED DIRECTLY BY AIRBORNE $\text{PM}_{2.5}$

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Background and Aims: The potential effects of airborne $\text{PM}_{2.5}$ on the innate immunity have raised concerns. As the first line of defense, Macrophage are able to be polarized and to induce inflammatory response. The aim of our research is to confirm that airborne $\text{PM}_{2.5}$ can directly affect macrophage polarization and to explore the role of Sirtuin1 in this process.

Methods: $\text{PM}_{2.5}$ samples were collected at central area of Beijing in the winter 2017. We used RAW264.7 cell line as a model system to demonstrate effects of airborne $\text{PM}_{2.5}$ on macrophage polarization. The expression of cytokines and key molecular markers were detected by real-time PCR. We investigated the effect of $\text{PM}_{2.5}$ on the expression of Sirtuin1 by Western blotting in vitro and in vivo experiments. The specific agonist and antagonist of Sirtuin1 were used to address the possible molecular mechanisms of $\text{PM}_{2.5}$ induced macrophage polarization.

Results: $\text{PM}_{2.5}$ increased the expression of interleukin-6 (IL-6) and induced Nitric oxide synthase (iNOS), but the expression of Arg-1 and CD206 had no significant change, which prompt that $\text{PM}_{2.5}$ enhanced the M1 polarization directly. $\text{PM}_{2.5}$ decreased the expression of Sirtuin1 both in vitro and in vivo experiments. Pretreatment of SRT1720, a specific agonist of Sirtuin1 prevented the increased expression of IL-6 and iNOS, and EX527 a specific antagonist of Sirtuin1 further increased the expression of IL-6 and iNOS.

Conclusion: $\text{PM}_{2.5}$ exposure significantly enhanced inflammatory M1 polarization through Sirtuin1 pathway, whereas activation of Sirtuin1 can inhibit $\text{PM}_{2.5}$ induced inflammatory M1 polarization. Sirtuin1 could

become an effective target for the intervention of inflammation induced by airborne $\text{PM}_{2.5}$.

AO076

FINDING A HIDDEN ASBESTOS RELATED LUNG CANCER: MULTI-CENTERED ACTIVE SURVEILLANCE SYSTEM IN KOREA

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Background and Aims: Various potential risk factors and long latent periods prevent clinicians diagnosing asbestos related lung cancer (ARLC). Therefore, it is necessary for researchers to find a hidden ARLC in the hospital. The aim of this study is to establish a surveillance program for hidden ARLC and evaluate the effect of surveillance program.

Methods: A total of 7 hospitals joined to find a hidden ARLC in this active surveillance program. The reading sheet of chest CT scan among incident lung cancer in all hospitals were collected for retrospective evaluation (2015.07–2017.06). After training of reading asbestos specific findings and need of intention of report those findings in the reading sheet for radiologists of chest division at each hospital, a prospective evaluation have been performed for 6 months (2017.07–2017.12). The searching keywords in the reading sheet of chest CT scan for asbestos exposure were 'plaque', 'asbestos', 'asbestosis'. The incident cases were calculated in both prospective and retrospective evaluation and compared before and after the active surveillance program.

Results: A total of 5,389 (No of CT scan = 17,503) those who eligible subjects diagnosed as incident lung cancer in retrospective evaluation and 2,030 (No of CT scan = 2,976) those diagnosed as incident lung cancer in prospective evaluation were enrolled and their CT scan finding reading sheet were evaluated. The numbers of those subjects with lung cancer who are estimated the exposure of asbestos were 29 cases (7.2 cases per 6 months) in retrospective evaluation and 12 cases per 6 months in prospective evaluation, respectively. Overall increase of finding ARLC (from 0.54% to 0.98%) after informing process for radiologist was shown.

Conclusion: A hospital-based surveillance program based on radiologists will make the numbers of underestimated the ARLC increase. Therefore, a stepwise expansion of this surveillance program in Korea should be needed to find hidden ARLC cases.

AO077

HYPERCAPNIC ACIDOSIS ATTENUATES DECOMPRESSION SICKNESS-INDUCED LUNG INJURY

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Background and Aims: Decompression sickness (DCS) remains the most important risk in both professional and recreational diving because standard decompression procedures sometimes fail to prevent bubble formation. Hypercapnic acidosis has been proved to have a protective effect on tissue injury in several animal models. We investigated

the effect of hypercapnic breathing on the air bubble- and DCS-induced lung injury.

Methods: First, rats were pressurized with air to 6 atmospheres absolute (ATA) for 60 or 120 min and then decompressed rapidly to the surface in 5 min to induced DCS and DCS-related lung injury. Hypercapnia was induced by replacement of compressed air with 3% CO₂ in 97% of air for 10, 30, and 60 min. Second, to differentiate the direct protective effect of hypercapnia from its preventive effect by reducing amount of bubble formation, we introduced intravenously a given amount of air into anesthetized rats (in vivo). Third, to exclude the effect of hemodynamic alterations by hypercapnia, we further verified the protective effects on the air bubble-induced tissue injury in an isolated rat lung model (ex vivo).

Results: Our results showed that brief hypercapnia for 10 min before decompression significantly attenuated acute lung injury and reduced the rate of animal death, whereas a prolonged hypercapnia during the whole bottom time augmented the DCS-induced lung injury. Our results also showed that brief hypercapnic ventilation before pulmonary artery air infusion attenuated in vivo or ex vivo air embolism-induced lung injury. Hypercapnia significantly attenuated acute lung injury by inhibition of the inflammation cascade.

Conclusion: In conclusion, our results suggested that brief hypercapnia before decompression may protect from DCS-induced lung injury via inflammation inhibition.

AO078

ASSOCIATION OF PHYSICAL ACTIVITY WITH LUNG FUNCTION IN DUSTY AREAS COHORT

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Background and Aims: We assessed associations between physical activity level and lung function in dusty areas cohort near cement plants.

Methods: In total, 504 participants in dust areas cohort completed the lung function test and collected physical activity information using questionnaire. We calculated MET score, physical activity time (min) and walking time (min) to assess physical activity level, and categorized them by median. Physical activity frequency (week) was categorized into groups less than 7 times per week and more than 7 times per week. We used the generalized linear model to compare lung function with physical activity level. Generalized linear model adjusted for age, sex, smoking status, pack-years.

Results: The average forced expiratory volume in 1 s (FEV₁) of participants was 86.5%. The median of MET score, physical activity time, and walking time were 1,270, 120(min), and 180(min), respectively. Using the generalized linear model in exploring the effect of physical activity on lung function with those who were inactivity (88.6%) as the reference group, showed that FEV₁ was 93.6% among those who were activity when adjusting for potential confounders (*P* value 0.037). FEV₁ was 95.9% in Met score ≤1,270 participants (*P* value 0.006). In addition, FEV₁ was 95.1% in participants with physical activity frequency per week < 7 (*P* value 0.046) and 96.9% in participants with physical activity time ≤120min (*P* value 0.004). The association between walking time (min) and lung function was not statistically significant.

Conclusion: This study showed that regular physical activity may have effect on lung function increase in participants in dusty areas cohort.

Table 1. Lung function according to physical activity level

	Lsmean ¹⁾	Mean Difference	P value
Physical activity			
inactivity (n=385)	88.6	ref.	ref.
activity (n=114)	93.6	5	0.037
MET Score			
inactivity (n=385)	88.6	ref.	ref.
≤1,270 (n=57)	97.1	8.5	0.006
>1,270 (n=57)	89.9	1.3	0.666
Physical activity/week			
inactivity (n=385)	86.6	ref.	ref.
<7 (n=52)	95.1	8.5	0.046
≥7 (n=62)	92.3	5.7	0.221
Physical activity time(min)/week			
inactivity (n=390)	88.0	ref.	ref.
≤120 (n=58)	96.9	8.9	0.004
>120 (n=56)	88.9	0.9	0.756
Walking time(min)			
inactivity (n=356)	88.6	ref.	ref.
≤180 (n=75)	92.1	3.5	0.223
>180 (n=67)	91.1	2.5	0.398

¹⁾ adjusted for age, sex, smoking status, pack-years

AO079

LUTEOLIN DECREASES THE PM2.5-INDUCED AUTOPHAGY OF MH-S BY SCAVENGING ROS

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Background and Aims: Luteolin (LUT) is a kind of flavonoids, which is generally present as a constituent of traditional Chinese herbs, and has been demonstrated to exhibit potent cytoprotective properties. Although LUT has various beneficial effects on health, further studies still need to be performed on the protection of lung. The present study investigated whether LUT can protect mouse alveolar macrophages (MH-S) from PM2.5 damage.

Methods: The effects of the PM2.5 on morphological of autophagy in MH-S were analyzed by transmission electron microscopy, GFP-LC3 puncta was observed by confocal fluorescence microscope. The cell viability was detected by MTT, the intracellular levels of ROS in MH-S cells were measured using DCFH-DA, The effects of LC3II and p62 in MH-S were observed with Western blotting following PM2.5 exposure; the role of autophagy in PM2.5-induced autophagy was examined using 3-methyladenine. PM2.5-induced mRNA expression of autophagy-related protein p62 and LC3II was also observed with RT-PCR.

Results: It was found that, following exposure to PM2.5, the MH-S exhibited autophagy, as observed by transmission electron microscopy, and reactive oxygen species (ROS) bursts, analyzed by fluorescence microscope. The cell viability showed both time- and concentration - dependent decrease when exposure to PM2.5, and compared with the MH-S cells treated with PM2.5 alone, LUT pretreatment can decreases PM2.5-induced cell death in a dose-dependent manner. Following pretreatment with micromolar concentrations of LUT, ROS production decreased and autophagy gradually declined. In addition, western blot analysis showed that the expression levels of classical autophagy-associated proteins, LC3-II and p62 were gradually decreased and increased with the PM2.5 exposure, following pretreatment with LUT.

Conclusion: These data indicated that PM2.5-induced autophagy was mediated by ROS, suggesting the possibility of protection against PM2.5 by certain natural antioxidants, including LUT.

Interstitial Lung Disease 1

AO081

AO080

NINTEDANIB AND PIRFENIDONE INHIBIT LYSOPHOSPHATIDIC ACID-INDUCED VASCULAR ENDOTHELIAL GROWTH FACTOR AND COLLAGEN PRODUCTION IN HUMAN PRIMARY LUNG FIBROBLASTS

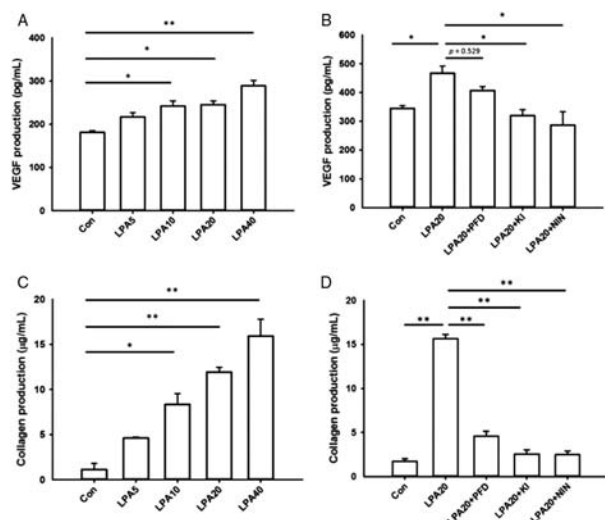
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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is characterized by uncontrolled lung fibroblast proliferation, excessive extracellular collagen deposition and profibrotic mediators release such as vascular endothelial growth factor (VEGF). Nintedanib (NIN) and pirfenidone (PFD) are two drugs recently approved for treatment of IPF based on studies that showed their anti-fibrotic effects in vitro and clinically delayed disease deterioration. However, the detail therapeutic mechanism remains largely unknown. Lysophosphatidic acid (LPA) is a potent bioactive phospholipid in tissues, plasma and body fluids. Activation of LPA can induce diverse cellular responses, including cell proliferation, migration, and cytokine release through G-protein coupled LPA receptors (LPARs). Increased LPA level was observed in bronchoalveolar lavage fluid of IPF patients in recent studies, indicating its role in the pathophysiology of IPF. We hypothesized that both NIN and PFD could inhibit LPA-induced VEGF and collagen production released by lung fibroblasts.

Methods: Human primary lung fibroblasts were exposed to various concentrations (5, 10, 20, and 40 μ M) of LPA for 24 h with or without pretreatment of selective LPAR1 inhibitor (Ki 16425, KI, 3 μ M), NIN (1 μ M) or PFD (20 μ M). Extracellular VEGF and collagen production released by fibroblasts were measured by the ELISA and Sircol collagen assay.

Results: Concentration-dependently increase of extracellular VEGF and collagen production (Figure 1A and 1C) were observed in human primary lung fibroblasts after LPA stimulation. Pretreatment of KI, NIN or PFD alleviated LPA-induced VEGF and collagen production (Figure 1B and 1D)

Conclusion: Both NIN and PFD inhibit LPA-induced VEGF and collagen production in human primary lung fibroblasts, suggesting their therapeutic mechanism involving LPA-regulated pulmonary fibrosis.



THE LONG TERM STUDY OF SIROLIMUS IN CHINESE POPULATION WITH LYMPHANGIOLEIOMYOMATOSIS

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Background and Aims: Definitely, sirolimus can stabilize the pulmonary function of LAM patients, and decrease the level of serum biomarkers of VEGF-D level. However, researchers found that some mild and severe impairment of lung function in LAM patients who continued to use sirolimus continued to deteriorate.

Methods: According to whether there were affiliated with TSC1 or TSC2 mutations, they were divided into TSC1/2 M (+) group included 21 cases and TSC1/2 M (-) group included 12 cases. After entering the group, sirolimus was given orally (maintenance of effective blood concentration 5–15 ng/ml). At the same time, lung function, serum VEGF-D and other clinical data were collected at baseline, follow up 3, 6, 12, 18, 24 months.

Results: Overall, sirolimus can stabilize the lung function indicators of Chinese LAM patients who suffered the moderate and severe pulmonary function damage, including FEV1, FVC, RV, TLC, DLCO and so on. Plus, sirolimus can reduce the serum VEGF-D level. Secondly, the subgroup analysis showed that sirolimus could stabilize and improve the pulmonary ventilation function and diffusion function in the TSC1/2 M (+) group of Chinese LAM population. The average monthly change of FEV1 increased by 5.57 ± 8.95 ml, the average monthly change of FVC increased by 9.04 ± 12.88 ml, and the average monthly variation of DLco increased by 0.04 ± 0.07 ml/mmHg/min. This group had a good response to sirolimus. The TSC1/2 M (-) group, responded poorly to sirolimus treatment. Finally, The level of serum VEGF-D in the TSC1/2 M (+) Group continued to decrease during the treatment.

Conclusion: The long-term treatment of sirolimus can stabilize and improve the TSC1/2 M (+) group of Chinese LAM patients with FEV1, FVC and DLco, prevent the decrease of lung function and reduce the serum VEGF-D level.

AO082

10 YEARS-EXPERIENCE OF USING PIRFENIDONE FOR IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is a progressive, poor prognostic interstitial lung disease with median survival ranging from 2.5 to 3.5 years. We use two antifibrotic agents for IPF nowadays. Pirfenidone has been approved in December 2008 in Japan. The aim of this study is to clarify efficacy and tolerability of 10 years-experience using of pirfenidone for IPF.

Methods: We retrospectively collected patients administered pirfenidone from December 2008 to April 2018. Baseline defined the day of starting pirfenidone. IPF was diagnosed by using the guideline of ATS/ERS/JRS/ALAT statement (AJRCCM 2011). IPF/UIP defined IPF confirmed by pathological findings of surgical lung biopsy (SLB) and clinical IPF defined IPF without SLB. Efficacy was evaluated decline of FVC after administration of pirfenidone, median survival time from starting pirfenidone in patients treated more than 52 weeks, and acute exacerbation rate in all patients with IPF. Tolerability was evaluated discontinuation ratio of pirfenidone at 52 weeks and whole period.

Results: 129 patients with IPF (IPF/UIP 44, clinical IPF 85) were enrolled in this study, excluded 25 patients with IPF diagnosed by disease behavior (unclassifiable IIPs 8, IPPFE 6, INSIP 1, chronic hypersensitivity pneumonia 7, other diseases 3). Median time from diagnosis to starting pirfenidone was 6.9 (IQR 2.1–84.8) weeks. 59 patients were treated more than 52 weeks {median treated periods was 117 (IQR 79–185) weeks}. Median decline of FVC was 90 (IQR –7 – 303) ml/year. Median survival time from starting pirfenidone and diagnosis was 4.1 and 6.8 years, respectively. Acute exacerbation ratio was 26% in all patients. Discontinuation ratio was 41% at 52 weeks and 62% at whole periods.

Conclusion: Efficacy for decline of FVC was similar to clinical trial reports. Median survival time was longer than previous reports. Discontinuation ratio was similar to post-marketing surveillance in Japan (Respir Investig 2015).

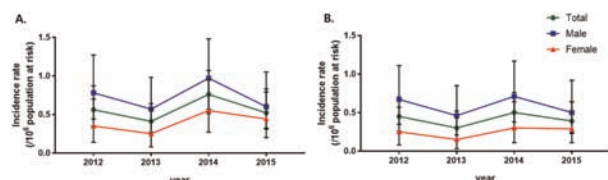
AO083

PULMONARY ALVEOLAR PROTEINOSIS IN KOREA: ANALYSIS OF PREVALENCE AND INCIDENCE BY A NATIONWIDE POPULATION-BASED STUDY

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Background and Aims: Pulmonary alveolar proteinosis (PAP) is a rare lung disease and data on prevalence and incidence of PAP are limited. The aim of this study is to investigate the prevalence and incidence of PAP by using nationwide claims data from Korean health insurance review and assessment service.



Methods: Cases of PAP were identified for any visit between 2010 to 2016 that listed the Korean Classification of Disease, 7th edition code of PAP (J84.0) and rare incurable disease exempted calculation code (V222). A narrow case was defined as follows: 1) more than two PAP-coded visits within 1 year of the first claim, 2) more than one claim for both chest computed tomography and diagnostic procedures (bronchoscopy or surgical lung biopsy) within 90 days of the first claim.

Results: A total of 182 patients (narrow, $n = 82$) visited medical institutions for PAP during the study period, and 89 patients (narrow, $n = 66$) were newly identified between 2012 and 2016. The prevalence of PAP was 4.44 (narrow: 4.39) per 10⁶ people and was highest between ages 60–69 years. The incidence was 0.56 (narrow: 0.41) per 10⁶ person-years, with the highest incidence rate between ages 50–59 years. The age- and sex-standardized annual incidence rates were constant from 0.56 (narrow: 0.45) per 10⁶ person-years in 2012 to 0.52 (narrow: 0.39) per 10⁶ person-years (figure). The highest incidence peak in men and women were 50–59 years, but the age distribution in women showed bimodal pattern due to second incidence peak in 20–29 years. For incidence cases, mean age was 50.8 years, the highest peak age was 50–59 years, and male predominance was observed (male-to-female ratio: 1.82).

Conclusion: The prevalence and incidence of PAP in Korea were low, similarly to those in other countries, and middle-aged men showed the highest risk.

THE PULMONARY MANIFESTATIONS OF TUBEROUS SCLEROSIS COMPLEX IN TAIWANESE PATIENTS

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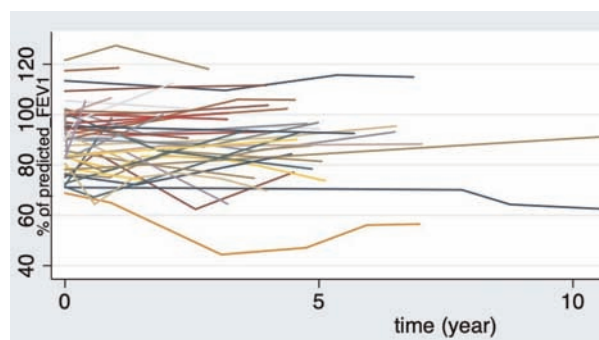
Background and Aims: Lymphangioleiomyomatosis (TSC-LAM) and multifocal micronodular pneumocyte hyperplasia (MMPH) are two major pulmonary abnormalities in patients with tuberous sclerosis complex(TSC). This study aimed to investigate the association between the pulmonary manifestations, genotypes, and the annual change of forced expiratory volume in one second (FEV1) in TSC-LAM and MMPH.

Methods: From 2010 to 2017, patients with suspected TSC by clinical manifestations or family history were screened. The diagnosis was made by genetic analysis or by diagnostic criteria 2012. The computed tomography of chest was reviewed to survey if LAM, MMPH, or combined LAM and MMPH existed. The pulmonary function tests were also collected, including FEV1, diffusion capacity, and forced vital capacity. We applied a linear mixed-effects model using FEV1 as the dependent variable. Fixed effects of the model included baseline age, LAM, time and the interaction between LAM and time.

Results: A total of 509 cases were screened and 183 patients was diagnosed as tuberous sclerosis complex. Finally 102 patients with CT images were included for analysis. The mean age was 34.9 ± 13.4 . Sixty four patients were female. TSC1 mutation was found in 12 patients and TSC2 mutation in 68 patients. The association between TSC-LAM & MMPH and TSC1&TSC2 mutations were listed in the table. The trend of FEV1 in all patients was showed in the Figure. There was no difference in FEV1 between patients with MMPH and no MMPH (92.3 ± 13.8 vs 91.2 ± 15.1). The linear mixed-effects model showed LAM was significant associated with the annual decline of FEV1 ($P = 0.05$).

Conclusion: In this Taiwanese cohort, LAM and MMPH mostly occurs among patients with TSC2 mutations. There was no difference in FEV1 decline between patient with MMPH or not. LAM was significant associated with the annual decline of FEV1.

	LAM(n=44)	MMPH(n=63)	LAM+MMPH(n=18)
Gender, female	42(95%)	41(65.1%)	18(100%)
Age	41.3 ± 13.7	37.8 ± 12.9	43.6 ± 12.0
TSC1 mutation	2 (4.5%)	10 (15.9%)	1 (5.6%)
TSC2 mutation	26 (59.1%)	42 (66.7%)	14 (77.8%)
unclassifiable	12 (27.3%)	7 (11.1%)	3 (16.7%)



AO085

MORPHOLOGICAL ANALYSIS OF ALVEOLAR MACROPHAGE IN PATIENTS WITH SARCOIDOSIS: LET'S REFLECT THE CELL ON A BRONCHOALVEOLAR FLUID SPECIMEN-PART 2.

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Background and Aims: It has been known that the cell count and fraction of bronchoalveolar lavage fluid: BALF specimen is useful to diagnose as interstitial lung disease including sarcoidosis. We have a hypothesis that alveolar macrophage: AM on BALF in sarcoidosis has the characteristic cell form because sarcoidosis is disease constitute granuloma due to epithelial cells.

Aim of this study is to determine the characteristic cell form of AM in sarcoidosis.

Methods: Fifteen cases of sarcoidosis were enrolled in this study. We analyzed the cell area, nuclear area, and NC ratio of AM on BALF specimen by digital microscope. Primary endpoint was a comparison of those findings in between sarcoidosis and healthy volunteer ($n = 5$). Also, we compared with those in pulmonary alveolar proteinosis: PAP ($n = 10$). Secondary endpoints were to investigate the following findings of AM on BALF in sarcoidosis: deviation of nuclear, chromatin hyperplasia of nuclear, phagosome, and ruffling.

Results: Median cell area and nuclear area of AM in sarcoidosis was 335 and 90 μm^2 , respectively. These findings were significant larger than those of healthy volunteer (90 and 26 μm^2 , respectively). They were as same as those of PAP (315 and 53 μm^2 , respectively). Although NC ratio of AM in sarcoidosis was as same as those of healthy volunteer, they were larger than those of PAP. Also, the following findings: chromatin hyperplasia of nuclear, phagosome, and ruffling were associated with the growth of cell size.

Conclusion: AM form in sarcoidosis was clearly difference from healthy volunteer. As compared with healthy volunteer, both cell area and nuclear area of AM increased in sarcoidosis. It suggested the above findings were caused by the increase of bubble appearance in nuclear and cytoplasm. Also, it is interesting the large AM tends to have the ruffling of cell surface. This result might be important finding to evaluate the activity in sarcoidosis in the future.

AO086

EXOSOMES-DERIVED FROM MACROPHAGES TREATED WITH ANGIOTENSIN II PROMOTE LUNG FIBROSIS VIA ACTIVATING TGF- β /SMAD2/3 PATHWAY BY SHIFTING RAS TO ACE/ANGII/AT1R AXIS

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Background and Aims: We hypothesized that AngII stimulated macrophages-released exosomes containing AT1R promoted collagen production and pulmonary fibrosis via activating AngII/AT1R axis.

Methods: In vivo, we established three animal models. The first model was treated with BLM and then was sacrificed at Day3, Day7, Day14, Day28, respectively. The second model was treated with GW4869, an exosomes inhibitor, after receiving BLM; The third model was treated with irbesartan, an AT1R inhibitor, along with exosomes injection once a week. In vitro, fibroblasts were pretreated with irbesartan before exposure to exosomes or AngII.

Results: In vivo, Macrophages were significantly increased in lung tissue and BALF during pulmonary fibrosis. GW4869 markedly attenuated BLM-induced pulmonary fibrosis with decreased AngII/AT1R levels. Exosomes promoted pulmonary fibrosis along with AngII/AT1R axis activation, which can be reversed by irbesartan. In vitro, AT1R containing exosomes-derived from macrophages treated with AngII activated TGF- β /Smad2/3 pathway and stimulated collagen product via upregulating AngII/AT1R axis. In turn, the increased AngII promoted the secretion of macrophage exosomes.

Conclusion: AT1R transported by exosomes-derived from macrophages treated with AngII initiated pulmonary fibrosis and activation of fibroblasts via up-regulating AngII/AT1R axis.

Respiratory Neurobiology and Sleep

AO087

CPAP PRESSURE IS ASSOCIATED WITH EFFECT OF MANDIBULAR ADVANCEMENT DEVICE FOR TREATING TREATMENT-NAÏVE PATIENTS WITH OSA

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Background and Aims: Continuous positive airway pressure (CPAP) is the standard treatment for obstructive sleep apnea (OSA) and mandibular advancement device (MAD) is an alternative. Recently, 4 studies showed the CPAP pressure could predict the MAD effect on reduction of apnea-hypopnea index (AHI). However, the cutoff of CPAP pressure, participants races and prior CPAP treatment was inconsistent across studies. Hence, this study aimed to investigate the association between CPAP pressure and the MAD effect in Taiwanese OSA patients who were treatment-naïve.

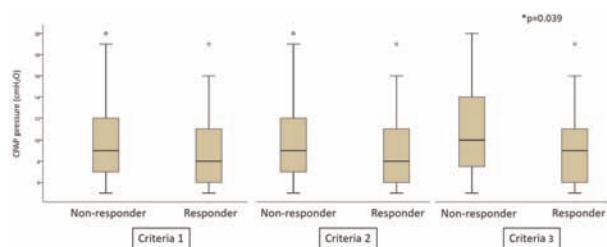
Methods: This retrospective study was conducted by reviewing medical records. Adult patients with OSA (AHI $\geq 10/\text{h}$), who were treatment-naïve and underwent CPAP titration were eligible. Those who refused CPAP treatment and were treated with 12-week MAD were recruited. Success of MAD treatment was classified according to 3 definitions,

namely criteria 1 (residual AHI < 5/h with >50% reduction), criteria 2 (residual AHI < 10/h with >50% reduction) and criteria 3 (reduction > 50%). The logistic regression analysis was applied to identify the association between the CPAP pressure and success of MAD treatment.

Results: Totally 90 patients were included with mean age of 53.8 years/o, BMI of 26.7 kg/m², and AHI of 41.8/h. The CPAP pressure was not associated with the MAD success based on criteria 1 and 2. In contrast, CPAP pressure [adjusted odds ratio 0.823, 95% CI (0.708, 0.958)] and AHI [1.049, (1.011, 1.089)] and waist circumference [0.937, (0.877–1.002)] was independently associated with criteria 3 MAD success which gave the AUROC 0.754 (95% CI 0.643–0.865). The best cutoff of CPAP pressure was 15 cm H₂O with sensitivity of 92.5, specificity of 26.1, likelihood ratio positive of 1.25, and likelihood ratio negative of 0.29.

Conclusion: The CPAP pressure < 15 cmH₂O was associated with AHI reduction >50% with MAD treatment in Taiwanese treatment-naïve OSA patients.

Acknowledgement: The work was supported by grants from National Taiwan University Hospital (NTUH 107-19), and 'Center for electronics technology integration (NTU-107L900502)' from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan, and NTU-NTUH-MediaTek Innovative Medical Electronics Research Center



AO088

RELATIONSHIP BETWEEN OBSTRUCTIVE SLEEP APNOEA, OTHER CARDIOVASCULAR RISK FACTORS AND CARDIOVASCULAR DISEASE

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Background and Aims: Data on the interaction of cardiovascular disease (CVD) risk factors and obstructive sleep apnea (OSA) in the pathogenesis of CVD are limited. We examined the cross-sectional associations and interactions between OSA, CVD risk factors and CVD in a large sleep clinic cohort.

Methods: Data from 4,100 consecutive patients who had in-laboratory polysomnography (PSG) at the Western Australian Sleep Disorders Research Institute between 2005–2010 (age 50.6 ± 14.1 years, 60.7% male) were analysed. The outcome was self-reported CVD (composite of heart failure, coronary and cerebrovascular disease) at presentation. We determined the odds ratio (OR) of CVD between patients with and without severe OSA [apnea-hypopnea index (AHI)>30 vs AHI < 30]. To assess the interaction between OSA and CVD risk factors (hypertension, diabetes and dyslipidaemia), ORs of CVD for patients with AHI < 30 with (+) the risk factor, AHI>30 without (-) the risk factor, and AHI>30+the risk factor were referenced to patients with AHI < 30-the risk factor.

Results: The OR for CVD in patients with severe OSA was 1.44 (95%CI 1.17–1.78, *P* = 0.0006). In the absence of severe OSA, each risk factor increased the OR for CVD (see Table). Compared to patients without severe OSA, those with severe OSA had greater CVD risk when there was co-existing hypertension, but not with co-existing diabetes or dyslipidemia.

Conclusion: The crude ORs for CVD are increased in patients with severe OSA and patients with CVD risk factors. Severe OSA amplified this risk in patients with hypertension, but not diabetes or dyslipidaemia. The influence of other co-variables will be modelled.

ORs (95%CI) of CVD

RISK CATEGORIES	Risk factor		
	Hypertension	Diabetes	Dyslipidemia
AHI>30+risk factor	3.15* [^] (2.38-4.18)	3.31* (2.40-4.57)	2.91* (2.15-3.92)
AHI>30-risk factor	1.17 (0.81-1.68)	1.63# (1.27-2.10)	1.71# (1.27-2.31)
AHI<30+risk factor	2.28* (1.68-3.09)	3.55* (2.52-4.99)	2.33* (1.72-3.17)
AHI<30-risk factor (Reference)	1.0	1.0	1.0

**p*<0.0001 & #*p*<0.001 c.f. reference

[^]*p*<0.05 c.f. AHI<30+risk factor

AO090

NON-APNOEA SLEEP DISORDER INCREASES THE RISK OF INCIDENT HEART FAILURE-A NATIONWIDE POPULATION-BASED COHORT STUDY

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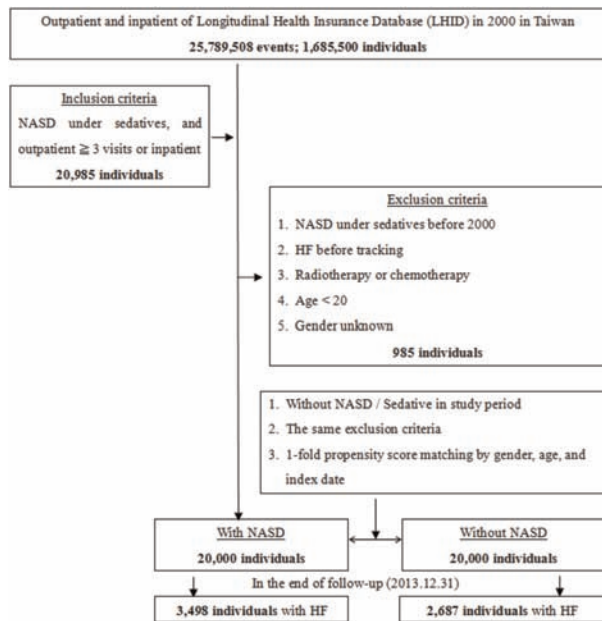
¹Tri-Service General Hospital, National Defense Medical Center, Taiwan

Background and Aims: Non-apnoea sleep disorder (NASD) increases the risk of cardiovascular events, such as hypertension and ischemic heart disease (IHD). Patients with heart failure (HF) are at higher risk for sleep disorder; however, there is no documentation on NASD's association with HF to date. Therefore, our study aimed to determine whether NASD increases the risk of incident HF.

Methods: Using the outpatient and inpatient data from Taiwan's Longitudinal Health Insurance Database, we conducted a nationwide cohort study of patients with a first-time diagnosis of NASD in the year 2000 and followed up the risk of incident heart failure until December 31, 2013. We calculated risks and incidence ratios of HF for patients with NASD compared with the general population. The cumulative incidence of NASD and the subsequent risk of HF are assessed by the Kaplan-Meier method and Cox regression using a matched comparison cohort of HF patients without NASD.

Results: The NASD cohort had an adjusted hazard ratio (HR) of incident HF 23.6% higher than that of the cohort without NASD (95% CI = 1.164–1.308; *P* < 0.001). In the NASD population, the mean interval to HF in males and females were 5.02 ± 3.65 years and 5.02 ± 3.70 years, respectively. The Kaplan-Meier analysis indicated that after the seventh year, the incidence of HF was higher in the NASD cohort than in the control cohort till the end of the follow up.

Conclusion: Our study demonstrates that NASD patients are at a higher risk of incident HF.



AO091

DOES CHRONIC INTERMITTENT HYPOXIA ALWAYS INCREASE BLOOD GLUCOSE LEVELS IN MICE?

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Background and Aims: Intermittent hypoxia (IH), one of the important pathophysiological components in sleep apnea, has been reported to increase blood glucose levels (BG) in animals (e.g., Obesity 2011;19:2167), although such findings have not consistently emerged across investigational groups. In addition, obstructive sleep apnea syndrome (OSAS) has been reported to be independently associated with insulin resistance (Am J Respir Crit Care Med 2002;165:670). To better understand the glycemic effect of IH, we evaluated the effect of two modalities of IH on BG levels in mice.

Methods: We exposed C57BL/6J male mice (4–5 week old) to either 12 h/day of mild IH (IHM, alternating F₁O₂-10–11% and normoxia (F₁O₂-21%) with 640 s total cycle duration, or 12 h/day of severe IH (IHS, alternating F₁O₂-6–7% and normoxia, 180 s cycle duration) or sham IH (SIH) every day for 8 weeks (*n* = 7/group, respectively). After IH (or SIH) exposures, all mice were kept under usual normoxic conditions for 5 weeks and BG levels were measured at around 7 PM.

Results: BG of SIH controls were 222 ± 23 mg/dl, while in IHM the BG concentrations were 186 ± 21 mg/dl and were significantly lower than SIH (*P* = 0.024). Similarly, BG levels of IHS were 190 ± 36 mg/dl and were also significantly lower than the levels found in SIH-exposed mice (*P* = 0.041).

Conclusion: Thus, chronic IH exposures mimicking different severities of sleep apnea do not consistently increase BG in mice.

AO092

DECREASED MIR-21-5P AND MIR-23-3P EXPRESSIONS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: A POTENTIAL PROTECTIVE EFFECT BY REGULATING TNF-ALPHA SIGNALING

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Background and Aims: The purpose of this study is to explore the anti-inflammatory role of microRNAs (miR)-21/23/146a/150/155 targeting the toll-like receptor pathway in response to chronic intermittent hypoxia with re-oxygenation (IHR) injury in patients with obstructive sleep apnea (OSA).

Methods: Gene expression levels of the five miRs, TLR2/4/6, and their down-stream mediators were assessed by quantitative RT-PCR method in peripheral blood mononuclear cells from 40 severe OSA patients and 20 matched subjects with primary snoring (PS). Human monocytic cell line THP-1 was induced to undergo apoptosis/necrosis with 7 cycles of IHR per day for 4 days versus continuous normoxic (NOX) condition.

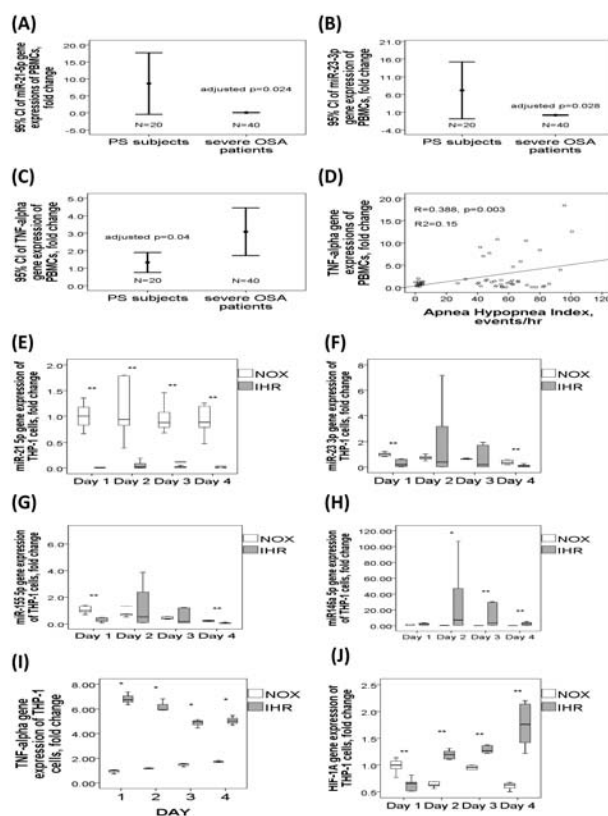
Results: Gene expression levels of miR-21-5p (adjusted *P* = 0.024) and miR-23-3p (adjusted *P* = 0.028) were significantly decreased in treatment-naïve OSA patients as compared with that in PS subjects, while TNF-α gene expression (adjusted *P* = 0.04) was significantly increased. Gene expression levels of both miR-21-5p, and miR-23-3p were negatively correlated with apnea hypopnea index (*r* = −.478, *P* < 0.001; *r* = −.446, *P* = 0.001) and oxygen desaturation index (*r* = −.45, *P* = 0.001; *r* = −.421, *P* = 0.001), while TNF-α gene expression was positively correlated with apnea hypopnea index (*r* = 0.388, *P* = 0.003). In vitro IHR treatment result in a significant decrease of miR-21-5p, miR-23-3p, and miR-155-5p gene expressions as compared with normoxic condition, but a significant increase of miR-146b-5p, TLR2, TLR6, TNF-α, HIF-1α, and HIF-2α gene expressions (all *P* values < 0.05). Both miR-21-5p and miR-23-3p gene expressions were negatively correlated with gene expressions of TLR2, TNF-α, and HIF-2α, and positively correlated with miR-155-5p gene expression. MiR-146a-5p gene expression was positively correlated with both TLR6 and HIF-1α gene expressions.

Conclusion: MiR-21-5p and miR-23-3p were down-regulated both in severe OSA patients and with in vitro IHR stimuli, while TNF-α was up-regulated. These findings provide biological insight into mechanisms by which IHR-suppressed miRs potentiate cell apoptosis and inflammation, and indicate that overexpression of the miR-21/miR-23 could represent a potential therapy for OSA.

Table 1. Demographic, biochemistry, and sleep data of all the 60 study participants

PS= primary snoring; HS= healthy subjects (non-snorers); BMI= body mass index; AHI= apnea hypopnea index; ODI= oxygen desaturation index; SaO₂= arterial oxyhemoglobin saturation; ESS= Epworth Sleepiness Scale; EDS= excessive daytime sleepiness; CKD= chronic kidney disease

	PS subjects (n=20)	Severe patients (n=40)	OSA p value
Age, years	44.6±14.3	47.6±11	0.392
Male Sex, n (%)	14 (73.7)	3 (82.5)	0.432
BMI, kg/m ²	25±3.1	25.9±2.7	0.262
AHI, events/hour	2.8±1.6	60.7±11.3	<0.001
ODI, events/hour	1.1±0.9	48.9±22.7	<0.001
Mean SaO ₂ , %	96.2±1.3	93.3±2.8	<0.001
Minimum SaO ₂ , %	89.2±3.5	70±12.6	<0.001
Snoring index, counts/hour	114±141	331±145	<0.001
ESS	8.5±4.5	11.6±5.2	0.034
EDS, n (%)	5 (25)	21 (53.8)	0.048
Smoking history, n (%)	3 (16.7)	15 (39.5)	0.208
Cholesterol, mg/dl	189.5±65	192.6±32.3	0.822
Triglycerides, mg/dl	155.3±224.9	149.9±77.8	0.893
Hypertension, n (%)	5 (25)	16 (40)	0.305
Diabetes mellitus, n (%)	1 (5.3)	4 (10)	0.542
Heart disease, n (%)	3 (15.8)	2 (5)	0.164
Stroke, n (%)	1 (5)	0	0.143
CKD, n (%)	1 (5)	1 (2.5)	0.584



PRENATAL CHRONIC INTERMITTENT HYPOXIA LEADS TO EARLY ATHEROSCLEROTIC LESIONS AND UPREGULATES CAVEOLIN-1 EXPRESSION IN RATS

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Background and Aims: Chronic intermittent hypoxia (CIH) has been associated with atherosclerotic lesions. However, whether prenatal exposure to CIH causes atherosclerosis after birth is unclear. The role of Caveolin-1 in the development of atherosclerosis remains controversial. The purpose of this study was to investigate the effects of prenatal and postnatal CIH exposure on the development of atherosclerotic lesions in adult rats, along with the potential role of Caveolin-1 during the process.

Methods: Sprague-Dawley rats were divided into four groups ($n = 8$): prenatal normoxia and postnatal normoxia (control group), prenatal CIH and postnatal normoxia, prenatal CIH and postnatal CIH, prenatal normoxia and postnatal CIH. Morphological changes of the aorta were examined by light microscopy. The protein expression of NF- κ B p65 and Caveolin-1 in the aorta was determined by western blot analysis.

Results: Prenatal CIH caused early atherosclerotic lesions and a significant thickening of the intima ($P < 0.001$). The expression of NF- κ Bp65 and Caveolin-1 was significantly increased in the CIH groups ($P < 0.01$). Prenatal CIH and postnatal CIH had synergistic effects on the thickening of the intima ($P < 0.05$), as well as the protein expression of NF- κ B p65 and Caveolin-1 ($P < 0.01$).

Conclusion: These results indicate that prenatal CIH exposure leads to early atherosclerotic changes and upregulates Caveolin-1 expression in the aorta in adult rats. In addition, prenatal CIH enhances postnatal CIH-induced formation of atherosclerotic lesions. These effects are likely mediated by increased oxidative stress caused by CIH, which activates the NF- κ B p65 signaling pathway and subsequent Caveolin-1 expression.

UPPER AIRWAY IMAGING DURING A NOVEL INTRA-ORAL NEGATIVE PRESSURE DEVICE THERAPY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Background and Aims: Obstructive sleep apnea (OSA) is characterized by periodic narrowing or obstruction of the upper airway when people sleep. Continuous positive airway pressure (CPAP) is the leading therapy for those symptomatic patients. For non-CPAP therapies, there is a novel tongue and soft palate retaining device through a negative pressure, iNAP[®] Sleep Therapy System. The aim of the study was to explore the anatomical mechanism of this intra-oral negative pressure device in treating adults with OSA.

Methods: This is a prospective, single center study. Subjects with OSA (apnea-hypopnea index, AHI, ≥ 5 /h), were enrolled. Those who were responders with the negative pressure device (treated AHI < 20 /h and AHI reduced $\geq 50\%$ from baseline) would undergo physical examinations with oral, nasal, and oropharyngeal check-up, followed by Müller maneuver and cephalometry studies. In addition, magnetic resonance imaging (MRI) would be done to precisely characterize the changes of upper airway when they used the new device, the iNAP[®] Sleep Therapy System (Somnics Inc., Hsinchu, Taiwan).

Results: At the supine position, the intra-oral negative pressure therapy significantly increased the size of the retro-palatal airway by moving

the soft palate anteriorly, and maintained the patency of the retro-glossal airway by setting the tongue forward. By using the real-time MRI method, the images revealed the soft tissue (soft palate and tongue) swung during breathing was significantly reduced by the device.

Conclusion: In those who responded to the intra-oral negative pressure therapy, the soft palate and tongue were moved forward (increased the size of the oropharyngeal airway) and set stable (prevented collapsed soft palate and dropped tongue), resulting in successfully diminished the apnea-hypopnea events.

Clinical Respiratory Medicine 2

AO095

LUNG INFLAMMATION, EMPHYSEMA, AND LUNG CANCER DEVELOPMENT IN A/J MICE IN RESPONSE TO CHRONIC EXPOSURE TO AEROSOL FROM A HEATED TOBACCO PRODUCT AND CIGARETTE SMOKE

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Background and Aims: Chronic exposure to cigarette smoke is the leading cause of chronic obstructive pulmonary disease and lung cancer. The A/J mouse model was used to evaluate lung inflammation, emphysema, and the underlying molecular changes upon lifetime exposure to cigarette mainstream smoke (CS) from the 3R4F reference cigarette or to aerosol from the Tobacco Heating System (THS) 2.2, a candidate modified risk tobacco product, at three concentrations.

Methods: A/J mice were exposed for 6 h per day, five days per week, for up to 18 months. Quantification of pulmonary inflammation, assessment of matrix metalloproteinase (MMP) activity in bronchioalveolar lavage fluid (BALF), lung function tests, lung morphometric assessments by stereological approach, histopathological evaluation, targeted proteomic analysis of BALF, transcriptome and proteome analysis of the lungs, and assessment of lung neoplastic changes were performed at selected interim and terminal dissections.

Results: Exposure to CS resulted in pulmonary inflammation, increased MMP activity, altered lung function, enlargement of distal airspaces in the lungs, and molecular changes, all indicative of emphysema. Only minimal effects on the lungs were observed following THS 2.2 aerosol exposure that were independent of THS 2.2 aerosol concentrations and exposure duration. Biological network analysis identified perturbed molecular processes that are consistent with CS exposure, but only minor perturbations of cell stress responses were noted following THS 2.2 aerosol exposure. At the terminal dissection time point, the incidence and multiplicity of bronchioalveolar adenomas and carcinomas was higher after CS exposure, but not in THS 2.2-exposed mice.

Conclusion: In summary, lung inflammation, emphysematous changes, molecular perturbations, and lung cancer were significantly lower in mice exposed to aerosol from THS 2.2 as compared with CS exposure.

AUTOMATED ALERTING AND DECISION SUPPORT FOR REPORTING OF PHYSIOLOGIC DETERIORATION VIA A CLINICAL ALERTING SYSTEM IN PATIENTS WITH PNEUMONIA ADMITTED TO THE GENERAL WARDS

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Background and Aims: For the risk of clinical deterioration pneumonia patients admitted to the general wards, earlier identification of physiologic abnormalities with timely aggressive management might provide chances of preventing serious critical illness and achieving better outcomes.

Methods: Between January 2017 and April 2018, the patients admitted to the general wards to receive antibiotics for pneumonia were retrospectively analyzed for the records of automated alerting, decision supporting, and reporting for their physiologic deterioration from the institutional Clinical Alerting System (CAS) database. Comparisons were made for cases with and without CAS alerting and reporting regarding the clinical outcomes.

Results: During the study periods, there were 3,448 cases of adult patients who received antibiotic treatment on admission to the general wards for pneumonia. Of the patients, 49.1% had malignancy, 21.0% had chronic airway-pulmonary conditions, and 18.6% had a stroke; 244 (7.1%) had at least one CAS alerting within 7 days of admission, 1,171 (34.0%) had at least one CAS reporting, and 223 (6.5%) had both. Of the first CAS alerting, 65.2% were followed by CAS reporting within 48 h. Cases with CAS alerting within 7 days had a higher rate of unplanned ICU transfer than those without (22.5% vs 4.7%, $P < 0.001$). Those with CAS reporting within 7 days also had a higher rate of unplanned ICU transfer than those without (11.0% vs 3.3%, $P < 0.001$). The overall in-hospital mortality rate was 18.9%; patients with CAS alerting (35.2% vs 17.7%, $P < 0.001$) and reporting (32.3% vs 12.0%, $P < 0.001$) also had higher in-hospital mortality rates than those without alerting or reporting.

Conclusion: Early physiologic deterioration within seven days of admission is associated with a higher risk of a poor outcome for patients with pneumonia admitted to the general wards. Adequate planning on patient deposition at the emergency room and early aggressive patient management after admission to the general ward is warranted.

AO097

FIRST SUCCESSFUL CASE OF CHEMICAL PLEURODESIS WITH OXYTETRACYCLINE THROUGH ROCKET® PLEURAL VENT™ - AMBULATORY PNEUMOTHORAX DEVICE FOR PNEUMOTHORAX

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Background and Aims: To report the first successful case of chemical pleurodesis through Rocket® Pleural Vent™ for pneumothorax.

Methods: A 79-year-old lady with asthma and idiopathic pulmonary fibrosis was admitted for a first episode right apical secondary spontaneous pneumothorax measuring 1.3cm in apico-cupolar distance. Due to a lack of pleural separation inside the safety triangle, Rocket® Pleural Vent™ was chosen and inserted at second intercostal space, mid-clavicular line instead. The lung fully re-expanded the next day, and chemical pleurodesis with oxytetracycline was performed with success.

There is no recurrence of pneumothorax and the patient is discharged 2 days afterwards.

Results: Rocket® Pleural Vent™ is designed for treatment of spontaneous, iatrogenic or traumatic simple pneumothorax. It consists of an 8F pigtail catheter mounted together with a heimlich valve in a T-shape configuration. It was proven to be effective and well tolerated for the ambulatory management of pneumothorax. This device provides more patient comfort as its insertion only requires a small incision and the whole device is small & lightweight. It allows full patient mobility as connection to underwater seal is unnecessary. This is especially attractive in loculated pneumothorax where conventional intercostal drain insertion can be technically challenging.

The T-shape arrangement in Rocket® Pleural Vent™, as opposed to a conventional heimlich valve, allows injection of therapeutic agents as well as connection to suction. Based on the above 2 factors, chemical pleurodesis can be attempted through this device. This is the first reported case of successful chemical pleurodesis through Rocket® Pleural Vent™ for pneumothorax, which may revolutionize the management of pneumothorax, especially secondary spontaneous pneumothorax which is indicated for pleurodesis after lung re-expansion.

Conclusion: Chemical pleurodesis through Rocket® Pleural Vent™ is a safe and feasible option for pneumothorax.

AO098

SOUND-SPECTROGRAM WILL BE USEFUL IN THE DIFFERENTIAL DIAGNOSIS OF WHEEZES: BRONCHOSPASM OR FIXED AIRWAYS NARROWING?

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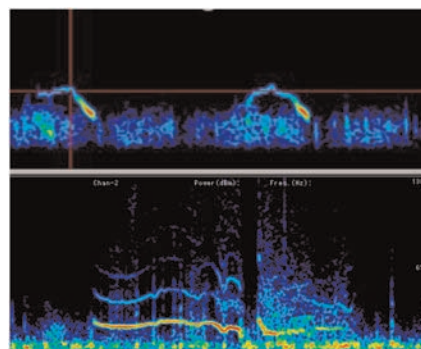
¹Rakuwakai Otowa Hospital, Japan

Background and Aims: Wheeze is a typical clinical sign of asthmatic fit. However, wheezes are also heard in patients with fixed airway stenosis caused by lung cancer, bronchial tuberculosis and others. They are likely to be confused with asthma. It is difficult to estimate the source of wheezes by auscultation alone, but this will be possible by using lung sound analysis.

Methods: We analyzed wheezes by a sound spectrometer (Kenzo Medico, LSA 2012). In sound spectrogram, frequencies are shown increasing up the vertical axis, time on the horizontal axis and the sound power by brightness and colour. Wheezes are recognized as rather horizontal bright lines. (Figure) When the wheeze contains harmonic components, we focused the shape of fundamental tone. When wheezes contain only one form of wheeze band (include harmonics), they were termed as monophonic wheezes. When there were more than two forms of frequency bands, they were termed as polyphonic wheezes. We recorded and analyzed wheezes from ten patients with bronchial asthma and ten patients with fixed airway narrowing.

Results: Wheezes of patients with asthma showed umbrella shaped bright lines visualizing fluctuation of wheeze frequency. (Figure, upper panel, two expiration-inspiration cycles) Polyphonic wheezes were recognized in patients with asthma. Wheezes from patients with fixed airway narrowing showed rather flat shape and monophonic (Figure, lower panel, one expiration-inspiration cycle, fundamental wheeze tone is the lowest bright line) in most cases. These wheeze sound changes were easy to find on the sound spectrogram but were difficult to recognize by auscultation alone.

Conclusion: The sound spectrogram is a useful tool to estimate the source of wheezes and to differentiate wheezes from asthma or fixed airways narrowing.



AO099

CLINICAL CHARACTERISTICS OF CHRONIC COUGH: ADULT CHRONIC COUGH COHORT STUDY OF SOUTH KOREA

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Background and Aims: Cough is basic defensive mechanism to protect human airway. Chronic cough is defined as cough more than 8 weeks in many adults cough guidelines. Clinical characteristics are different by country, ages, and ethnicity. In this study, we set multi-centre, prospective, and observational cohort study to evaluate clinical characteristics of chronic cough of South Korea.

Methods: Total 19 university hospitals were joined. Participants were recruited from 1st March 2016 to 28th February 2018. Older than 18 year-old was included. Participants were excluded who had active or chronic respiratory disease. Smoker, pregnancy, and angiotensin-converting enzyme inhibitor user were excluded. Treatments were done by following treatment algorithm of Korean Association of Tuberculosis and Respiratory Disease (KATRD) cough guideline 2014. Outcomes were evaluated at 1st week and 4th week of treatment. Treatment response was measured by changing of cough numeric rating scale (NRS). Lowering more than 50% of initial cough NRS and decrease of 4 or more cough NRS were defined good response outcome. Paired *t*-test and Pearson's Chi-square test were used to evaluate statistical difference and risks.

Results: Total 431 participants were enrolled. Clinical characteristics of cohort study was shown in Table 1. Upper airway coughing syndrome (UACS) and cough variant asthma (CV asthma) were top two cause of chronic cough (54.1% and 47.6% each). Gastro-oesophageal reflux (GERD) and eosinophilic bronchitis (EB) were followed (14.0% and 8.0% each). Overall response after 4 weeks treatment was 70.8%. Allergic skin test (66.1%) and immunoglobulin E (64.6%) were mostly used as additional tests.

Conclusion: UACS and CV asthma were most common cause of chronic cough in South Korea. Management according to KATRD guideline showed good response outcome (70.8%). In this study, we defined clinical characteristics of chronic cough and showed efficiency of KATRD cough guideline 2014.

Baseline Characteristics (n=431)	
Age, year	49.40±15.45
Sex, male (n, %)	106 (24.8%)
Duration, week	63.49 ± 175.36
Initial cough NRS	5.34±1.63
NRS after 1 week	2.60±1.87
NRS after 4 weeks	1.21±1.38
Response after 1 week	235 (54.5%)
Response after 4 weeks	305 (70.8%)

AO100

A COMPARATIVE STUDY ON THE DIAPHRAGM MUSCLE THICKNESS AND RAPID SHALLOW BREATHING INDEX (RSBI) AS A PREDICTOR FOR SUCCESSFUL EXTUBATION AMONG CRITICALLY ILL ADULT PATIENTS

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Background and Aims: Several indexes that has been used in clinical practice to assess the patient's ability to recover spontaneous breathing has shown limitations and disadvantages. The rapid shallow breathing index (RSBI) was found to be one of the most accurate predictors but values of sensitivity and specificity for the suggested threshold were highly variable in different studies. Bedside ultrasonography, which is already crucial in several aspects of management for critically ill patients, has been recently proposed as a simple, inexpensive, non-invasive and readily available and reproducible method of quantification of diaphragmatic contractile activity.

Methods: All intubated patients admitted at the critical care units of St. Luke's Medical Center were assessed every day for readiness to be weaned from assisted mechanical ventilator. All patients who met the criteria for readiness to wean were included in the study. Patients underwent ultrasound of the diaphragm muscle to measure its thickness and spontaneous breathing parameters (SBP) to measure rapid shallow breathing index (RSBI). Patients were followed through weaning until successfully extubated from assisted mechanical ventilation, regardless of the ultrasound and RSBI result.

Results: ROC curve analysis of RSBI resulted in an area under the curve of 0.587, suggesting that RSBI is not a significant predictor for successful extubation ($P = 0.6262$). ROC curve analysis determined >3.2 mm as the best cut-off score for diaphragm muscle thickness on inspiratory phase [DTM (Insp)]. Moreover, resulting area under the curve of 0.707 indicates that DTM (Insp) can significantly predict successful extubation with a sensitivity of 73.3% and a specificity of 80%.

Conclusion: This study found that in ICU patients who have met the criteria for weaning, a diaphragm muscle thickness of >3.2 mm can be a predictor of successful weaning. Based on outcome measure comparison done, diaphragm muscle thickness can successfully predict success in weaning as much as RSBI can.

QUALITY CHANGES OF CLINICAL PRACTICE GUIDELINES FOR RESPIRATORY DISEASES IN CHINA: A SYSTEMATIC APPRAISAL

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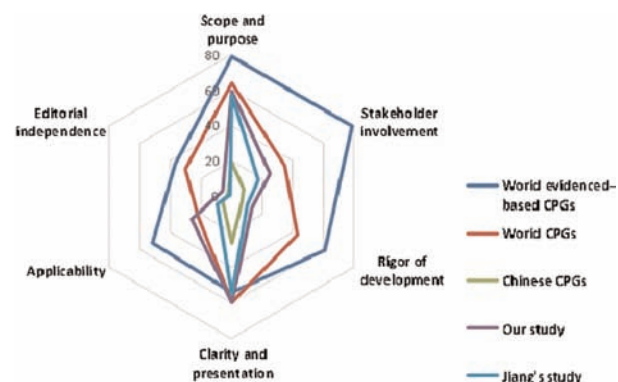
Background and Aims: Jiang et al reported the low quality of Chinese clinical practice guidelines (CPGs) for respiratory diseases. But the publication of CPGs for respiratory diseases in China is increasing significantly in 2013–2017 and the quality and potential impact is unknown. We are to evaluate the quality of these Chinese CPGs published in 2013–2017 by using the Appraisal of Guidelines for Research and Evaluation instrument II (AGREE II) and provide methodological reference for the formulation and updating of future CPGs.

Methods: We searched the CPGs for chronic respiratory diseases published in 2013–2017 by retrieving four Chinese databases (the WANFANG database [WANFANG], the Chinese National Knowledge Infrastructure [CNKI], the VIP database [VIP] and the Chinese Biomedical Literature database [CBM]). Four reviewers assessed the relevant CPGs independently by using AGREE II. Assess the overall assessment consistency among reviewers by using the Intra-class Correlation Coefficient (ICC).

TABLE 2] AGREE II Scores of the Guidelines

Domain	Mean, Range (%) Before 2013	Mean, Range (%) After 2013
Scope and purpose	57.3 (4.2–80.6)	58.9 (40.3–80.6)
Stakeholder involvement	17.6 (0.0–62.8)	25.2 (5.6–62.5)
Rigor of development	10.2 (2.6–70.3)	13.2 (3.1–59.9)
Clarity and presentation	55.2 (5.6–83.3)	60.3 (6.1–84.7)
Applicability	9.3 (0.0–37.5)	25.8 (9.4–58.3)
Editorial independence	1.1 (0.0–50.0)	5.9 (0.0–97.9)

AGREE=Appraisal of Guidelines for Research and Evaluation.



Results: One hundred and forty-two guidelines published in 49 medical journals from 2013 to 2017 were identified and evaluated. The overall agreement among reviewers was considered to be consistent (ICC, 0.810; 95% CI, 0.801–0.819). The scores of the six AGREE domains are relatively low: scope and purpose (mean, 59.1%; range, 4.2%–80.5%), stakeholder involvement (mean, 25.3%; range, 2.8%–54.2%), rigor of development (mean, 13.8%; range, 0%–27.1%), clarity and presentation (mean, 58.8%; range, 22.2%–80.6%), applicability (mean, 26.1%; range, 0%–22.9%) and editorial independence (mean, 6.2%; range, 0%–16.7%). Only 2 guidelines (1.4%) were strongly recommended for clinical practice.

Conclusion: The overall quality of the guidelines for respiratory diseases in China from 2013 to 2017 is low but slightly higher than previous CPGs from 1987 to 2013. The quality of CPGs can be improved,

especially in the domains of Rigor of development, Applicability and Editorial independence. Most guidelines were based on low-quality evidence. There was an urgent need for high-quality clinical studies to provide evidence for CPGs.

AO102

CLINICAL PATHWAY AND DURATION OF HOSPITALIZATION IN PATIENTS WITH ACUTE EXACERBATION OF BRONCHIECTASIS

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Background and Aims: Acute exacerbations of bronchiectasis impose significant morbidity on patients, and contribute to a large burden in healthcare costs. Length of hospitalization stay (LOS) is an important component of this cost. Clinical pathways (CP) have been shown to be effective in reducing LOS in other respiratory conditions such as chronic obstructive pulmonary disease and asthma. However, CP has not been established to optimise outcomes in bronchiectasis. The objective of this study was to determine the effect of implementing CP on the management of patients with acute exacerbations of bronchiectasis.

Methods: A retrospective analysis on all adult patients admitted with acute exacerbations of bronchiectasis between 2015 and 2017 was conducted. Demography, LOS, and co-morbidities were established. Patients were divided into (1) CP group, and (2) non-CP group. The primary endpoint was LOS, and the secondary endpoint was the event rate of recurrent hospitalisation with bronchiectasis exacerbation within 30 days of discharge.

Results: A total of 594 patients were identified with 242 patients in CP group and 352 patients in non-CP group. Age, gender, body mass index, smoking history and sputum microbiology were similar in both groups. The median (IQR) LOS was significantly shorter in CP than non-CP (5.5 (4–7) days versus 6 (4–8) days, $P = 0.028$). There was no significant difference on 30 days readmission rate ($P = 0.2$), and time to readmission ($P = 0.5$).

Conclusion: Our study demonstrated that implementation of a CP specifically designed for patients with acute exacerbations of bronchiectasis had the potential of reducing hospital LOS.

Bronchoscopy and Interventional Techniques 2

AO103

THE PROGNOSTIC PREDICTORS OF PATIENTS WITH AIRWAY INVOLVEMENT DUE TO ADVANCED OESOPHAGEAL CANCER AFTER METALLIC AIRWAY STENTING USING FLEXIBLE BRONCHOSCOPY

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Background and Aims: Advanced oesophageal cancer patients with airway involvement had poor prognosis. Self-expandable metallic stents (SEMSs) implantation via bronchoscopy can immediately relieve airway stenosis and offer the opportunity of survival improvement. The purpose of this study was to determine the factors that predict survival in patients with airway involvement due to advanced oesophageal cancer after SEMSs implantation.

Methods: We conducted a retrospective study, from February 2007 to July 2013, in a university hospital. A total 42 advanced oesophageal cancer patients with airway involvement were included during this period. These patients underwent flexible bronchoscopy with electrosurgery and SEMSs implantation under bronchoscopic visualization and local anaesthesia without fluoroscopic guidance throughout the procedure.

Results: The total 42 patients were included in analysis. Acute respiratory failure was found in 14 patients (33.3%). After SEMSs implantation, additional anti-cancer therapy was performed in 28 patients (66.7%). The median survival after procedure was 83 days. Longer survival was seen in subjects with further anti-cancer therapy (HR, 0.146; CI, 0.06–0.34; $P < 0.001$). Persistent pneumonia and poor PFS may be potential factors that make patients without further therapy. Patients with anti-cancer therapy before procedure (HR, 3.429; CI, 1.54–7.60; $P = 0.002$) and acute respiratory failure (HR, 5.224; CI, 2.23–12.26; $P < 0.001$) had poorer survival. Patients with the residual diameters of obstructive trachea < 0.77 cm had high risk of acute respiratory failure.

Conclusion: SEMSs insertion with flexible bronchoscopy provide patients with airway involvement by advanced oesophageal cancer an opportunity of survival improvement. The patients with anti-cancer therapy before procedure and acute respiratory failure had poor prognosis. ARF easily occurred if the residual diameters of obstructive trachea was less than 0.77 cm. On the contrast, available post airway stenting therapy improved these patient's survival.

AO104

A MULTICENTRE, PROSPECTIVE TRIAL OF ELECTROMAGNETIC BRONCHOSCOPIC AND ELECTROMAGNETIC TRANSTHORACIC NAVIGATIONAL APPROACHES FOR THE BIOPSY OF PERIPHERAL PULMONARY NODULES (ALL IN ONE)

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Background and Aims: Pulmonary nodules are a common but difficult issue for physicians as most identified on imaging are benign but those identified early that are cancerous are potentially curable. Multiple diagnostic options are available but each technique has differences in diagnostic yield and complication rates with no established gold standard. With the recent advent of electromagnetic navigation (EMN), a combined bronchoscopic and transthoracic approach is now feasible in a single, staged procedure. Here, we present the study design and initial nodule characteristics for a single-arm trial evaluating a staged approach for the diagnosis of pulmonary nodules. (NCT03338049)

Methods: Participants with 1–3 cm, intermediate to high-risk pulmonary nodules will undergo a staged approach with endobronchial ultrasound (EBUS) followed by EMN-bronchoscopy (ENB), then EMN-transthoracic biopsy (EMN-TTNA) with the procedure terminated at any stage after a diagnosis is made via rapid onsite cytopathology. (Figure 1) We aim to recruit 150 EMN participants from eight academic and community settings in the United States to show significant improvements over other historic bronchoscopic guided techniques. The primary outcome is overall diagnostic yield of the staged approach.

Results: 53 patients have been enrolled since trial initiation began in February 2018 and have undergone a Veran guided EMN procedure. 35

nodules were in the periphery of the lung and amenable to EMN-TTNA as determined a priori by a radiology core laboratory utilizing planning software. Mean nodule size is 1.78 cm with nodules located 2.2 cm from the pleura. There have been no bleeding complications to date. 10 patients (18%) who underwent EMN-TTNA had a pneumothorax of which only 5 (9%) required drainage.

Conclusion: This is the first study designed to evaluate the diagnostic yield of a staged procedure using EBUS, ENB and EMN-TTNA for the diagnosis of pulmonary nodules. If effective, the staged procedure will increase minimally invasive procedural diagnostic yield for pulmonary nodules.

Conclusion: Cryobiopsy has a great potential to break through the diagnostic bronchoscopy for PPLs.

AO106

EVALUATION OF TRANSBRONCHIAL LUNG CRYOBIOPSY FREEZING TIME, CRYOBIOPSY SIZE, HISTOLOGICAL QUALITY AND INCIDENCE OF COMPLICATION:

A PROSPECTIVE CLINICAL TRIAL

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Background and Aims: Transbronchial cryobiopsy (TBCB) is a novel way to obtain large lung biopsies without crush artefact. However, correlation of freezing time with cryobiopsy size and complications has not been evaluated in vivo. The aim of this study is to reveal the correlation between cryobiopsy freezing time and size of cryobiopsy specimens, and evaluate incidence of complications and histological quality of the cryobiopsy specimens in different freezing times.

Methods: Individual cryobiopsies were obtained from patients who had suspected ILD based on clinical information, laboratory tests and HRCT with atypical findings requiring lung biopsy. The freezing time was increased incrementally from 3 to 6s to achieve individual cryobiopsies.

Results: 33 patients were enrolled and 142 transbronchial cryobiopsies were taken in this study. The mean size of the cryobiopsy ranged from 9.2 ± 0.82 to 18.83 ± 1.27 mm². A significant positive correlation between increased freezing times and cryobiopsy sizes was observed in this study, but no statistical difference in diagnostic yield was observed between each group. A significant higher proportion (22.86%) of specimen swelling was observed when the freezing time exceeded 5s. Haemorrhage occurred in 103(72.54%) individual cryobiopsies and 4(12.12%) cases of pneumothorax were found by X-ray. As the freezing time prolongs, the risk of severe bleeding significantly increases and reaches the highest level at 5s.

Conclusion: The optimal freezing time begins with 3 or 4s, which is easily achievable and provides an adequate biopsy size whilst creating a safety threshold from complications.

AO107

FEASIBILITY AND SAFETY OF CRYOBIOPSY IN INTERVENTIONAL BRONCHOSCOPY

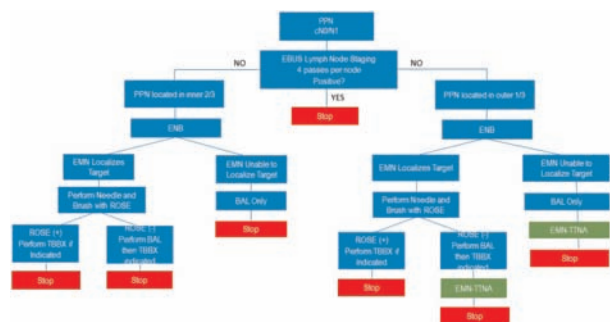
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Background and Aims: The flexible cryoprobe is primarily used for cryoextraction of malignant airway stenosis and was introduced as an alternative method for mechanical tumour debunking, which is immediately effective. Because of extraordinarily well-preserved tissue samples from cryorecanalization procedures, the technique has been transferred to the biopsy of endobronchial or peripheral lesions. The aim of this study was to assess the diagnostic yield and to show the feasibility and safety of cryobiopsy using the flexible bronchoscope and semi-rigid pleuroscope.

Methods: In a single-centre, observational, retrospective study, patients underwent cryobiopsy using the flexible bronchoscope and semi-rigid pleuroscope were evaluated between January 2015 to May 2018. Patient's characteristics including age, sex, lesion size, procedural complications, and the final pathologic diagnosis were recorded.

Results: A total of 238 patients were included in this study. 104 patients underwent cryobiopsy using semi-rigid pleuroscope due to



AO105

CRYOBIOPSY – A POTENTIAL TO BREAK THROUGH THE DIAGNOSTIC BRONCHOSCOPY FOR PERIPHERAL PULMONARY NODULES -

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Background and Aims: Despite the improvement of diagnostic ability of bronchoscopy with advanced techniques for peripheral pulmonary lesions (PPLs), it has still been insufficient compared to transthoracic needle aspiration/biopsy. We focused on cryobiopsy that enables us to obtain tissues with large quantity and high quality; nowadays, it has become the first option for the diagnosis of interstitial lung diseases. Thus, we applied cryobiopsy for PPLs, and investigated the utility.

Methods: Consecutive patients who underwent diagnostic bronchoscopy with cryobiopsy for PPLs at our hospital from June to November 2017 were collected. The cases with the purpose of rebiopsy were excluded. All procedures were performed with the same setting: using radial endobronchial ultrasound (R-EBUS), virtual bronchoscopy, and X-ray fluoroscopy under local anaesthesia. After usual sampling (forceps, brush, or aspiration needle), cryobiopsy was performed where the same location was estimated by X-ray fluoroscopy. The diagnostic value and the safety of cryobiopsy were reviewed.

Results: We performed cryobiopsy for 116 cases with PPLs in this period. The median (range) size was 22.7 (7.1–115.4) mm, and the features (solid, part-solid, nonsolid) were 68.1%, 25.9%, 6.0%, respectively. Besides, the PPLs mainly located at peripheral 1/3 (69.8%), and 21.6% showed negative bronchus sign. The diagnostic yield was 91.4%, and 10 cases were diagnosable only by cryobiopsy (the additional effect was 8.6%). This advantage was different among each R-EBUS findings (within, adjacent to, invisible); the diagnostic yield improved from 95.4%, 71.4%, 50.0% to 96.9%, 85.7%, 50.0%, respectively. On the other hand, 1 case (0.9%) caused mild pneumothorax, and 39 cases (33.6%) caused moderate to severe bleeding. However, no case needed any intervention or admission.

unknown aetiology of exudative pleural effusion. 96 patients (92.3%) were established definitive diagnoses after cryobiopsy. 115 patients underwent cryobiopsy using the flexible bronchoscope due to endobronchial tumour and 111 patients (96.5%) were established definitive diagnoses after cryobiopsy. Still 19 patients underwent cryobiopsy using the flexible bronchoscope due to peripheral lung lesion and 15 patients (79%) were established definitive diagnoses after cryobiopsy. Mild bleeding occurred in 14 cases (5.8%), moderate bleeding occurred in 5 case (2.1%), and no severe bleeding occurred in these patients. Moreover there were still 4 patients (1.7%) with pneumothorax after procedure.

Conclusion: Cryobiopsy using the flexible bronchoscope and semi-rigid pleuroscope is safe and useful to obtain histological samples for diagnosis. Larger tissue samples can be obtained by cryoprobe.

AO108

EFFICACY AND SAFETY OF ARGON PLASMA COAGULATION (APC) PLUS PARTIALLY SPRAYED ADHESIVE VIA THORACOSCOPY IN THE TREATMENT OF SPONTANEOUS PNEUMOTHORAX PATIENTS WITH SUBPLEURAL BLEBS DISEASES

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Background and Aims: To evaluate the preliminary efficacy and safety of argon plasma coagulation (APC) plus medical adhesive assisted thoracoscopy in the treatment of spontaneous pneumothorax caused by subpleural blebs.

Methods: 51 patients of spontaneous pneumothorax with subpleural blebs diseases treated in Pneumology Department of Rizhao city Hospital of Traditional Chinese Medicine from July 2015 to June 2017 were retrospectively analyzed. Among the 51 patients, 59 target bullae were found, 1.157 ± 0.703 on average, with the diameter ranging from 0.5 to 5 cm and an average diameter of 2.64 ± 1.015 cm. 21 patients were treated with APC, and 30 were treated with APC+ (APC plus medical adhesive). The rate of stopping air leakage within 24 h after operation, the rate of stopping air leakage within one week after operation, and the disappearance rate of target subpleural blebs in CT scans one week after operation, as well as the incidence of postoperative fever, chest pain, pleural effusion, haemorrhage, and infection after operation were observed and compared between the two groups. The efficacy and safety of APC+ subpleural cavity in the treatment of spontaneous pneumothorax was compared.

Results: The air leakage rate in APC+ group is significantly higher than that in APC group 24 h after operation (90.0% vs 52.4%, $P < 0.05$), and the rate in APC+ group is also significantly higher than that in APC group one week after operation (96.7% vs 66.8%, $P < 0.05$). There is no significant difference in the disappearance rate of target subpleural blebs in CT scans one week after operation and the incidence of shrinking target subpleural blebs and alveolar wall thickening (both $P > 0.05$). There is no significant difference in the incidence of postoperative complications such as fever, chest pain and pleural effusion (all $P > 0.05$).

Conclusion: The treatment of spontaneous pneumothorax with subpleural blebs by APC+ is safer and more effective.

COPD 2

AO109

EARLY MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Prevalence of COPD increased by 67% from 2004 to 2015 in China (13.7% in >40 years population). [Wang C. Lancet. 2018, Fang LW. Lancet Res Med. 2018]. Among patients population >92% were characterized as stage I & II, which are always neglected by physicians and patients.

Methods: By using Endobronchial Optical Coherence Tomography and exercise test, those patients present with apparent small air way remodelling and less exercise tolerance. [Ding M. Chest. 2016] The earlier the staging, the faster the annual declining of FEV1. [Dransfield MT. AJRCCM. 2017] Patients may not present with dyspnoea (even exercise dyspnoea) until their FEV1 dropped to $\leq 50\%$ predicted. Early intervention may ameliorate disease progression. Community based integrated intervention (medical education, smoking cessation, improved air pollution and short course SAMA) significantly reduced the incidence of COPD and annual decline of FEV1. [Zhou YM. BMJ. 2010]

Results: In a two years 'Tie-COPD' study, we have firstly demonstrated that regular use of inhaled Tiotropium significantly improved trough FEV1 (127-169 mL), FVC (116-164 mL), annual post bronchodilator FEV1 decline rate, CAT score, CCG score and exacerbation rate in stage I to II patients, even in the subgroup with CAT < 10. [Zhou YM, Zhong NS. NEJM. 2017] suggesting an active intervention of stage I to II COPD may greatly improve lung function and reverse (or partly reverse) disease progression.

Conclusion: Whether the strategy of the management of COPD may move to the upstream of the disease, similar to early stage of hypertension or diabetes is worthwhile elucidating.

AO110

THERAPEUTIC TARGETING OF THE IL-6 TRANS-SIGNALLING IN PULMONARY EMPHYSEMA

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Background and Aims: Emphysema is the major debilitating component of COPD, the 4th leading cause of death worldwide with no current treatments. Lung inflammation triggered by exposure to environmental factors (tobacco) is strongly linked to emphysema. My research has discovered that expression of interleukin (IL)-6 is consistently increased in emphysema patients, and in a genetic mouse model for spontaneous emphysema (gp130F/F) to drive the onset of emphysema. Although IL-6 signals using 2 distinct modes, classical signalling via its membrane-bound IL-6 receptor, and trans-signalling (TS) via a naturally-occurring soluble IL-6R (sIL-6R), the precise mechanism(s) by which IL-6 promotes emphysema remains to be elucidated. Our aim is to identify IL-6TS mediated emphysematous molecular/cellular processes.

Methods: The genetic and therapeutic blockade of gp130F/F emphysema mouse model was used to prove the specific role of IL-6TS in driving disease. Emphysema patient lung biopsies and serum during stable disease, with their own corresponding acute exacerbation samples were used for identifying IL-6TS in human emphysema development and exacerbations.

Results: Here, we demonstrate that lung tissues and serum from emphysema patients, as well as from spontaneous (gp130F/F) and cigarette smoke-induced emphysema mouse models, are characterized by excessive production of the soluble IL-6 receptor, which is essential for pathogenic IL-6TS. Genetic and therapeutic blockade of IL-6TS in emphysema mouse models with the antagonist sgp130Fc prevented emphysema by suppressing augmented alveolar type II cell apoptosis. Finally, we also reveal that IL-6TS components are up-regulated in serum from emphysema patients during exacerbation.

Conclusion: Collectively, we define that hyper-activation of the IL-6TS components in the lung augment cell apoptosis, which in turn cause emphysema. These data have considerable translational potential for biomarker discovery and early disease detection, as well as patient stratification for potential responders that may gain the most benefit from selective anti-IL-6TS directed therapies during development and exacerbation.

AO111

MMP-12 ACTIVATES PROTEASE ACTIVATED RECEPTOR (PAR)-1, UPREGULATES PLACENTA GROWTH FACTOR AND LEADS TO PULMONARY EMPHYSEMA

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Background and Aims: Due to the expansion of aging and smoking populations, chronic pulmonary obstructive disease (COPD) is predicted to be the third leading cause of death worldwide in 2030. It is therefore pertinent to develop effective therapy to improve management for COPD. Cigarette smoke-mediated protease-antiprotease imbalance is a major pathogenic mechanism for COPD and results in massive pulmonary infiltration of neutrophils and macrophages, releasing excessive neutrophil elastase (NE) and matrix metalloproteinases (MMPs). Our previous studies indicated that placenta growth factor (PGF) and PGF-triggered downstream signalling molecules mediate NE-induced lung epithelial cell apoptosis, which is a major pathogenic mechanism for pulmonary emphysema. However, the relationship between MMPs-directed COPD and PGF remains elusive. We hypothesize MMPs may upregulate PGF expression and be involved in MMPs-mediated pathogenesis of COPD.

Methods: ELISA assay were used to analysis PGF secretion and caspase activity. Luciferase reporter assay were used to detect PGF promoter activity. Western blot assay were used to proved PGF and Egr-1 protein expression, PGF-activated signalling pathways, PAR-1 activation and caspase activity. We intratracheally instilled MMPs, siRNA and inhibitors into the lung of C57BL/6 WT and PGF KO mice weekly for one month. IHC, H&E stain and TUNEL assay were used to analysis PGF expression, emphysema and apoptosis level in mice lung.

Results: In this study, we demonstrate that only MMP-12 can increase the expression of PGF by increasing early growth response protein 1 (Egr-1) level through the activation of protease activated receptor 1 (PAR-1). The PGF-mediated downstream signalling molecules drive caspase-3 and - dependent apoptosis in bronchial epithelial cell. Both the upregulation of PGF by MMP12 and PGF downstream signalling molecules with pulmonary apoptosis and emphysema were also demonstrated in animals.

Conclusion: Given these findings, we suggest that both human COPD-associated elastases, NE and MMP-12, upregulate PGF expression and promote the progression of emphysema and COPD.

AO112

THE PROTECTIVE ROLE OF BRONCHIAL EPITHELIAL CELLS DERIVED EXOSOME IN COPD

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Background and Aims: Chronic obstructive pulmonary disease is a multi-pathogenesis disease mainly induced by cigarette smoke (CS) exposure. The absorbance of noxious materials from toxic gases and particles could lead to a series of disorder in lungs, for example, an excess of epithelial-mesenchymal transition (EMT) in bronchial epithelial cells. Exosome could encapsulate microRNAs and proteins, acting as a messenger in intracellular crosstalk and pathogenesis. The exosome contents vary with the extracellular environment. We therefore wondering the functions of exosome from bronchial epithelial cells in response to cigarette smoke exposure.

Methods: We identified the characteristics of exosome derived from BEAS-2B cells and detected the level of exosome microRNA-21 after being stimulated by cigarette some extract (CSE) or not. The THP-1 cells were stimulated by PMA to generate macrophages and then the M2 macrophage biomarkers (CD163, CD206, TGF- β) were observed after different exosomes intervention. bronchial epithelial cells were co-cultured with M2 macrophages and the EMT biomarkers (E-cadherin, α -SMA and N-cadherin) were observed.

Results: The morphology of exosome was ensured by transmission electron microscope, surface markers by flowcytometry and particle size by nanoparticle tracking analysis (NTA). The level of microRNA-21 in exosome was decreased after CSE stimulating ($P < 0.05$). The internalization of exosome by macrophages were observed by fluorescence microscope. The level of M2 macrophage, such as CD163, cd206 and TGF- β were decreased in macrophages after CSE-induced exosome intervention compared with non-CSE exosome ($P < 0.05$) and this phenomenon was reconfirmed by microRNA-21 mimics and inhibitors. Being co-cultured with IL-4 induced M2 macrophages, the level of E-cadherin was decreased in BEAS-2B cells ($P < 0.05$) and α -SMA and N-cadherin were increased ($P < 0.05$).

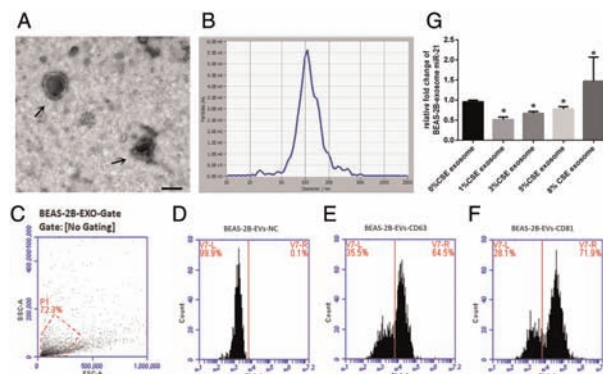


Figure 1. Characteristics of BEAS-2B cells derived exosomes. A. the transmission electron microscope (TEM) photo of exosomes. B. the particle size distribution of exosomes by nanosight tracking analysis (NTA). C. the gate of flow cytometry of BEAS-2B cells derived exosome. D. negative control of BEAS-2B cells derived exosome by flow cytometry. E. CD63 of BEAS-2B cells derived exosome by flow cytometry. F. CD81 of BEAS-2B cells derived exosome by flow cytometry. G. the expression level of BEAS-2B cells derived miR-21 in different cigarette smoke extra concentration. * $p < 0.05$.

Conclusion: These findings demonstrated that the noxious materials from cigarette smoke could change the components of bronchial epithelial cells derived exosome. Those altered exosomes could suppress the EMT process of bronchial epithelial cells by alleviating M2-directed macrophages polarization, acting as a protective role in COPD.

AO113

ANDROGRAPHOLIDE SIMULTANEOUSLY AUGMENTS NRF2 ANTIOXIDANT DEFENSE AND FACILITATE AUTOPHAGIC FLUX BLOCKADE IN CIGARETTE SMOKE-EXPOSED HUMAN BRONCHIAL EPITHELIAL CELLS

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Background and Aims: Cigarette smoking is the leading cause of chronic obstructive pulmonary disease (COPD). Cigarette smoke heightens oxidative stress and impairs autophagy, advancing COPD progression. Andrographolide is a bioactive diterpenoid lactone isolated from the plant *Andrographis paniculata* which has been a traditional medicinal herb for respiratory diseases. As airway epithelial cells form the first interface to be exposed to cigarette smoke, this study aimed to explore the modulatory effects of andrographolide on oxidative stress and autophagy in human bronchial epithelial BEAS-2B cells exposed to cigarette smoke extract (CSE).

Methods: CSE was generated by pumping a single stick of 3R4F cigarette smoke via a peristaltic pump into 10 ml of media and diluted accordingly. BEAS-2B cells were pre-treated with DMSO/andrographolide for 30 min before exposure to filtered CSE for 6/24/48 h and then lysed or fixed for further analysis.

Results: CSE (2%) exposure increased autophagic markers p62 and LC3B-II levels in BEAS-2B cells. Andrographolide alone increased p62 and p-p62 (S349) in BEAS-2B cells. However, in the presence of CSE, andrographolide was able to simultaneously increase LC3B-II level and enhance antioxidant defence by decreasing oxidative stress and increasing total antioxidant capacity, through upregulation of nuclear Nrf2 via the p62-Nrf2 positive feedback loop. Using RFP-GFP-LC3B transfected BEAS-2B cells exposed to CSE, andrographolide was found to impair autophagosome fusion with lysosome, which may account for the minor drop in mitochondrial membrane potential and the moderate increase in activated caspase 3/7 and annexin V levels.

Conclusion: Our findings revealed for the first time that andrographolide simultaneously upregulated antioxidant defence through the p62-Nrf2 loop and moderately induced cell death through impairment of autophagic flux in CSE-exposed bronchial epithelium. Andrographolide facilitates cigarette smoke-induced cell death may protect against chronic inflammation and aberrant DNA repair, and validation of these *in-vitro* findings in an experimental COPD model by andrographolide is warranted.

AO114

PRMT6 MEDIATES INFLAMMATION VIA THE ACTIVATION OF NF-κB/P65 PATHWAY ON CIGARETTE SMOKE EXTRACT-INDUCED MURINE EMPHYSEMA MODEL

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Background and Aims: To investigate whether PRMT6 could attenuate the inflammation of lung tissue and investigate the relationship

between PRMT6, histone 3 and NF-κB signaling pathway in CSE-induced murine emphysema model.

Methods: BALB/c mice were treated with PRMT6-overexpressed lentiviral vectors intratracheally and injected with CSE for three times. The lung functions were measured on day 28 right before the sacrifices, and the pathology of lung tissues were examined in all mice. The expression and location of NF-κB in mice lung tissue were measured by immunohistochemistry. The expressions of PRMT6, H3R2me2a, H3K4me3 protein, and interleukin-1β (IL-1β), tumour necrosis factor α (TNFα) were detected in lung homogenates by Western-blotting. The mRNA expression of IL-1β and TNFα were measured by RT-qPCR.

Results: The increased MLI and DI, the morphology measures, were partly recovered by the intratracheal instillation of PRMT6 in the CSE-induced mice. In CSE + Lenti-PRMT6 group of mice, the overexpression of PRMT6 was successfully detected, which reversed the expression of H3R2me2a and H3K4me3. After overexpression of PRMT6, the nuclear activated NF-κB/p65 induced by CSE was significantly reduced. The expression of H3K4me3 was positively correlated with p65 positive cell numbers. Meanwhile, overexpression of PRMT6 inhibited the expression of IL-1β and TNFα in the lungs of mice with CSE-induced emphysema.

Conclusion: The overexpression of PRMT6 might partially protect against CSE-induced emphysema in mice through NF-κB/p65 pathway, mediated by H3R2me2a.

AO115

THE INFLAMMATORY CYTOKINE ENVIRONMENT OF COPD ALTERS THE AIRWAY EPITHELIAL RESPONSES TO VIRAL AND BACTERIAL STIMULI

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Background and Aims: COPD is a chronic airway inflammatory disease associated with a Th1/Th17-biased inflammatory milieu. Respiratory infections are the major triggers of acute exacerbations of COPD (AECOPD) which are episodes of worsening symptoms associated with exaggerated airway inflammation. However, the mechanisms which drive the enhanced inflammatory response to infections in COPD remain poorly defined. In this study, we characterised the responses of airway epithelial cells (AECs) to infectious stimuli in COPD and established a novel model to study how the Th1/17-biased environment alters the phenotype of AECs.

Methods: Cytokine production by AECs from patients with COPD and healthy controls were assessed in response to virus-like stimuli (poly I:C or imiquimod), or bacterial endotoxin (LPS). Primary AECs from healthy controls or human bronchial Calu-3 cells were cultured in the absence or presence of the Th1/17 cytokines. After 48 h cells were stimulated with viral or bacterial stimuli for 4 h. Expression of pro-inflammatory and antiviral genes, and pattern recognition receptors was measured by qRT-PCR.

Results: Primary AECs from COPD patients and controls exhibited similar responses to viral stimuli, including increased expression of pro-inflammatory and antiviral genes. However, the magnitude of these response was greater in COPD AECs for most genes. LPS induced expression of a few of cytokines in only COPD AECs. Primary AECs and Calu-3 cells pre-treated with Th1/Th17 cytokines exhibited increased baseline expression of pro-inflammatory and antiviral cytokines and expression was further enhanced by viral dsRNA. Upregulated production of viral receptors, but not bacterial receptors, was observed in cells pre-treated with Th1/17 cytokines.

Conclusion: Th1/17-biased inflammatory environment in COPD promotes pro-inflammatory and antiviral responses to viral and bacterial

stimuli in distinct ways. Increased signalling via pattern-recognition receptors may contribute to the exaggerated inflammation in virus-induced AECOPD. Calu-3 cells pre-treated with Th1/17-cytokines may be an appropriate model to study altered phenotype of AECs in COPD.

AO116

CCL-1/CCL-2 INHIBITION BY ROLIPRAM IN MONOCYTES OF COPD

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Background and Aims: COPD (chronic obstructive pulmonary disease) is aware as a global health problem increasingly and statistically it affects more than 300 million patients in the world. Monocytes recruitment to the lungs is also an important step in COPD. The pulmonary macrophages in COPD smokers are resulted from monocytes as a response to the chemotactic chemokines. PDE4 inhibitors play the roles in airway smooth muscle relaxation and inflammatory cells activation inhibition.

Methods: The CCL-1, CCL-2 and IP-10 concentrations of the cell supernatants were measured using commercially available ELISA assay (R & D system, Minneapolis, MN) following the manufacturer's instruction.

Results: Following the stimulation of LPS, TLR4 mediates CCL-1 and CCL-2 through the MAPKs and NF κ B pathway. Also, the epigenetic modification of H3 is also involved in their secretions. Rolipram, a PDE4 inhibitor, inhibits the PDE4 activity which leads to cAMP accumulation inside cells following PKA activation. Following the stimulation of LPS, TLR4 mediates CCL-1 and CCL-2 through the MAPKs and NF κ B pathway. Also, the epigenetic modification of H3 is also involved in their secretions. Rolipram, a PDE4 inhibitor, inhibits the PDE4 activity which leads to cAMP accumulation inside cells following PKA activation.

Conclusion: In conclusion, our results provided an exciting data that Rolipram inhibited LPS induced CCL-1 (I309)/CCL2 expression via MAPKs and epigenetic modifications. Further study into the possible candidates in COPD treatment or other cytokines/chemokines in COPD pathogenesis might be necessary.

AO117

SODIUM TANSINONE IIA SULFONATE INHIBITS CIGARETTE SMOKE-INDUCED INFLAMMATION AND OXIDATIVE STRESS IN MICE VIA INHIBITING AKT/HIF-1 α SIGNALING PATHWAY

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Background and Aims: Hypoxia-inducible factor (HIF)-1 α signaling was activated during cigarette smoke (CS)-induced chronic obstructive pulmonary disease (COPD). Tanshinone IIA was reported to be able to inhibit HIF-1 α expression in LPS-induced lung injury. This present study aimed to investigate the effects of sodium tanshinone IIA sulfonate (STS), a water-soluble derivative of tanshinone IIA, on CS-induced COPD in mice and the underlying mechanisms.

Methods: The role of STS in cigarette smoke extract (CSE)-induced inflammation, oxidative stress was investigated using RAW 264.7 cells. The in vivo effects of STS were evaluated in a mouse model of CS-induced COPD.

Results: Here, we found that STS improved pulmonary function, ameliorated emphysema and decreased the infiltration of inflammatory cells in the lungs of CS-exposed mice. STS reduced CS- and CSE-

induced upregulation of tumour necrosis factor (TNF)- α and interleukin (IL)-6 in the lungs and macrophages. STS also inhibited CSE-induced reactive oxygen species (ROS) production, as well as the upregulation of heme oxygenase (HO)-1, matrix metalloproteinase (MMP)-9 and MMP-12 in macrophages. In addition, STS suppressed HIF-1 α expression *in vivo* and *in vitro*, and pretreatment with HIF-1 α siRNA reduced CSE-induced elevation of TNF- α , IL-6 and HO-1 content in the macrophages. Moreover, we found that STS inhibited CSE-induced AKT phosphorylation in macrophages, and inhibition of this signaling molecule significantly repressed CSE-induced TNF- α , IL-6, HO-1 and HIF-1 α expression. It indicated that STS inhibits CSE-induced HIF-1 α expression likely by blocking AKT signaling. Furthermore, STS also promoted HIF-1 α protein degradation in CSE-stimulated macrophages.

Conclusion: STS prevents COPD development possibly through the inhibition of AKT/HIF-1 α signaling, and may be a novel strategy for the treatment of COPD.

Paediatric Lung Disease

AO118

POST-OPERATIVE OUTCOME OF PAEDIATRIC EMPYEMA TREATED WITH VIDEO ASSISTED THORACOSCOPIC SURGERY (VATS)

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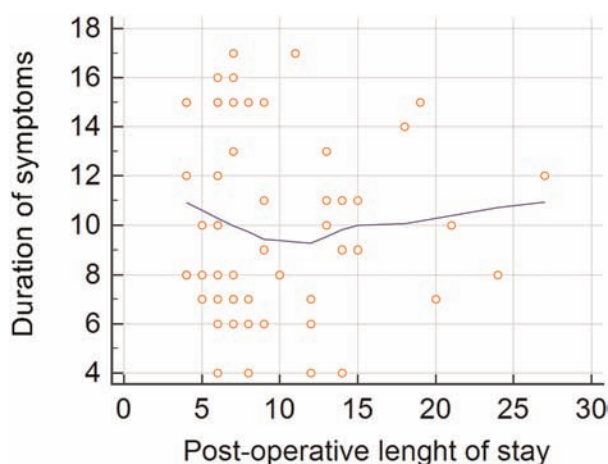
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Background and Aims: VATS is commonly performed in children with empyema, however, there is no data regarding the post-operative outcomes (after discharge) following the procedure.

Methods: A 5-year (2013–2018) retrospective review was performed on children treated with VATS and chest drain for empyema. The study was approved by the local ethics committee (RES-18-0000-071Q). Statistics: results are reported as number of cases (%) and median (range). Correlation and logistic regression analysis were performed.

Results: We identified 62 children, 36 (58%) males, with a median age of 3.6 (0.4–14.5) years treated over the 5-year period. Presentation was: autumn 12 (19%), winter 19 (31%), spring 19 (31%) and summer 12 (19%) patients. Median post-operative follow-up was 47 (9–489) days.

Streptococcus species were identified in 35 (56%) of cultures from pleural fluid. Chest drain was left in situ for a median of 4 (2–13) days. Four (6%) children required a second procedure (3 VATS, 1 thoracotomy).



Median duration of pre-operative symptoms before the VATS procedure was 9 (4–17) days.

Median post-operative length of stay was 8 (3–28) days and duration of oral antibiotics therapy after discharge was 28 (3–42) days. Thirty-nine (63%) required post-operative oxygen therapy for 3 (1–16) days.

There was no correlation between the duration of pre-operative symptoms at the time of VATS and post-operative length of stay ($r = -.03$ [95% CI $-0.3 - 0.2$]; $P = 0.7$) (Figure)

Post-operative x-ray was available for 56 (90%) patients and documented persisting lung or pleural abnormalities in 47 (84%). Logistic regression analysis failed to identify any predisposing factors for persisting x-ray abnormalities ($P = 0.63$).

Conclusion: We found a significant incidence of persisting abnormalities on post-operative x-ray following VATS with chest drain for empyema in children. Long-term follow-up of children following VATS might be indicated to identify patients at risk of chronic respiratory problems.

AO119

COMMUNITY-ACQUIRED NECROTIZING PNEUMONIA DUE TO METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS SECRETING PANTON-VALENTINE LEUKOCIDIN IN 4 PATIENTS ADMITTED TO CHILDREN'S HOSPITAL 1 IN NOVEMBER 2017: CASE SERIES REPORT

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Background and Aims: Community-acquired pneumonia due to *Staphylococcus aureus* is an infrequent but potentially lethal infection. It is often associated with the production of Pantone-Valentine leukocidin (PVL), which is responsible for extensive tissue necrosis and a high mortality rate. We describe four young children presented within November-2017 to Children hospital 1 at Ho chi minh city with community acquired necrotizing pneumonia due to MRSA-PVL.

Methods: The patients admitted to Children hospital 1 with necrotizing pneumonia and pleural effusion. We implemented the pleural sample and blood culture. Patients with MRSA-PVL necrotising pneumonia will be observed until discharging.

Results: All four patients in this case series were young immunocompetent children presenting with a short non specific symptoms, but developed respiratory distress acutely. The minimum age was 1.5 months, the maximum one was 22 months, 2 remaining cases were 13 months and 16 months respectively. 3 cases of patients were resident in central areas of Ho Chi Minh city whereas 1 case was resident in suburb. Overall 100% of presentations occurred in November.

The median time from symptom onset to hospital admission was only 2 days. The second patient had a prodrome of diarrhoea whereas the others had a prodrome of influenza like illness.

All of them were critically ill and admitted to the emergency room of respiratory department and all required assisted ventilation.

All patients developed pneumothoraxes, pleural effusions that required VATS procedure.

Three cases showed to be responded with the combination of Vancomycin and Clindamycin. However, only 1 case was prescribed Linezolid after 28 days of Vancomycin treatment and VATS due to persisted high fever and skin lesions appearance.

Conclusion: A young healthy immune-competent child with respiratory distress may be having PVL producing community acquired MRSA. High index of suspicion, early diagnosis and appropriate antibiotics is important since untreated community acquired MRSA has a high mortality rate.

CHANGES AFTER AUTOMATED CONTROL OF INSPIRED OXYGEN CONCENTRATION IN PRETERM INFANT WHO UNDERWENT CPAP

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Background and Aims: To examine changes before and after the automated control of inspired oxygen concentration ('automated control') in preterm infants who underwent CPAP.

Methods: The subjects of our study were preterm infants hospitalized in our NICU. They underwent CPAP with automated control. We retrospectively investigated the number of changes to their FiO₂, the average FiO₂, the rate that SpO₂ fell within the target range, the rate that SpO₂ fell less than -% of the target, and the index of oxygenation (SpO₂/FiO₂ ratio) between before and after automated control.

Results: A total of 23 automated control were performed on 20 infants. The median (smallest - largest values) of their length of gestation were 26 weeks (22–31) and their weight at the start were 870 g (515–1,814). The number of FiO₂ changes per hour before and after automated control were 0 (0–2.3) and 110 (7.3–189, $P < 0.01$); the average FiO₂ was 0.29 (0.22–0.44) and 0.27 (0.21–0.49, $P = 0.72$); the rate that SpO₂ fell within the target range was 37% (1.3–75) and 55% (3.2–84, $P < 0.01$); the rate that SpO₂ fell less than -% of the target value was 1.9% (0.1–31) and 1.5% (0.2–9.4, $P = 0.01$); the average SpO₂/FiO₂ ratio was 335 (207–443) and 349 (189–458, $P = 0.01$).

Conclusion: By automated control of inspired oxygen concentration, their FiO₂ changed more frequently, the rate that SpO₂ falls within the target range increased, and the frequency that it dropped decreased for preterm infants who underwent CPAP. In addition, as the index of oxygenation (SpO₂/FiO₂ ratio) increased, it was shown that excessive use of oxygen was avoided. Using automated control for preterm infants might help avoid their exposure to low oxygen or excessive oxygen levels, which might lead to the reduction of complications and improvement of impairment with oxygen-induced toxicity.

AO121

SPONTANEOUS PNEUMOMEDIASTINUM WITH SUBCUTANEOUS EMPHYSEMA IN AN 8 YEAR OLD FEMALE: A CASE REPORT

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Background and Aims: Bronchial asthma is a disease characterized by chronic airway inflammation. Severity of which is variable and determined upon clinical presentation. Despite its common incidence, complications such as spontaneous pneumomediastinum with subcutaneous emphysema is considered a rare occurrence in the paediatric population.

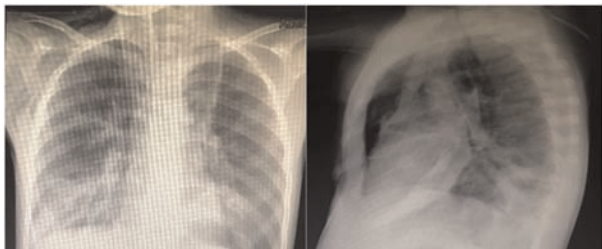
This case report aims to present a case of an 8 year old female diagnosed with pneumomediastinum and subcutaneous emphysema as a result of a severely exacerbated bronchial asthma. This study also aims to discuss the incidence, etiology, diagnosis and management of spontaneous pneumomediastinum with subcutaneous emphysema.

Methods: This case report was based on the thorough review of the chart data on history, physical examination findings and pertinent laboratory results of the index case.

Results: This is a case of a 8 year old female who came in to the emergency department in apparent respiratory distress associated with dyspnea and chest pain. Patient clinically presented with signs and symptoms consistent with bronchial asthma in severe exacerbation. Upon chest radiography, it revealed presence of spontaneous pneumomediastinum and subcutaneous emphysema over the right supraclavicular and

axillary region. Subsequently, patient was admitted at the paediatric intensive care unit for further management and close monitoring. Patient was eventually discharged well after a total of 8 hospital days.

Conclusion: Subcutaneous emphysema is a common symptom associated with spontaneous pneumomediastinum. Both conditions are considered a sequelae to bronchial asthma in severe exacerbation. Although asthma in exacerbation is a common occurrence, spontaneous pneumomediastinum is an uncommon condition seen in the paediatric population. Diagnosis, however, may be made by simple radiographic imaging. Management is conservative and geared towards symptomatic relief. No deadly complications rooted from spontaneous pneumomediastinum has been reported.



AO122

DIAGNOSTIC VALUE OF SALIVARY LIQUEFIED CARBOHYDRATE ANTIGEN KL-6 IN CHILDREN WITH PNEUMONIA

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Background and Aims: To investigate the diagnostic value of salivary liquefied carbohydrate antigen KL-6 and the relationship with the severity in children with pneumonia.

Methods: A total of 269 children with pneumonia and 112 children with non-pulmonary disease were collected from the First Affiliated Hospital of Guangzhou Medical University. The age of them was under 16 years old. Serum levels of KL-6 were detected.

Results: The serum KL-6 level of pneumonia group was higher than the non-pulmonary disease group [170.0(121.0, 272.0) U/ml vs 119.5 (88.3, 156.0) U/ml], the difference had statistically significant ($Z = -4.63$, $P < 0.001$). The AUC of the diagnostic test was 0.82 (95% CI: 0.71 to 0.94, $P < 0.001$). The Youden index of 0.506 was selected as the cutoff point. The sensitivity was 65.50%, the specificity was 92.60%, the accuracy rate was 78.57%, the positive predictive value was 90.48%, and the negative predictive value was 71.43%. The Kappa value was 0.58 [0.37, 0.78]. The serum KL-6 level of severe pneumonia group was higher than the mild to moderate pneumonia group [277.0(204.0, 395.0) U/ml vs 163.5 (116.0, 248.8) U/ml], the difference had statistically significant ($Z = -2.41$, $P < 0.001$). The AUC of diagnostic test was 0.89 (95% CI: 0.81 to 0.96, $P < 0.001$). The Youden index of 0.452 was selected as the cutoff point. The sensitivity was 93.20%, the specificity was 78.00%, the accuracy rate was 85.88%, the positive predictive value was 82.00%, and the negative predictive value was 91.43%. The Kappa value was 0.72 [0.57, 0.86]. There was no significant difference of KL-6 level among the children with bacterial pneumonia, mycoplasma pneumonia and viral pneumonia.

Conclusion: The serum KL-6 level has certain clinical application value in the diagnosis of paediatric pneumonia and the prediction of severe pneumonia in children, but there is no specificity between different pathogens induced pneumonia.

PNEUMONIA DUE TO BURKHOLDERIA PSEUDOMALLEI IN CHILDREN AT THE CHILDREN'S HOSPITAL NO 1, HOCHIMINH-CITY, VIET NAM

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Background and Aims: Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*. Until recent years of 21st century, melioidosis is more considerable because of high mortality rate and difficult therapy. The early diagnosis and bacterial prediction will help to choose appropriate antibiotics and can reduce the mortality. We report some septicæmia, severe pneumonia, acute respiratory failure cases caused by *Burkholderia pseudomallei* in children admitted to the Children's hospital No 1, HoChiMinh-city, Viet Nam. Determine the epidemiological, clinical, paraclinical and treatment characteristics of pneumonia due to *Burkholderia pseudomallei* and status of antibiotic susceptibility of *Burkholderia pseudomallei* to antibiotics recommended for treatment.

Methods: Case series

Results: There were 6 patients (4 males, 2 females) (median age: 60 months). The definitive diagnosis were confirmed by lung infiltrations on the chest radiographies and the positive blood or body fluids of *Burkholderia pseudomallei*. 4/6 children were under 2 years old. Almost were hospitalized in rainy season. Three children came from Cambodia. One cases had underlying disease (beta thalassemia). All 6 cases had typical clinical presentation of acute pneumonia, 5/6 cases had respiratory failure. 5/6 children (83.3%) had septicæmia. Other clinical appearances included skin abscesses (40%), soft tissue abscesses (60%), and septic arthritis (16.7%). The chest radiographies findings vary widely: nodal patchy consolidation (6/6 cases), and especially pneumatocele (4/6 cases), pleural effusion (almost right lung) (6/6 cases), fibrosis (1/6 cases). Necrotizing pneumonia was found in 3/6 children. *Burkholderia pseudomallei* were completely sensitive to ceftazidime and TMP-SMX. Two cases were sensitive to ciprofloxacin, ticarcilin, cefotaxim, carbapenem. Especially, the resistance to carbapenem were found in 4/6 children. These children had a prolonged hospital stay: median LOS were 27 days. Commonly used antibiotics: ciprofloxacin, ceftazidime, meropenem, imipenem, TMP-SMX. One case relapsed of this disease without subsequent eradication therapy (TMP-SMX). During hospitalization, 33% of the patients died (2/6 cases).

Conclusion: Melioidosis represent an important cause of morbidity, mortality, and fatal community-acquired bacteremic pneumonia.

AO124

PRIMARY CILIARY DYSKINESIA IN JAPAN

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Background and Aims: Primary ciliary dyskinesia (PCD) is a rare genetic disease characterized by functional cilia impairment. Patients with PCD would miss the opportunity to receive appropriate diagnosis due to various physical symptoms. In Japan, there has been no or few nationwide survey of PCD.

Methods: To investigate the current status of patients with PCD in Japan, we conducted the first nation-wide survey of PCD for 1823 institutes in 2016, in collaboration with the Diffuse Lung Diseases Research Group from the Ministry of Health, Labour and Welfare, Japan.

Results: In this survey, questionnaire answers were obtained from 481 institutes (response rate; 26.4%). There were 51 institutes with the patients who were diagnosed as PCD. Overall, 116 cases were reported as patients with PCD and total 73 patients were followed by the institutes at the time of this survey. The diagnostic methods are transmission electron microscopy (76 cases), high-speed video analysis (17 cases), nasal nitric oxide measurement (16 cases), and others (24 cases). The numbers of the patients diagnosed by genetic analysis were 11 cases.

Conclusion: This first nation-wide survey of PCD in Japan provided the basis for further analysis of clinical characteristics in patients with PCD by the second survey and establishment of appropriate diagnosis criteria in Japan.

AO125

UTILITY OF FRACTIONAL EXHALED NITRIC OXIDE (FENO) LEVELS IN DIFFERENTIATING UPPER RESPIRATORY TRACT INFECTION AND BRONCHIAL ASTHMA FROM HEALTHY NORMAL SCHOOL CHILDREN CRESTITA GORME¹

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Background and Aims: Nitric oxide is a biological mediator produced by the human lung and is present in the exhaled breath. This agent is implicated in the pathophysiology of lung diseases. Existing studies already established FeNO as a biomarker of airway inflammation, especially in asthma. It is therefore essential to define the normal values among healthy children and compared it with those with respiratory symptoms as occurred in upper respiratory tract infection (URTI) and bronchial asthma. It is also equally important to determine any factors that affect the levels of FeNO.

Methods: The study was conducted among grade school children in a public school. Parents were asked to answer questionnaires for presence of probable asthma and URTI. The children were categorized into three: healthy, URTI, and asthma groups. FeNO levels were measured among subjects.

Table 1. Baseline Demographic Characteristics of Study Population

Characteristics (N=49)	Healthy Children (n=23)	Bronchial Asthma (n=4)	Upper Respiratory Tract Infection (n=22)	TOTAL
Age (in years)				
6-10 years old	19	3	17	39 (79.59%)
11- 14 years old	4	1	5	10 (20.41%)
>14 years old	0	0	0	0
Sex				
Male	7	3	16	26 (53.06%)
Female	16	1	6	23 (46.94%)
BMI				
Z score -3	0	0	1	1 (2.04%)
Z score -2	1	0	1	2 (4.08%)
Z score -1	2	0	1	3 (6.12%)
Z score 0	10	3	6	19 (38.78%)
Z score 1	10	0	4	14 (28.57%)
Z score 2	0	1	9	10 (20.41%)
TOTAL	23	4	22	49

Table 2. FeNO levels according to presence of URTI and bronchial asthma

	Normal (n= 24)	URTI (n= 21)	Bronchial Asthma (n=4)
Feno Levels (ppb) (median)	9.6 (6-15.3)	12.6 (9.3- 35)	31.8 (15.3-62.15)

Results: The median FeNO level of the study population is 12.0 ppb (11.6 – 21.3 ppb). The median FeNO level among healthy subjects is 9.6 ppb (6.0- 15.3 ppb). For those with URTI and asthma, the median FeNO levels are 12.6 ppb (9.3-35 ppb) and 31.8 (15.3–62.15 ppb) respectively. The levels of the asthma group were significantly higher than the healthy children with a *P* value of 0.0488 . There was no significant difference in the FeNO levels between the asthma and the URTI group. Body mass index, weight and height do not alter FeNO measurement. However, FeNO levels of the males and the younger age group (6–11 years old) are significantly higher with *P* values of 0.0337 and 0.0061 respectively.

Conclusion: FeNO concentration is higher among children with probable asthma compared to healthy children. Male gender and younger age have significant correlation with an elevated FeNO. BMI, weight, and height do not affect FeNO.

Critical Care Medicine 2

AO126

PATHOGEN IDENTIFICATION WAS NOT ASSOCIATED WITH MORTALITY IN PATIENTS ADMITTED TO A MEDICAL INTENSIVE CARE UNIT WITH PNEUMONIA

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Background and Aims: Pneumonia remains one of the leading causes of death worldwide. Patients with pneumonia usually receive empirical antibiotic treatment right after cultures being collected. If pathogens are identified, the antibiotic treatment may be adjusted to a definite treatment accordingly. Theoretically, patients whose causal pathogens are identified will receive more appropriate definitive antibiotic treatments thus may have a better outcome. The aim of this study was to investigate whether pathogen identification influences clinical outcomes in critically ill patients with pneumonia.

Methods: We conducted a retrospective observational cohort study of pneumonia patients admitted to the medical intensive care unit (MICU) in a tertiary hospital from January 2012 to October 2013. Clinical information and culture reports were collected. We set ICU mortality as the primary outcome.

Results: A total of 665 patients with pneumonia were enrolled in this study, and 232 (34.9%) patients died in the ICU. Pathogens were identified in 260 patients (39.1%), with Gram-negative bacteria in 71% of patients, Gram-positive bacteria in 15%, and polymicrobial infection in 14%. *Klebsiella pneumoniae* (67, 25.8%) was the most commonly identified pathogen, followed by *Pseudomonas aeruginosa* (57, 21.9%), and *Acinetobacter baumannii* (41, 15.8%). Patients without pathogens identified had similar mortality rate compared to patients with pathogens identified (33.6% vs 33.9%, *P* = 0.405; adjusted OR = 0.97, 95% CI = 0.68–1.38, *P* = 0.845). However, we found a trend that hospital-acquired pneumonia (HAP) patients without pathogen identified had higher mortality rate than those with pathogen identified (48.9% vs 34.9%, *P* = 0.053), while community-acquired pneumonia (CAP) patients without pathogen identified had lower mortality rate than those with pathogen identified (22.7% vs 37.9%, *P* = 0.014).

Conclusion: Pathogen identification was not associated with mortality in critically ill patients with pneumonia. However, we found a trend that pathogen identification may be associated with a lower mortality in HAP and a higher mortality in CAP.

AO127

PREDICTORS OF OUTCOME AMONG LUNG TRANSPLANTATION PATIENTS SUPPORTED WITH EXTRACORPOREAL MEMBRANE OXYGENATION

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Background and Aims: ECMO is increasingly being applied as life-support for lung transplantation patients. The aim of this study was to determine. However, the outcomes of this procedure in Lung transplantation patients have not yet been characterized. The aim of this study was to evaluate the outcome of in Lung transplantation patients supported with ECMO and to identify potential predictors of mortality in these patients.

Methods: Patients underwent lung transplantation treated with ECMO in Guangzhou Institute of Respiratory Diseases between January 2015 to August 2017 were retrospectively reviewed. Patient demographics and clinical variables were collected and analyzed. Univariate and multivariable logistic regression was performed to identify predictors of outcome in lung transplantation patients treated with extracorporeal membrane oxygenation.

Results: During the study period, 67 patients underwent lung transplantation at our institution, 21 patients were treated with ECMO. 14 patients (66.6%) were survived at 6 months. Significant predictors of survival in lung transplantation patients based on a multivariate logistic regression analysis, were advanced age and long times of preoperative mechanical ventilation and preoperative intensive care unit, a higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score.

Conclusion: Age, long times of preoperative mechanical ventilation and preoperative intensive care unit, a higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score may be the major predictors of the prognosis in lung transplantation patients supported with ECMO based on a multivariate analysis.

AO128

SEROTONIN AND VASCULAR PERMEABILITY (SEROTONIN BEYOND THE BRAIN) --- ANALYSIS OF SEROTONIN IN SEPSIS AND ARDS

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Background and Aims: Septic shock or ARDS is characterized by a dysregulated vascular permeability and its treatment outcome remains poor. Most of the cases require intensive care, and its disease burden on health economics is high. Recently, we reported that macrophage phagocytosis dysfunction was regulated by serotonin (5-hydroxytryptamine; 5-HT) through Rho kinase activation (Tanaka et al. JBC.2014). We focused on endothelial cells and we hypothesized that vascular permeability on endothelial cells would be regulated by 5-HT through Rho kinase activation. To prove this, we conducted *in vitro* experiment and 5-HT kinetics was assessed in clinical patient samples.

Methods: *In vitro* experiment, permeability upon 5-HT stimulation of endothelial monolayer determined by albumin transfer using human pulmonary microvascular endothelial cells (HPMEC). For clinical samples analysis, plasma and urine samples from healthy volunteers controls ($n = 7$), sepsis and ARDS ($n = 46$) patients in ID ward, ICU and ER at Nagasaki University Hospital were acquired after obtaining the informed consent, then serotonin metabolite (5HIAA) was measured.

Results: 5-HT significantly increased the permeability of the endothelial cells compared with the control. Treatment with Y-27632 (Rho kinase inhibitor) significantly inhibited the permeability that was induced by 5-HT stimulation. Plasma 5HIAA levels in clinical samples were significantly higher in sepsis patients compared with controls. And these elevated levels were significantly correlated with the severity indexes (SOFA score, APACHE-II score, P/F ratio, use of renal-replacement therapy) and ICU discharge rate.

Conclusion: 5-HT increased the vascular permeability of endothelial cells via the Rho kinase pathway and elevated 5HIAA were seen in severe septic shock patients, suggesting a novel mechanism by which 5-HT may disrupt the endothelium barriers and contribute to the pathogenesis of severe shock status with a vascular leak of sepsis or ARDS.

AO129

PROTECTION EFFECT OF OVERWEIGHT AND OBESITY IN CRITICALLY ILL ADULT PATIENTS WITH INFLUENZA: A MULTICENTER RETROSPECTIVE COHORT STUDY IN TAIWAN

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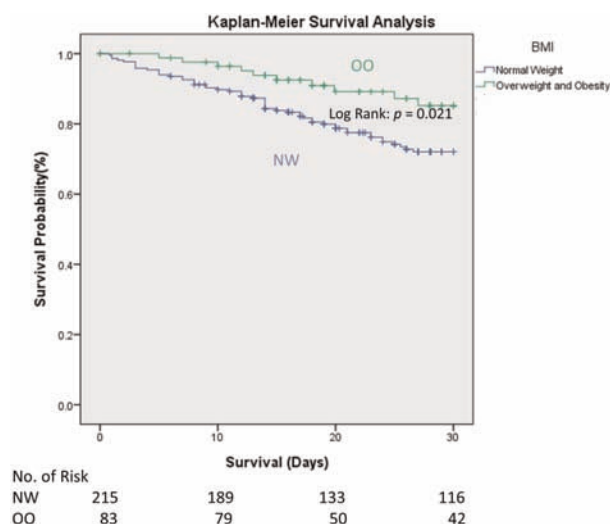
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Background and Aims: Previous studies suggest that obesity may be a risk factor for complications from pandemic influenza A (H1N1) or seasonal influenza infection. We aimed to examine the association between overweight/obesity and normal weight in adult critically ill patients with seasonal influenza infection in Taiwan.

Methods: This is a multicenter retrospective cohort study conducted by Taiwan Severe Influenza Research Consortium (TSIRC) which includes eight tertiary referral medical centres. Patients with virology-proven influenza infection admitted to intensive care unit between January and March 2016 were included for analysis. After excluding underweight patients, the patients were categorized in two groups by body mass index (BMI), overweight/obesity (OO, BMI ≥ 27.5 kg/m²) and normal weight (NW, $27.5 > \text{BMI} \geq 18.5$ kg/m²) according to local cut-point.

Results: A total of 303 patients were enrolled, and 97.4% of them with respiratory system involvement. The patients in OO group were younger than NW group (55.9 ± 13.3 years vs 62.8 ± 14.8 , $P < 0.001$), and less organ dysfunction (Sequential Organ Failure Assessment Score, SOFA score) (9.2 ± 3.5 vs 10.7 ± 4.5 , $P = 0.02$). Among other severity evaluation, there were no significant difference in APACHE II score, C-reactive protein, lactate, and platelet count. The 30-day mortality was also lower in OO group (11% vs 24.4%, $P = 0.008$). Using Kaplan-Meier survival analysis to evaluate the association of 30-day mortality with different BMI category, the result showed positive correlation (log-rank test, $P = 0.021$). In a multivariate Cox proportional hazard regression model adjusted for sex and APACHE II (including to age factor), the normal weight comparing with overweight/obesity was independently associated with a higher 30-day mortality rate (aHR 2.027, 95% CI: 1.027–4.001, $P = 0.042$).

Conclusion: The normal weight comparing with overweight/obesity was independently associated with a higher 30-day mortality rate in critically ill patients with influenza in Asian population. Further prospective study is warranted.

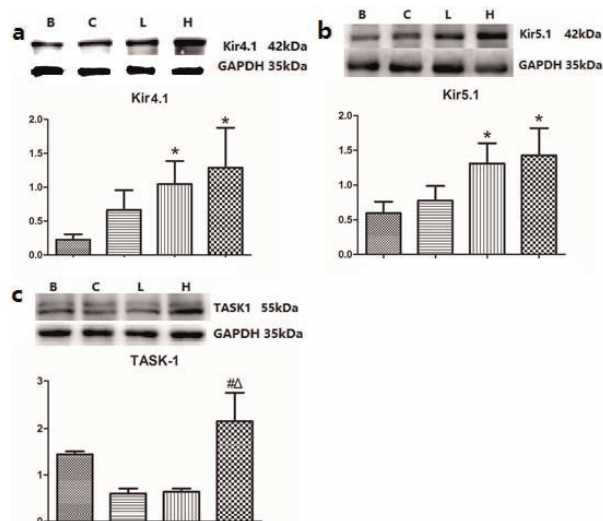


AO130

HIGH TIDAL VOLUME MECHANICAL VENTILATION REDUCES RESPIRATORY CENTER DRIVE BY POTASSIUM CHANNELS ALTERATION

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Background and Aims: TWIK-related acid-sensitive potassium channel (TASK) and inwardly rectifying potassium channel (Kir) are closely related to respiratory centre control. We aimed to investigate the effect of MV on TASK and Kir's functions and explored the respiratory centre drive alteration using a rat model.



Methods: 32 Male Sprague-Dawley rats were randomized to 4 groups: (1) H: MV for 6 h with Vt at 20 mL/kg; (2) L: MV for 6 h with Vt at 5 mL/kg; (3) C: anesthetized and unventilated animals; (4) B: sacrificed immediately after being anesthetized to serve as basic reference. The ventilation strategy was volume controlled mode. We measured lung histology (haematoxylin-eosin staining) and diaphragm discharge

(physiological instrument) and determined TASK1, Kir4.1, Kir5.1 levels (western blotting) in rat brainstems. The potassium channels of TASK1, Kir4.1 and Kir5.1 acted as markers of respiratory centre activity.

Results: The lung injury was significantly severer in Group H. Kir4.1 and Kir5.1 levels were significantly higher in the MV groups compared to Group B (Group H, $P = 0.039$, $P = 0.006$; Group L, $P = 0.002$, $P = 0.006$) and Kir5.1 level was also significantly higher in the Group H to Group C ($P = 0.007$). The protein of TASK-1 in Group H was significantly higher than Group C and L ($P = 0.007$, $P = 0.008$). The EMGdi frequency in Group H decreased significantly than Group C and L ($P = 0.004$, $P = 0.001$).

Conclusion: Mechanical ventilation affects the regulation of the respiratory centre by interfering TASK-1 and Kir4.1-5.1 channels expression.

AO131

UTILITY OF 6-MIN WALK TEST IN PREDICTING POST-OPERATIVE PULMONARY COMPLICATIONS AMONG PATIENTS UNDERGOING CARDIOTHORACIC SURGERIES

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Background and Aims: Postoperative pulmonary complications (PPC) are common and are an important cause of perioperative morbidity and mortality. Standard pre-operative spirometry and cardiopulmonary testing (CPET) have limitations, hence, a simple 6-min walk test (6MWT) was used to evaluate PPC among patients undergoing heart and thoracic surgeries.

Methods: A prospective cohort study was conducted among patients undergoing open heart and thoracic surgeries. 6MWT was done pre-operatively and patients were observed for occurrence of PPC within 48 h after surgery. Diagnostic accuracy analysis and area under the receiver-operating characteristic (ROC) curve were used to analyze variables and compare performance of 6MWT and development of PPC.

Table 1. Baseline demographic and clinical characteristics of patients who underwent cardiothoracic surgeries.

CHARACTERISTICS n=62	WITH PPC n = 19 (31%)	WITHOUT PPC n = 43 (69%)	p-value
Frequency (%); Mean $\pm$ SD			
Age	53.21 $\pm$ 14.13	48.60 $\pm$ 14.46	0.249
Sex Male (38/61%)	11 (58%)	27 (63%)	0.781
Female (24/39%)	8 (42%)	16 (37%)	
Weight (kg)	62.08 $\pm$ 16.18	62.90 $\pm$ 15.89	0.852
Height (meters)	1.60 $\pm$ 0.07	1.62 $\pm$ 0.09	0.366
BMI (kg/m ²)	24.39 $\pm$ 6.51	23.83 $\pm$ 5.01	0.712
Co-morbidities			
Hypertension (n=31)	11	20	0.582
Diabetes mellitus (n=11)	3	8	1.000
Asthma	0	0	
Chronic kidney disease (n=1)	1	0	0.306
Cerebrovascular disease (n=5)	2	3	0.638
Coronary artery disease (n=24)	8	16	0.781
History of PTB (n=7)	1	6	0.422
History of COPD (n=12)	7	5	0.034
Smoking history			
Never smoker (n=37)	8	29	0.022
Smoker (n=25)	11	14	
Type of Surgery			
CABG (n=23)	7	16	1.000
Valve Surgery (n=34)	13	21	0.177
Vascular Surgery (n=5)	2	3	0.638
CHD Surgery (n=6)	1	5	0.657
Lung Surgery (n=4)	2	2	0.580
6-minute walk distance	247.53 $\pm$ 83.97	325.03 $\pm$ 69.88	0.004

Results: A total of 62 participants were included in the study. 6MWT was done in all cases. The average 6MWD was 301.27 $\pm$ 82.10 m. Among the 62 patients, 19 (31%) developed post-operative pulmonary complications. Subjects who walked above the clinical 6MWD cut-off of 300 m showed a decreased chance of developing PPC post-operatively with a sensitivity of 78.9% and specificity of 62.8%. The clinical pre-operative 6MWD of 300 m was selected as cut-off for predicting PPC risk

with an area under curve of 0.2393 indicating that for every meter increase in 6-min walk test, it is 1.38% less likely to have complications with an odds ratio of 0.986 (95% C.I. 0.978 to 0.995; $P = 0.002$).

Conclusion: Six-min walk test is a simple, non-invasive and feasible test that may be used for pre-operative evaluation. A 6-min walk distance of >300 m is more likely to result to better outcomes in terms of post-operative pulmonary complications. However, a 6-min walk distance of < 300 m cannot consistently predict the development of post-operative pulmonary complications especially among COPD patients.

AO132

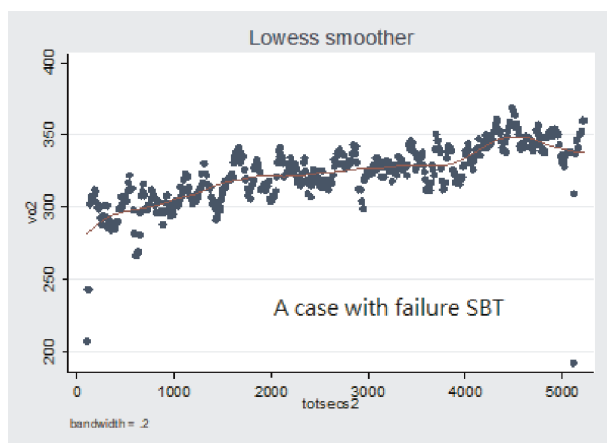
KINETICS OF OXYGEN UPTAKE DURING THE SPONTANEOUS BREATHING TRIAL PREDICTS WEANING OUTCOMES FOR PATIENTS WITH PROLONGED MECHANICAL VENTILATION: A PROSPECTIVE ANALYSIS AT A WEANING UNIT

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Background and Aims: The relationship between oxygen uptake (VO₂) during spontaneous breathing trial (SBT) and weaning outcome was rarely reported. We hypothesized that the VO₂ will increase if the work rate of SBT was above anaerobic threshold. We aimed to analyze the kinetics of VO₂ during SBT and its prognostic significance in tracheostomized patients with prolonged mechanical ventilation (PMV).

Methods: We used an open circuit method to continuously measure the breath-by-breath VO₂ (by CARESCAPE Monitor B650, GE Healthcare, US) during SBT for PMV patients with tracheostomy at a weaning unit. The kinetics of VO₂ during SBT were analyzed and compared between patients grouped by the result of SBT



Results: Between January and June 2018, 24 patients completed the study, aged 68.7 ± 13.6 years and had 43.9 ± 26.1 days of MV before inclusion. The most common reasons for initiating MV were pneumonia (54%) and heart failure (21%). The VO₂ data were collected with a duration of 781 ± 393 min [30–1440], and 20 patients successfully passed the SBT. The overall mean VO₂ level was 237.1 ± 44.3 ml/min. The SBT success cases had a significantly lower level of mean VO₂ than the failure cases (224.4 ± 32.6 vs 297.4 ± 23.4 ml/min; $P < 0.001$). The time

proportion of VO₂ >250 ml/min was $28 \pm 28\%$ in the success cases, in contrast to $91 \pm 12\%$ who failed; the time proportion was highly correlated to SBT results, with an AUC of ROC curve of 0.98 (Youden index 0.90). Using the time proportion of 64.6% as a cutoff for predicting SBT failure, the sensitivity and specificity was 90% and 100%, respectively.

Conclusion: Patients with PMV who exhibit successful and failed SBT attempts differ significantly with their kinetics of VO₂ during the trial. The kinetics of oxygen uptake during SBT is valuable in predicting the weaning outcome of tracheostomized patients with PMV.

AO133

NEUTROPHIL EXTRACELLULAR TRAPS AUGMENTED ALVEOLAR MACROPHAGES PYROPTOSIS IN LPS INDUCED ALI/ARDS

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Background and Aims: Systemic inflammation is the main feature in lipopolysaccharide(LPS)/severe infection-induced acute lung injury(ALI)/acute respiratory distress syndrome (ARDS), our previous study demonstrated alveolar macrophages pyroptosis confers a critical role in LPS-induced ALI. Furthermore, our another previous study show neutrophil extracellular traps also contribute to the pathogenesis of ALI/ARDS while NETs did not result in systemic inflammation directly. Then we hypothesize that NETs may upregulate alveolar macrophages pyroptosis resulted in aggravation of ALI/ARDS.

Methods: the authors analyzed whether NETs are involved caspase-1 in the supernatant of bronchial aspiration and clinically involved in ARDS patients caused by severe bacterial infection. Then the authors used an LPS-induced ALI model to investigate whether targeting NETs can suppress alveolar macrophages pyroptosis and be protective in the mouse model. NETs degradation agents (DNase) and NETs inhibitor (PAD4) were administered to mice.

Results: Analysis of supernatant of bronchial aspiration from ARDS patients ($n = 20$) showed elevated NETs and Caspase-1 were significantly correlated with the degree of ARDS and were higher in nonsurvivors (1865 ± 191.6 , 35.7 ± 3.097 , $n = 7$) than in survivors (1300 ± 119.7 , 26.94 ± 1.659 , $n = 13$). DNase and PAD4 inhibitor markedly attenuated the pyroptosis ratio of alveolar macrophages and the intensity of ARDS.

Conclusion: NETs may play a contributory role to ARDS by promoting pyroptosis of alveolar macrophages and systemic inflammation, thus may become a marker reflecting disease activity. Targeting NETs may be a potential therapeutic strategy.

Pulmonary Circulation

AO134

CLINICAL COURSE AND OUTCOMES OF PATIENTS WITH SUBMASSIVE PULMONARY EMBOLISM

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Background and Aims: The standard treatment of massive pulmonary embolism (PE) was known as systemic thrombolysis. However, the

treatment of submassive PE was not well established yet. Also, data regarding the clinical course and outcome of submassive PE is still lacking.

Methods: A multicenter retrospective study was conducted with patients admitted to the hospital due to submassive PE in three tertiary referral centres between Jan 2003 and Jan 2018. The demographic and clinical data were collected.

Results: Total 132 patients were enrolled in this study. The median age was 71 years old and 76 (58%) patients were females. Immobilization and recent surgery were the most common risk factors and provoked PE was 48%. Their pulmonary embolism severity index (PESI) was 100 ± 34 . The main location of submassive PE was main or lobar pulmonary artery. Half of patients (56%) had D-shape left ventricle on echocardiography. The initial right ventricular systolic pressure was 62 ± 18 mmHg. The mainstay treatment of submassive PE was anticoagulation alone (75%). During the hospitalization, only 4 patients (3%) had progressive hemodynamic instability. Their PE-related hospital mortality was 1.5%. The long-term follow-up chest CT and subsequent echocardiography were done in 56 (42%) and 58 (44%) patients, respectively. Among 76 patients with long-term follow-up, 19 (25%) had progression to chronic PE.

Conclusion: The clinical outcome of most patients with submassive PE was favourable with anticoagulant therapy alone. A prospective multi-centre study will be needed.

AO135

PREVALENCE OF VENOUS THROMBOEMBOLISM AMONG ADULT PATIENTS DIAGNOSED WITH CANCER AT ST. LUKE'S MEDICAL CENTER FROM 2010-2015

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Background and Aims: Venous thromboembolism (VTE) and its complications are reported to be the second most common cause of mortality in patients with cancer.⁸ In Asia, incidence of VTE is underestimated probably due to limited epidemiological data, genetic predisposition, underdiagnoses or low awareness.¹⁹ Although malignancy is a known common risk factor for VTE, there is no published local data made as to its prevalence and risk factors across different cancer subtypes and staging. This is a retrospective institutional review on prevalence of Venous Thromboembolism in a 600 bed-capacity Philippine tertiary hospital.

Methods: This is a single-centre retrospective cross-sectional study which included all patients aged 18 years old and above histologically diagnosed with cancer, and who had computed tomography pulmonary angiography and/or venous duplex done in St. Luke's Medical Center Quezon City from 2010 to 2015.

Results: A total of 10,577 cancer patients were recorded from the St. Luke's Medical Center- Quezon City Cancer Institute Logbook from 2010-2015. Among cancer patients recorded 2,926 of them had undergone venous duplex and/or CTPA combined. Positive VTE cancer patients were 208. Ninety one patients (43.8%) had acute thromboembolism, 98 (47.1%) had sub-acute to chronic VTE, while 19 patients (9.1%) had pulmonary embolism. Mean age is 61.33 with a female predominance with 60.0% and mean BMI of 25.63 (SD = 6.22). Most patients had hypertension 47.8% and diabetes 31.7%. Most patients presented with swelling and enema with 53.4% followed by pain (33.3%). Breast carcinoma is the most common (17.7%) among the cancer subtype from the samples with cancer. This was followed by lung carcinoma which was approximately 14.8%. Out of 208 patients, 57.9% were in stage I-III.

Conclusion: Despite modern advances and recent researches, VTE is still underestimated and underrecognized. Adequate work-up is

warranted and local registry is recommended to keep track of the actual national prevalence and/or incidence in general.

Distribution of venous thromboembolism according to cancer subtypes

Cancer Subtypes:	Acute	Subacute	Pulmonary Embolism	Total
Breast	11(5.3%)	23(11.1%)	3(1.4%)	37(17.8%)
Lung	10(4.8%)	15(7.2%)	6(2.9%)	31(14.9%)
Cervical	13(6.2%)	4(1.9%)	1(0.5%)	18(8.7%)
Endometrial	6(2.9%)	0(0%)	0(0%)	6(2.9%)
Ovarian	6(2.9%)	7(3.4%)	2(1.0%)	15(7.2%)
Colon, Rectal	8(3.8%)	22(10.6%)	2(1.0%)	32(15.4%)
Esophageal, gastric	9(4.3%)	1(0.5%)	1(0.5%)	11(5.3%)
Thyroid	1(0.5%)	0(0%)	0(0%)	1(0.5%)
Lymphoma	3(1.4%)	2(1.0%)	1(0.5%)	6(2.9%)
Others	13(6.2%)	14(6.7%)	0(0%)	27(13.0%)
Pancreatic, hepatocellular	11(5.3%)	10(4.8%)	3(1.4%)	24(11.5%)
Total	91(43.8%)	98(47.1%)	19(9.1%)	208(100.0%)
Staging:				
Stage I – III	52(43.3%)	63(52.5%)	5(4.2%)	120(100.0%)
Stage IV	39(44.3%)	35(39.8%)	14(15.9%)	88(100.0%)
Total	91(43.8%)	98(47.1%)	19(9.1%)	208(100.0%)

AO136

FACTORS RELATED TO PULMONARY HYPERTENSION IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Background and Aims: HIV patients are likely to have cardiovascular events when compared with the general population. This may be due to combination of traditional risk factors, inflammation associated with HIV infection, and the effects of Anti Retroviral Therapy (ART). Pulmonary hypertension is one of the cardiovascular complications of HIV infection associated with significant mortality. Pulmonary hemodynamic evaluation through echocardiography aims for early detection and prevention of morbidity. This study aims to determine the incidence of pulmonary hypertension in HIV/AIDS patients and analyze the factors affect it.

Methods: We studied 59 HIV patients at Wahidin Sudirohusodo Hospital Makassar using an observational cross sectional method. Each subject underwent an echocardiography examination to measure the value of Mean Artery Pulmonary Pressure.

Results: Mean age was 31 years, male dominated by 44 people (74%) with BMI 16.6 kg/m². There were 36 patients (61%) who detected PH with mPAP 30.44 mmHg. There was a significant correlation between Cluster of Differentiation 4 with mPAP ($P = 0.03$, $R = -0.276$) and IMT value with mPAP ($P = 0.007$, $R = -0.349$). Subjects with PH had lower CD4 values than non-PH subjects (162 vs 245, $P = 0.04$), lower BMI values (16 vs 17, $P = 0.005$), higher levels of C-Reactive Protein non-PH subjects (43 vs 17, $P = 0.03$), and on PH subjects had an average of 7 months of ART treatment compared to non-PH subjects who had a mean duration of ART at 12 months ($P = 0.04$). In this study it was also found that Tuberculosis Coinfection did not affect the incidence of pulmonary hypertension in HIV patients ($P = 0.35$).

Conclusion: A decrease in CD4 cell count is inversely related to an increase in mPAP value. Other factors such as BMI, CRP and duration of ART did not show a direct relationship to HP incidence.

AO137

TRENDS IN HOSPITALIZATION AND MORTALITY OF VENOUS THROMBOEMBOLISM FROM 2007 TO 2016 IN CHINA

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Background and Aims: Venous thromboembolism (VTE) has emerged as a major public problem in the western countries. But data on VTE burden in China mainland is seldom reported.

Methods: We collected data on patients with principal diagnose of VTE, pulmonary embolism (PE) or deep vein thrombosis (DVT) using the International Classification of Diseases-10 (ICD-10) from 90 hospitals across nearly whole China mainland. The trends in the hospitalization rate, mortality, length of stay (LOS) and comorbidities from 2007 to 2016 were analyzed.

Results: Totally, 105, 723 cases with VTE were identified, consisting of 43, 589 cases as PE and 62,134 cases as DVT alone. For VTE patients, the age-sex adjusted hospitalization rate increased from 3.2 to 17.5 per 100,000 population and in-hospital mortality decreased from 4.7% to 2.1% ($P < 0.001$). In addition, the mean LOS declined from 14 days to 12 days ($P < 0.001$). We further analyzed the data in 2016 and found the hospitalization rate of VTE was higher in elderly male patients (male vs female, 155.3 vs 125.4 per 100,000 population in ≥ 85 years old, $P < 0.001$) and northern China (north vs south, 18.4 vs 13.4 per 100,000 population, $P < 0.001$). Higher mortality rates were found in patients with cancer and Charlson Comorbidity Index > 2 . Similar trends were also observed in PE and DVT alone patients.

Conclusion: The hospitalization rate and comorbidities burden of VTE increased steadily, while the mortality rate sustained a decline. As a recent nationwide epidemiology research of VTE in China, this study provides important information of VTE burden.

Asthma 2

AO138

ALTERED AIRWAY TRANSCRIPTOMICS AFTER BRONCHIAL THERMOPLASTY TREATMENT IN SEVERE ASTHMATICS

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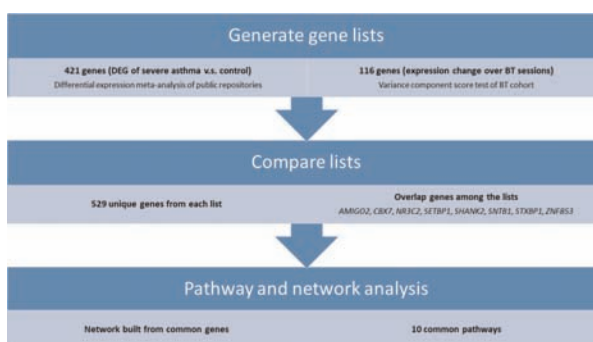
¹University of California-Davis, United States

Background and Aims: Bronchial thermoplasty is a non-pharmacologic, device-based treatment option for a select population of severe asthmatics that are resistant to standard therapies. However, the specific biological processes and pathways affected are poorly understood. The purpose of the study is to identify the pathways altered by bronchial thermoplasty using a transcriptomic approach and combining meta-analysis of public repositories and time-course longitudinal analysis of our bronchial thermoplasty dataset.

Methods: Patients undergoing bronchial thermoplasty were recruited to the study and a bronchial brushing sample was obtained before each bronchial thermoplasty session and sent for RNA sequencing. The schematic of our analysis work is shown in Figure 1. We first modelled gene expression changes over sequential bronchial thermoplasty sessions using the variance component score test. We then performed differential expression meta-analysis using data from public repositories. Overlapping genes between the identified gene lists were included for downstream pathway and network analyses using MetaCore.

Results: 12 patients were enrolled in the study with 25 RNA sequencing gene expression data sets obtained at sequential bronchial thermoplasty sessions. A total of 133 severe asthma cases and 107 healthy controls from the public repositories were included in the meta-analysis. The Rho GTPase family and 8 overlapping genes; including AMIGO2, CBX7, NR3C2, SETBP1, SHANK2, SNTB1, STXBP1, and ZNF853 were identified. Those overlap genes were included for downstream pathway and network analysis. Multiple pathways were found to be associated with neurophysiological processes and the cystic fibrosis transmembrane conductance regulator (CFTR).

Conclusion: These results establish that bronchial thermoplasty treatment alters several gene networks associated with neurophysiological processes involving CFTR and Rho GTPase family members. Future studies focused on these identified pathways will provide insight into how these changes lead to reduced asthma symptoms, and potentially identify specific asthma phenotypes that will benefit from this intervention.



AO139

CORRELATION BETWEEN FUNGAL ALLERGEN EXTRACTS AND COMPONENTS OF ASPERGILLUS FUMIGATUS SIGE SENSITIZATION IN PATIENTS WITH RESPIRATORY TRACT ALLERGIC DISEASES IN SOUTHERN CHINA

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Background and Aims: *Aspergillus fumigatus* is the most common airborne mycotic allergen. There is still a lack of detailed studies investigating allergy caused by crude mycotic allergen extracts allergy, and their correlation with *A. fumigatus* components. Objective: Analyse the sensitive of the mycotic allergen in patients with allergic respiratory diseases in Southern China.

Methods: We included 4033 patients with respiratory diseases that had undergone *A. fumigatus* allergen sIgE tests, and randomly selected 145 *A. fumigatus*-positive adults and 50 *A. fumigatus*-negative adults to simultaneously detect seven mycotic allergens including *A. fumigatus*, *Penicillium chrysogenum*, *Cladosporium herbarum*, *Mucor racemosus*, *Candida albicans*, *Alternaria alternate*, and *Helminthosporium halodes*, along with total IgE levels, and analyzed their correlation. Next, 72 *A. fumigatus*-positive patients and 7 *A. fumigatus*-negative patients were chosen for determining *A. fumigatus* components, Asp f 1, Asp f 2, Asp f 3, Asp f 4, and Asp f 6.

Results: In 4033 patients, 7.30% were positive for *A. fumigatus* allergen sIgE, with an average sIgE level of 1.10 (0.54–3.79) kU/L. Majority of fungus-positive incidents showed *A. fumigatus* accounting for 23.3% of all fungus-positive cases. Each tested fungus had a high positivity rate in the combined sIgE sensitization with *A. fumigatus* (84.6–100%).

A. fumigatus also showed correlation with all other fungi (0.51–0.82, $P < 0.05$). The correlation between *A. fumigatus* and Asp f 2 was the strongest ($r = 0.73$, $P < 0.01$). The positivity rate and sIgE levels of Asp f 6 were significantly higher in patients with ABPA than in patients with AS ($P < 0.05$).

Conclusion: Fungi have important sensitization effects in asthma and ABPA patients. Asp f 6 has a higher positive rate and concentration in ABPA patients, which can help identify ABPA and asthma.

AO140

SHORT TERM EFFICACY OF BENRALIZUMAB FOR SEVERE ASTHMATIC PATIENTS IN JAPAN

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Background and Aims: Benralizumab has been approved as an IL-5 target therapy for severe asthma in Japan since April 2018. Previous clinical trials demonstrated that benralizumab reduced asthma exacerbation, reduced systemic steroid use, and improved pulmonary function in severe eosinophilic asthma. Until now, there is no report of benralizumab use in severe asthmatic patients in clinical practice.

Methods: Eight severe asthmatic patients were received subcutaneous injection of benralizumab 30 mg per month. We assessed the asthma control (ACT, ACQ-5), asthma-related QOL (AQLQ), forced expiratory volume in one second (FEV1), symptom, exhaled nitric oxide (FeNO) level and reduction of systemic steroid use after one or two month-treatment of benralizumab.

Results: The mean age was 57.6 years, and the average duration of asthma was 33.8 years. The mean eosinophil count was 420.7 /microliter and the mean IgE level was 514.1 IU/ml. Half of the patients used oral corticosteroids (OCS) and 5 patients were treated with mepolizumab prior to benralizumab. The mean severe exacerbation rate was 3.8 per year under the GINA step 4 or 5 treatment. After one-month treatment, ACT score improved from 14.5 to 18.4, and ACQ-5 improved from 2.1 to 1.3 with complete depletion of peripheral eosinophils. AQLQ improved from 3.8 to 4.8 and 134 ml of FEV1 increased. FeNO level did not change. The reduction of OCS use was observed in two out of five patients. The comorbidity of eosinophilic sinusitis also improved in one patient.

Conclusion: Compared to mepolizumab, short term use of benralizumab improved asthma control, QOL, pulmonary function and reduced OCS use with complete elimination of peripheral eosinophils in Japanese patients with severe uncontrolled asthma.

AO141

EFFECTIVENESS OF ASTHMA EDUCATION FOR NURSES USING AN ASTHMA CARE APPLICATION COMPARED TO A WRITTEN ASTHMA ACTION PLAN IN THAILAND

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Background and Aims: Asthma education is crucial to prevent exacerbated symptoms and death. An Asthma Care Application (the app) was developed to provide self-care knowledge to reduce incidence of acute exacerbation of symptoms. The effectiveness, in terms of asthma

knowledge and satisfaction among nurses, of the app was compared to traditional written directions for asthma prevention and treatment.

Methods: Nurses dealing in one Bangkok Metropolitan Area (BMA) hospital's asthma care attended an asthma knowledge workshop organized by the Center of Excellence for Allergy, Asthma and Pulmonary Diseases, Thammasat Hospital. They were randomly divided into two groups, one using the app and the other a written asthma action plan as educational instruments. Workshops were presented by lecturers on two consecutive days. Data about asthma knowledge and sample satisfaction was obtained by questionnaire before and after each group's workshop. Group scores were compared to determine effectiveness.

Results: Forty-four nurses were enrolled in the seminar; 25 (57%) used the app, half of them in emergency department. This group revealed a significant increase in post-test asthma knowledge scores compared to pre-test statistics (91%, 75% respectively; $P = 0.002$). By contrast, the written asthma action plan group showed less significant improvement in post-test scores (89%, 80% respectively; $P = 0.135$). The app group also reported higher satisfaction scores in terms of ease of asthma action plan usage, reducing the number of hospital admissions, with convenient access due to portability ($P < 0.001$, $P = 0.026$, $P = 0.026$ respectively).

Conclusion: The app might be introduced to improve asthma knowledge and satisfaction among nurses in Thailand, compared to current written asthma action plans. More research on long-term benefits of the app with asthma patients would be indicated.

AO142

THE CLINICAL AND PATHOPHYSIOLOGICAL FEATURES OF COUGH-PREDOMINANT-ASTHMA

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Background and Aims: Asthma is a heterogeneous disorder presenting with many phenotypes, and recent interest is concentrated on the identification of phenotypes based on the pattern of inflammation in the airways and clinical symptoms. There are three types of asthma in our study, including cough variant asthma (CVA), cough predominant asthma (CPA) and classic asthma (CA). It is little known about the differences in clinical features and pathophysiology mechanisms of CVA, CPA and CA.

Methods: Asthmatic patients were enrolled and divided into CVA, CPA and NCPA. Questionnaires, spirometry, capsaicin cough challenge test, induced sputum test were performed in all patients. Cough severity was evaluated with VAS, symptom score and LCQ.

Results: A total of 461 patients with asthma were enrolled, with 111 CVA, 198 CPA and 152 CA. The prevalence of symptoms was as following: dyspnea (80.6%), wheeze (86.4%), cough (96.1%), chest tightness (56.4%). The major troublesome symptoms were dyspnea (43.6%), wheeze (41.9%), cough (60.4%), chest distress (7.8%). Compared with CA, patients with CPA had higher VAS score ($P < 0.001$) and lower LCQ score ($P < 0.001$). There were no significant differences in Eos% and Neu%, age, gender and combined diseases (AR, ST, GER and bronchiectasis) between CVA, CPA and CA. FEV1%pred, FEV1/FVC% and MMEF%pred were similar between CPA and CA. There was a higher trend of cough hypersensitivity in CPA patients as compared with CA (64% vs 36.4%, $P = 0.059$). Compared to the patients received standardized treatment (>3 months) and under controlled, patients received standardized treatment but without controlled had higher cough sensitivity and eosinophils in sputum ($P < 0.05$).

Conclusion: Cough is the most common and disturbing symptom in asthmatic patients, and mostly presented as the initial symptom. Cough hypersensitivity and eosinophilic airway inflammation may contribute to

the development of CPA. Further studies are needed for the mechanisms of CPA.

AO143

HIGH FRACTIONAL EXHALED NITRIC OXIDE LEVELS PREDICT SHORT-TERM WORSENING OF RESPIRATORY RESISTANCE

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Background and Aims: High fractional exhaled nitric oxide (FeNO) levels have been regarded as an indicator of asthma exacerbation. However, little is known about the effect of high FeNO levels on short-term course of lung function. The aim of this study was to assess whether high FeNO levels (> 35 ppb) would predict the short-term worsening of lung function.

Methods: This was a multicentre prospective observational study. Subjects included asthmatic patients who had routine check-ups at each institution from April 2015 to December 2016. Patients received standard treatment, including ICS and other medications, according to the asthma guidelines and the medications were not changed for at least 3 months. The asthma control test (ACT), spirometry, and forced oscillation technique (FOT) were performed before and after observation period. The patients were classified into high and low FeNO groups (FeNO $\geq$ 35 ppb or < 35 ppb) based on the baseline FeNO levels and the results were compared between the 2 groups.

Results: One hundred and four patients (mean age, 52 years and 49 males) completed the study without exacerbation. Overall, FeNO levels significantly decreased (mean, ppb: 34.7 to 31.1; $P = 0.0243$). However, there was no change in the ACT scores or lung function. A comparison between the groups revealed that FeNO improved significantly in the high FeNO group but not in the low FeNO group (mean, ppb: 58.9 to 44.7 and 23.9 to 25.1, respectively; $P < 0.001$). The difference between respiratory resistance at 5 Hz and 20 Hz (R5-R20), a parameter of FOT, significantly worsened in the high FeNO group but not in the low FeNO group (mean, cm H₂O/L/s: 0.41 to 0.54 and 0.49 to 0.48, respectively; $P = 0.032$). There was no difference in the ACT scores, spirometry, and other FOT parameters between the groups.

Conclusion: High FeNO levels predicts short-term worsening of respiratory resistance.

AO144

CAN FASTER ESCALATIONS IMPROVE THE EFFECTIVENESS OF ASTHMA ACTION PLANS?

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Background and Aims: Self-administered asthma action plans (AAPs) promote long term asthma control. The effectiveness of escalating inhaled corticosteroids in this setting is uncertain. (N Engl J Med 2018; 378:950-952). We hypothesize that delays in taking appropriate action steps may contribute to the failure of AAPs. Thus, the aim of this study was to evaluate the effectiveness of more rapid escalations of AAPs in the management of acute asthma exacerbations (AAEs).

Methods: This is a before Vs after study of consecutive adult patients attending an asthma clinic all of whom had previously received training in

AAPs. During the intervention period, we actively promoted the rapid escalation of self-management steps during AAEs with a 'KILAT' (lightning) AAP training program. We compared patient behaviour and clinical outcomes in AAEs before Vs after implementing the KILAT AAP. APP failure was defined as any unscheduled doctor and/or hospital visit for an AAE.

Results: When the KILAT APP was taught to the first 297 patients only 78 (26%) remembered it. After several iterations, this improved to 52%. The rapid escalation KILAT APP was applied in 418 AAEs. Before the KILAT escalation plan was implemented the APP failure rate was 109/342 (32%, 95%CI: 27%-37%) afterwards it was 111/418 (27%, 95%CI: 22%-31%) ($P > 0.05$). Rates of emergency department and/or hospital admissions were reduced from 56/342 (16%, 95%CI: 12%-20%) to 47/418 (11%, 95%CI: 8%-14%), $P < 0.05$. There was also a reduction in the % of patients who took oral prednisolone during AAEs from 64% (95%CI: 60%-69%) to 15% (95%CI:12%-18%).

Conclusion: We conclude that, despite poor adherence, faster escalations may improve the effectiveness of AAP in treating asthma exacerbations. Following our intervention there was a marked reduction in the use of oral steroid bursts. More robust studies are needed on the impact of adherence and timeliness on the effectiveness of AAPs.

AO145

THE CHARACTERISTICS OF SERUM HYDROXY- EICOSATETRAENOIC ACIDS IN ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

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Background and Aims: Hydroxy-eicosatetraenoic acids (HETEs) are a class of monohydroxy fatty acids that are metabolized by arachidonic acid (AA). They may be involved in the pathogenesis of asthma, but little is known about their potential roles in allergic bronchopulmonary aspergillosis (ABPA). This study was performed to evaluate serum HETEs in ABPA patients and to observe the changes of HETEs levels during treatment.

Methods: Sera from ABPA (N = 20), fungal associated asthma (FAA, N = 15), non-fungal associated asthma (NFAA, N = 23) patients and the healthy controls (N = 12) were assessed for 14 eicosanoids by using ultra-high performance liquid chromatography-quadrupole-time of flight/MS (UHPLC-Q-TOF/MS). In addition, sera from 12 ABPA patients were collected at 1, 2, 3, 6 months after treatment in our hospital.

Results: Compared with FAA and NFAA subjects, ABPA subjects expressed lower levels of serum AA, 15(S)-HPETE, 12(S)-HPETE and 5(S)-HPETE ($P < 0.05$). However, their levels of serum 15(S)-HETE and 12(S)-HETE were higher than in NFAA subjects and HC groups ($P < 0.05$). After treatment, the serum levels of 15(S)-HETE, 12(S)-HETE, 11(S)-HETE, 8(S)-HETE and 5(S)-HETE in ABPA subjects all decreased with the decrease of Af. sIgE concentration. Additionally, in ABPA subjects, there was a positive correlation between serum AA and tIgE ($\rho = 0.649$; $P < 0.05$). Serum 11(S)-HETE was positively correlated with Af. sIgE, FVC and FEV1 respectively ($\rho = 0.659$, $P < 0.05$; $\rho = 0.753$, $P < 0.01$; $\rho = 0.800$, $P < 0.01$). Serum 15(S)-HETE was positively correlated with the ratio of FEV1/FVC ($\rho = 0.632$, $P < 0.05$). Simultaneously, both 12(S)-HETE and 15(S)-HETE showed a positive correlation with peripheral blood eosinophil count ($\rho = 0.683$, $P < 0.05$; $\rho = 0.681$, $P < 0.05$).

Conclusion: Our data suggest that the increased release of 15(S)-HETE, 12(S)-HETE and 11(S)-HETE in ABPA subjects might, at least partially, be a mechanism underlying ABPA. Furthermore, the novel

finding of serum levels of HETEs in ABPA patients during treatment indicates that HETEs may help in future in monitoring the progression of ABPA.

AOL002

VIETNAM HEALTHY LUNG PROGRAM – A SOLUTION TO FULFIL THE GAPS IN ASTHMA AND COPD MANAGEMENT

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Background and Aims: In Vietnam, unmet needs in respiratory diseases are quite challenging. National data showed only 29.1% of asthmatics were treated with preventative therapy[#] and 37.5% of COPD patients were reported severely symptomatic^{##}. Healthy Lung (HL) Program, a region-wide AstraZeneca initiative has been applied in Vietnam since 2017, focusing on improving care to patients. This program targets 3 main pillars: partnership and awareness, capacity and access, understanding and skills over 3 years with 1 million USD investment.

Methods: Healthy Lung (HL) program has been implemented in collaboration among: Medical Service Administration, MOH, Vietnam Tuberculosis and Lung Disease Association, Vietnam Respiratory Society, Society of Asthma–Allergy–Clinical Immunology of Ho Chi Minh City, and AstraZeneca. HL will establish, upgrade 150 Units for Management of Asthma, COPD Outpatient, maintain other well-performed units via various activities: patient clubs to raise awareness; screening programs for early diagnosis, treatment; medical education programs to improve healthcare provider capability in diagnosis, treatment, management; equipment sponsorship for diagnosis, treatment. To measure the impact of HL program (both clinical and economic outcomes), 2 studies are conducted on patients one year before and after admission to program

Results: Up to Sep'18, the program has supported to screen 1660 respiratory patients, educate 19 HCPs, increase awareness for 5745 patients, provide 1 spirometers, 434 nebulizers, 6 nebulizing stations. First unit was established in May 2018 at provincial hospital with high appraisal from hospital, community. Last 4 months of 2018, program aims to support the establishment, upgrading of 30 Units, providing access for 4,500 patients, 30 patient clubs to educate 1,800 patients; 12 screening programs to early diagnose 1800 patients; educate 60 doctors, nurses, technicians; 16 spirometers, 178 nebulizers, 100 nebulizing stations

Conclusion: HL program now and in the future, will fulfil the gaps in asthma, COPD management, thus reduce morbidity and lessen social economic burden in Vietnam

Tuberculosis 2

AO146

LYMPHOCYTE LEVELS ASSOCIATION WITH BACTERIAL LOAD AND PULMONARY LESION FORM IN MDR TB PATIENT FARAH VIDIAST^{1*}, ANDI PUJI PRATIWI¹, SARAH NAURA IRBAH¹, DIAH HANDAYANI²

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Background and Aims: Multi-drug resistant tuberculosis (MDR TB) is still a burden in Indonesia. There were 2.293 of cases registered in

2016 with only 54% of succeeded treatment in 2014. This disease severity shown in various manifestation, including bacterial load and lesion form. Many research has mentioned the great role of CD4 T lymphocyte in representing these manifestations. However, measuring CD4 T lymphocyte is still beyond Indonesian clinical practice. This study aims to analyze whether the regularly done lymphocyte levels measurement has association with these disease severities for its role in managing the disease.

Methods: This study uses cross-sectional design and 99 subjects from consecutive sampling at the biggest centre of MDR TB in Indonesia during May-September 2017. Subjects were diagnosed by Xpert MTB/Rif. The lymphocyte count and chest x-ray were conducted before treatment. Lymphocyte count was divided into 2 categories (normal, under normal) then its associations with bacterial load (positive, negative) and pulmonary lesion form (cavitary, no cavitary) were analyzed by chi-square using SPSS version 20.

Results: There were 54 males and 45 females in 41.9 ± 11.4 average of age. Majority of subjects has lymphocyte levels under normal (67.6%), +2 bacterial load (27.3%), no cavitary lesion (57.6%), and no diabetes (66.7%). Significant association of under normal lymphocyte level with positive bacterial load was found ($P = 0.008$) while cavitary lesion shows otherwise ($P = 0.854$). Therefore, the cross-tabulation shows there are proportional differences in each relation, which are 73.2% and 16.4% respectively.

Conclusion: It is possible to use lymphocyte level as a representation of disease severity in bacterial load aspect. Not being the major determinant of cavitary formation might underlie its insignificant finding in association with pulmonary lesion form. Majority of subjects has under normal lymphocyte level which indicates that MDR TB patient encounters immunity problem. Therefore, it should be included in the focus when treating the patients.

AO147

THE ADHERENCE AND ADVERSE EFFECT OF USING PREVENTIVE THERAPY FOR LATENT TUBERCULOSIS THERAPY AMONG KIDNEY TRANSPLANT CANDIDATES

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Background and Aims: For further control of tuberculosis (TB), one of the most common infectious disease worldwide, screening latent tuberculosis infection (LTBI) in high risk group and give preventive therapy is an important strategy. Three-month high-dose weekly isoniazid (H) and rifapentine (P) (3HP) are well-known for LTBI treatment in general population but the adherence and adverse effects (AE) of are not clear among kidney transplant candidates.

Methods: We enrolled kidney transplant candidates in a tertiary referred centre in northern Taiwan and screened the LTBI status using QuantiFERON-Gold In-tube. We suggested those with positive LTBI status receive preventive therapy and monitored the adherence and AE.

Results: There were 23 kidney transplant candidates enrolled. Ten of them received 3HP and Thirteen received 9-month daily isoniazid (9H). The average age and sex were similar between the two groups. There were two (20%) in the 3HP group and six (46%) in the 9HP group discontinued the treatment ($P = 0.192$). The discontinuation reason was drug AE in 100% ($n = 2$) and in 17% ($n = 1$) in the 3HP and the 9HP groups, respectively ($P = 0.035$). For those without drug AE, the adherence was higher patients received 3HP than the 9H group (100% vs 58%, $P = 0.035$). In regard to the AEs, one (7%) patient in the 9H group had Grade 2 malaise and vomiting whereas eight (80%) in 3HP group had $\geq$ Grade 2 AEs ($P < 0.001$) including two with $\geq$ Grade 3. Generalized

weakness and malaise required rest (50%) were the most common AE and vomiting (20%) as well as fever (20%) were the second common.

Conclusion: For kidney transplant candidates, the adherence of 3HP regimen for LTBI treatment is better than that of 9H regimen. But the overall occurrence of AEs is higher in the 3HP treatment, which needs further investigation and improvement.

AO148

TREND OF MULTIDRUG-RESISTANT TUBERCULOSIS OVER 20 YEARS: DRUG RESISTANCE, TREATMENT OUTCOMES, AND ADVERSE EVENTS

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Background and Aims: Multidrug-resistant (MDR)-tuberculosis (TB) still remains as a global health threat. The aim of this study is to investigate the trend of drug resistance, treatment modalities and outcomes, and adverse events over the last two decades in a referral centre in South Korea, a country with intermediate TB burden.

Methods: MDR-TB patients who were treated at Seoul National Hospital University between 1996 and 2015 were divided by five years according to the date of initial diagnosis. The changes of demographic characteristics, drug resistance, drugs used, treatment outcomes, and adverse events over time was evaluated using nonparametric test for trend across ordered groups.

Results: Between 1996 and 2015, 418 patients were treated as MDR-TB; 86 patients between 1996 and 2000 (cohort 1), 125 between 2001 and 2005 (cohort 2), 123 between 2006 and 2010 (cohort 3), and 84 between 2011 and 2015 (cohort 4). Body mass index of patients have been increasing gradually from 19.0 kg/m² in cohort 1 to 20.9 kg/m² in cohort 4 ($P = 0.007$). The proportion of patients with positive acid-fast bacilli staining of sputum (from 60.5 to 29.7%, $P < 0.001$) or cavities (from 86.0% to 40.5%, $P < 0.001$) on chest radiographs decreased over time. Resistance to pyrazinamide, fluoroquinolone, cycloserine, and p-aminosalicylic acid decreased over time. For treatment, later-generation fluoroquinolone (from 77.9 to 90.5%) and linezolid (from 0 to 26.2%) were more frequently prescribed recently. The treatment success rate increased from 45.3 to 88.1% over 20 years ($P < 0.001$). However, neurologic adverse events including peripheral neuropathy increased from 4.7 to 13.1% ($P = 0.027$).

Conclusion: Over last 20 years, MDR-TB patients were presented with less severe disease with better resistant profiles. With more frequent use of FQs and new drugs, treatment outcomes have been improving continuously.

AO149

INITIAL IMPLEMENTATION OF SHORTER REGIMEN FOR MDR-TB IN DR. SOETOMO HOSPITAL, SURABAYA: THE PROPORTION BETWEEN ELIGIBILITY AND INELIGIBILITY SOEDARSONO^{1,2}

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Background and Aims: In May, 2016, WHO launched new guidelines for the management of MDR-TB, including a recommendation of Shorter Regimen (STR). The following criteria for eligibility for the STR in Indonesia are: no resistant to fluoroquinolone/ second-line injectable drugs;

no contact with pre/XDR TB patients; no exposure for ≥ 1 months to second-line medicines in the STR; no intolerance to medicines in the STR; no pregnancy; no severe extra pulmonary TB; no severe lung defect with underweight BMI. Indonesia started to implement the STR since October 2017 where the target aimed was 80% of MDR-TB patients received the STR. The purpose of the study is to evaluate the eligibility of MDR TB patients to be given STR as the first choice of regimen as recommended by WHO, applied by Dr. Soetomo Hospital, which is the centre of East Indonesian MDR-TB referral hospital.

Methods: This was a descriptive study. From the data of registry, we analyzed phenotypic DST results to the constituent drugs, taking history, laboratory and chest X-Ray of all RR cases diagnosed based on gene Xpert in, from October 2017 to July 2018, to determine their eligibility for this regimen.

Results: There are 150 RR/MDR-TB patients. 105 (70%) are Eligible STR and 45 (30%) are Ineligible. From 45 Ineligible STR patients, there are 17 (37.8%) patients are resistant to fluoroquinolone/ second-line injectable drugs, 1 (2.2%) is exposed for ≥ 1 months to second-line medicines, 1 (2.2%) has contact with XDR patients, 2 (3.4%) are intolerance to medicines in the STR, and 24 (53.3%) have severe lung defect with underweight BMI.

Conclusions: There are 105 (70%) patients are eligible to STR and 45 (30%) are ineligible from total 150 RR/MDR TB patients. The major cause of ineligibility in this study is due to the severe lung defect with underweight BMI.

Keywords: MDR-TB, Shorter Regimen.

AO150

CHYLOUS EMPYEMA AND SECONDARY SPONTANEOUS PNEUMOTHORAX COMPLICATING PULMONARY TUBERCULOSIS

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Background and Aims: Empyema is a complication of a parapneumonic effusion. Chylothorax is caused by traumatic and non-traumatic aetiologies. Secondary spontaneous pneumothorax occurs in those with pulmonary diseases. An aetiology which can cause the occurrence of all these three diseases is PTB. Reports of an exudative effusion fulfilling the criteria for both chylothorax and empyema, complicated with pneumothorax, on the background of PTB, are rare.

Methods: We report the case of a patient with infected chylothorax and pneumothorax secondary to PTB.

Results: A 76-year-old, male, with a complaint of cough, dyspnea and weight loss. Medical history was significant for hypertension, diabetes and COPD. Physical examination revealed crackles heard on the right lung and decreased breath sounds on the left. The intercostal tube drained 0 to 200 cc of non-foul-smelling, turbid, milky fluid per day. HIV test was negative. CXR and chest CT showed multiple bilateral pulmonary nodules, cavitations, pneumonia with consolidation and pneumothorax on the left. Upon centrifugation, the pleural fluid remained milky. Pleural fluid analysis yielded an exudative effusion with the following results: pH 6.5, wbc 5.9×10^9 , lymphocytes 76%, glucose, total cholesterol 23 mg/dl, TG 17 mg/dl. Pleural fluid/serum cholesterol ratio was 0.18, while pleural fluid/serum TG was 0.11. Pleural fluid culture grew *Acinetobacter* sp. Pleural fluid and endotracheal aspirate TB culture were positive for *Mycobacterium tuberculosis*. No evidence of malignancy was detected after thorough investigation. He was started on antibiotics and anti-TB therapy.

The coexistence of empyema and chylothorax is rare because of the bacteriostatic nature of chyle, more so is TB as a cause of chylothorax. In

a systematic review, only 37 cases of chylothorax secondary to PTB have been reported in literature.

Conclusion: Fascination on the rarity of the case described above lies in that it concurrently fulfilled the criteria for both empyema and chylothorax secondary to PTB.

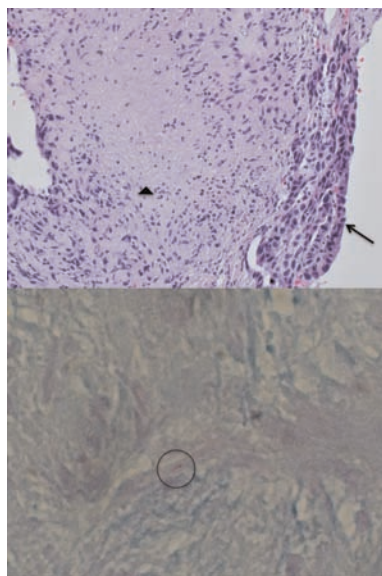
AO151

LUNG CANCER AND TUBERCULOSIS: COMPLEXITIES IN DIAGNOSIS AND MANAGEMENT

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Background and Aims: A 64-year old male, never smoker was hospitalized for increasing dyspnea due to a right malignant pleural effusion. CT thorax performed 3 weeks ago at another hospital reported a right upper lobe nodule with pleural effusion and ascites. He underwent thorascopic pleural biopsy, and talc poudrage. Repeat CT showed a spiculated right upper lobe nodule, mediastinal lymphadenopathy, pericardial effusion, ascites, peritoneal nodules and splenic nodules presumed to be metastatic disease. However, the pleural biopsy revealed acid-fast bacillus (AFB), caseating granulomas with Langhans' giant cells co-existing with adenocarcinoma stained TTF-1 positive (see image of pleural biopsy sample histology, showing necrotizing granulomatous inflammation (arrowhead) coexisting with adenocarcinoma cells (arrow) and acid fast bacillus (circle)). A transthoracic echocardiogram showed effusive-constrictive pericarditis supported by signs of distended jugular venous pressure and bilateral leg edema consistent with right heart failure. The patient underwent pericardial window creation as well as abdominal paracentesis. Pericardium, pericardial fluid and abdominal fluid were negative for malignancy, but cultures from peritoneal fluid and pericardium were positive for mycobacterium tuberculosis complex sensitive to first line anti-tuberculosis drugs. He was treated for TB with resolution of splenic and peritoneal disease and ascites.



Methods: nil

Results: This case illustrates the unique challenge of diagnosis and management of concurrent lung cancer and tuberculosis (TB). When TB and lung cancer are present in an individual, it is difficult to diagnose since both share similarities in symptoms, signs and imaging. Their confluence also raises management considerations such as duration of TB treatment, role of steroid therapy for TB pericarditis, and assessment of clinical response to lung cancer treatment.

Conclusion: Prompt diagnosis and early institution of anti-TB therapy together with afatinib are key to the favourable clinical response observed in our patient.

AO152

RESISTANCE PATTERN AMONG DRUG-RESISTANT TUBERCULOSIS PATIENTS IN INDONESIA

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Background and Aims: Background: Drug-resistant tuberculosis is a problem of tuberculosis eradication program in Indonesia. Resistance pattern of Mycobacterium tuberculosis become important to understand. The aim of this study is to know the pattern of tuberculosis drug resistance based on patients characteristics and the type of drug resistance.

Methods: Method: This is a descriptive analysis using baseline data from ongoing TB cohort study on drug resistance (TRIPOD). This study started to enrol the subjects on February 2017. Of 88 tuberculosis patients, 48 (54%) patients were drug resistance tuberculosis. Method: This is a descriptive analysis using baseline data from ongoing TB cohort study on drug resistance (TRIPOD). This study started to enrol the subjects on February 2017. Of 88 tuberculosis patients, 48 (54%) patients were drug resistance tuberculosis. Method: This is a descriptive analysis using baseline data from ongoing TB cohort study on drug resistance (TRIPOD). This study started to enrol the subjects on February 2017. Of 88 tuberculosis patients, 48 (54%) patients were drug resistance tuberculosis.

Table 1. Resistance pattern based on drug resistance type and patient characteristics

Drug resistance type	Age (years) mean (range)	Male n (%)	Comorbid n (%)	Resistance Pattern
Mono resisten (n=8)	42 (24 – 52)	6 (75%)	HIV=0 DM=3 (38%)	Resistant to R (n= 4) H (n=1) S (n=1) E (n=2)
Poli resisten (n=7)	41 (20 – 66)	4 (57%)	HIV=0 DM=3 (43%)	Resistant to H-S (n=1) R-E (n= 2) E-S (n=1) R-Oflox (n=1) R-S (n= 2)
MDR (n=31)	42 (19 – 61)	14 (45%)	HIV=0 DM=9 (30%)	Resistant to R-H (n=5) R-H-S (n=2) R-H-E (n=10) R-H-E-S (n=14)
Pre XDR (n=2)	32 (23 – 41)	1 (50%)	HIV=0 DM=1 (50%)	Resistant to R-H-E-Oflox (n=1) R-H-E-S-Oflox (n=1)
XDR (n=0)	-	-	-	-

R=Rifampicin, H=Isoniazid, E=Ethambutol, S=Streptomycin, Oflox=Ofloxacin

Results: Results: Of 48 drug resistant tuberculosis patients, 8% was Rifampicin monoresistance, 8% was other monoresistance, 15% was polyresistance, 65% was MDR-TB, and 4% was Pre-XDR-TB. All type of drug resistance have Diabetes Mellitus as a co-morbid in about 40%

patients. Resistance pattern based on drug resistance type and patient characteristics can be seen in following table.

Conclusion: Conclusions: MDR-TB was the highest number of drug-resistant tuberculosis. Diabetes Mellitus was a co-morbid in all drug resistance type.

AO153

SEVEN DAYS OF FLUOROQUINOLONE EXPOSURE PRIOR TO TUBERCULOSIS DIAGNOSIS IS ASSOCIATED WITH AN INCREASED RISK OF MORTALITY

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Background and Aims: Empirical use of fluoroquinolones (FQs) prior to tuberculosis (TB) diagnosis may improve the initial clinical symptoms and delay the initiation of anti-tuberculosis therapy. This study aimed to investigate the impact of the duration of FQ use prior to TB diagnosis on clinical outcomes in northern Taiwan.

Methods: 306 TB patients were diagnosed at Tri-Service General Hospital, Taipei, Taiwan between 2013 and 2015. Groups of patients who were exposed to FQ for at least 7 days or for less than 7 days prior to TB diagnosis were defined as long-term FQ (days; LT-FQ) and short-term FQ (ST-FQ) groups, respectively.

Results: Long term FQ exposure prior to TB diagnosis significantly increased the risk of mortality (Odds ratio = 3.00; 95% CI for OR = 1.21–7.47). Of the 306 patients identified, 21 (6.86%) were in the LT-FQ group and 285 (93.14%) were in the ST-FQ group. Compared to the ST-FQ group, patients in LT-FQ group were older (LT-FQ vs ST-FQ = 75 vs 62); with a decreased positive rate of acid-fast bacilli (AFB) smear in initial sputum examinations (19% vs 41%) and increased rate of mortality (43% vs 20%). The rate of TB PCR tests performed was significantly lower in LT-FQ group than in ST-FQ group (43% vs 68%; $P = 0.02$). However, there are no significant differences between the rates of TB cultures (91% vs 86%) and TB PCR (89% vs 75%).

Conclusion: Fluoroquinolone exposure for at least 7 days prior to tuberculosis diagnosis is associated with a lower rate of positive AFB smears and a higher rate of mortality. TB PCR could be a good method for patients with a history of FQ use.

Cell and Molecular Biology

AO154

IMMUNOLocalization of Zinc Transporters and Metallothioneins Supports a Potential Role of Zinc in Endothelium-Smooth Muscle Cross Talk in Vascular Physiology and COPD

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Background and Aims: Cardiovascular-related comorbidities are known contributors to morbidity and mortality in COPD. Zinc homeostasis has vital physiological functions throughout the body and we have shown its dysregulation in the epithelium in response to cigarette smoke. Its role however, in mechanisms underlying vasculature dysfunction/inflammation in COPD are unknown. We hypothesized that zinc flux may also regulate signalling pathways in the microvasculature in COPD. As a first step in tackling this hypothesis we analyzed the expression of proteins responsible for zinc homeostasis in endothelium and smooth muscle of human microvasculature. Immunolocalization was related with components of the eNOS/MAPK axis, the key regulators in vasculature physiology and COPD.

Methods: Microvessels were isolated from adipose tissue biopsies donated by 12 non-smoker patients undergoing hernia surgery. Expression/localization of zinc transporters (ZIPs, isoforms 1, 2, 4, 8, 12 and 14), zinc binding/storage proteins metallothioneins (MTs, isoforms 1/2 and 3), eNOS, and p38 MAPK (including their phosphorylated isoforms) were investigated by immunofluorescence and confocal microscopy and ImageJ quantification.

Results: In the human microvasculature, the endothelium was found to be the major harbour of all tested ZIPs (ZIP1, ZIP8, ZIP12, ZIP4, ZIP14 and ZIP2, in order of brightness), with abundant expression of p38 MAPK and eNOS. ZIPs were less abundantly in the smooth muscle, revealing mostly nuclear patterns. Metallothioneins however showed brighter immunofluorescence in the smooth muscle than endothelium. Furthermore the active forms of eNOS (Ser1177-phosphorylated) and p38 MAPK (Thr180/Tyr182-phosphorylated) were localized to different compartments of the microvasculature, with eNOS-P mostly in the smooth muscle but p38 MAPK-P in the endothelium. Correlation analyses are pending.

Conclusion: We show, for the first time, expression of proteins responsible for zinc homeostasis in human microvasculature. Their differential immunolocalization and the eNOS/p38 MAPK phosphorylation suggests a potential role of zinc flux in microvasculature endothelium-smooth muscle cross talking in vasculature physiology and COPD.

AO155

MITOFUSINS IN TYPE 2 ALVEOLAR CELLS ARE REQUIRED FOR METABOLIC ADAPTATION IN PULMONARY FIBROSIS

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Background and Aims: Mitochondrial dynamics are required for metabolic adaptations under stress. Growing evidence suggests mitochondrial damage and altered mitochondrial dynamics in alveolar type 2 (AT2) cells might be related to the pathogenesis of idiopathic pulmonary fibrosis (IPF). However, the roles of mitofusins (MFN) in the biology of AT2 cells and in IPF pathogenesis are still unknown.

Methods: To elucidate the AT2 cell-specific function of MFN1 and MFN2, we employed an inducible knockout strategy to selectively delete *MFN1* and *MFN2* genes in adult murine AT2 cells. We further examined whether loss of MFN1 or MFN2 in AT2 cells could potentiate bleomycin-induced pulmonary fibrosis. Multidisciplinary approaches, including ultrastructural and histology examination, transcriptomic and lipidomic analyses, were applied to explore the mechanisms.

Results: We report the striking phenotype of spontaneous pulmonary fibrosis in mice with MFN1 and MFN2 deletion specifically in AT2 cells. Deletion of mitofusins in AT2 cells results in accumulation of damaged mitochondria, activation of mitochondrial stress responses, and profound inhibition of lipid synthesis. Through bleomycin model of pulmonary fibrosis, we find bleomycin-induced mitochondrial damage in AT2 cells are

accompanied by increased lipid synthesis. We further uncover both MFN1 and MFN2 are essential in upregulating lipid synthesis in AT2 cells after bleomycin exposure, and show mice with deficiency of MFN1 or MFN2 in AT2 cells are more susceptible to bleomycin-induced pulmonary fibrosis and mortality.

Conclusion: Our data together reveal the novel function of MFN1 and MFN2 in lipid metabolism, and highlight 'maladaptive' mitochondrial damage in AT2 cells as a potential pathogenic mechanism of pulmonary fibrosis.

AO156

NEW INSIGHTS OF THE PATHOLOGY OF PULMONARY FIBROSIS REVEALED BY METABOLOME ANALYSIS ~ANTI-FIBROTIC FACTOR STANNIOCALCIN1 (STC1) AND SYSTEMIC DAMAGE RESPONSE~

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Background and Aims: In previous study, we showed that stannioalcin-1 (STC1) released from mesenchymal stem cells (MSCs) control the mitochondrial uncoupling respiration of alveolar macrophages and lung epithelial cells under oxidative and endoplasmic reticulum stresses though upregulation of uncoupling protein 2 (UCP2). STC1 intra-tracheal injection ameliorate bleomycin induced pulmonary fibrosis in animal model. However, STC1 has myriad functions in injured tissue such as keeping calcium and phosphate homeostasis, inducing early wound healing and inhibiting activities of activated macrophage. Uncoupling respiration could not cover STC1 myriad functions. Therefore, we intended to the metabolome analysis for explaining the myriad function of STC1 to keep homeostasis.

Methods: Human lung epithelial (A549, H1299) and fibroblast (MRC5, HFL1) cell lines were cultured with/without recombinant STC1 50 ng/ml (Bio-vendor) for 48 h. Metabolome (capillary electrophoresis and liquid chromatography-mass spectrometry (LC/MS)) were done by Human metabolome Technology (HMT, Tokyo) and Tohoku University Tohoku Medical Megabank Organization (ToMMO, Sendai). Bisulfite analysis was done using Bisulfite Conversion Kit and DNA Polymerase (291-78501, 293-78501 Wako Fujifilm, Tokyo).

Results: The results showed that STC1 control the cysteine and methionine metabolism strongly. This pathway regulates the methylation and de-methylation of DNA and histone and the synthesis of DNA, reactive sulfur species (RSS) with redox activities, and manage the stress response of the organs. Bisulfite analysis reveal that STC1 reduce methylation of anti-fibrotic gene X and upregulates gene X expression. These things suggest new insights of pathology of pulmonary fibrosis to us.

Conclusion: STC1 derived from MSCs may manage epigenetics and redox balances in fibrotic environment and keep homeostasis in lung.

EXPERIMENTAL LUNG INJURY REDUCES KRÜPPEL-LIKE FACTOR 2 TO INCREASE ENDOTHELIAL PERMEABILITY VIA REGULATION OF RAPGEF3-RAC1 SIGNALING

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Background and Aims: Acute respiratory distress syndrome (ARDS) is caused by widespread endothelial barrier disruption and uncontrolled cytokine storm. Genome-wide association studies (GWAS) have linked multiple genes to ARDS. Although mechanosensitive transcription factor Krüppel-like factor 2 (KLF2) is a major regulator of endothelial function, its role in regulating pulmonary vascular integrity in lung injury and ARDS-associated GWAS genes remains poorly understood. The objectives of this study are to examine KLF2 expression in multiple animal models of acute lung injury and further elucidate the KLF2-mediated pathways involved in endothelial barrier disruption and cytokine storm in experimental lung injury.

Methods: Animal and in vitro models of acute lung injury were used to characterize KLF2 expression and its downstream effects responding to influenza A virus (A/WSN/33 [H1N1]), tumor necrosis factor- α , LPS, mechanical stretch/ventilation, or microvascular flow. KLF2 manipulation, permeability measurements, small GTPase activity, luciferase assays, chromatin immunoprecipitation assays, and network analyses were used to determine the mechanistic roles of KLF2 in regulating endothelial monolayer integrity, ARDS-associated GWAS genes, and lung pathophysiology.

Results: KLF2 is significantly reduced in several animal models of acute lung injury. Microvascular endothelial KLF2 is significantly induced by capillary flow but reduced by pathologic cyclic stretch and inflammatory stimuli. KLF2 is a novel activator of small GTPase Ras-related C3 botulinum toxin substrate 1 by transcriptionally controlling Rap guanine nucleotide exchange factor 3/exchange factor directly activated by cyclic adenosine monophosphate, which maintains vascular integrity. KLF2 regulates multiple ARDS GWAS genes related to cytokine storm, oxidation, and coagulation in lung microvascular endothelium. KLF2 overexpression ameliorates LPS-induced lung injury in mice.

Conclusion: Disruption of endothelial KLF2 results in dysregulation of lung microvascular homeostasis and contributes to lung pathology in ARDS.

AO158

TREATMENT WITH TRICHOSTATIN A RESTORES SENSITIVITY TO GEFITINIB AND IMPAIRS CANCER STEM CELLS FEATURES IN EGFR-MUTANT NON-SMALL CELL LUNG CANCER CELLS

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Background and Aims: The epigenetic modifications in cancer stem cells (CSCs) that result in chromatin condensation are mediated by histone deacetylase (HDAC). We have previously investigated the presence of gefitinib-resistant-persisters (GRP) population within the non-small cell lung cancer (NSCLC) cells that possess CSCs features. In the current study, we aimed to examine the possible impact of HDAC inhibition on the stem CSC features and EGFR sensitivity in NSCLC with EGFR mutation.

Methods: NSCLC cell lines with EGFR mutation, PC9 and HCC827, were treated with high concentration of gefitinib and the remaining small population of surviving cells were termed as gefitinib-resistant-persisters (GRPs). HDACs, including HDAC1 until HDAC11, were used as markers of chromatin compaction in GRP of PC9 and HCC827 cells. We injected PC9 cells into immuno-deficient mice and, once the tumor growth, we started the treatment with gefitinib. Gefitinib-resistant tumor (GRT) was established by obtaining the remaining tumor in PC9-injected mice after two weeks of gefitinib treatment.

Results: Among all HDACs that were tested, we found high expressions of HDAC1, HDAC2, and HDAC5 in PC9-GRP and HCC827-GRP cells. HDAC1 mRNA and protein were also showed upregulation in PC9-GRT as compared to the naïve PC9 tumor. Importantly, treatment with HDAC inhibitor Trichostatin A increased the sensitivity of PC9 and HCC827 cells, as well as GRP cells, to gefitinib. Furthermore, inhibition of HDAC reduced stem cells factors expressions and reduced sphere numbers of GRP. Finally, HDAC1 was also highly observed in lung cancer biopsy specimens from lung cancer patients with acquired resistance to gefitinib.

Conclusion: These findings suggest that HDAC inhibition by Trichostatin A might be considered to impairs the CSC features and eventually restores the sensitivity of NSCLC to EGFR-TKI.

AO159

REGULATIONAL MECHANISM OF CELL MOTILITY AND GM-CSF SECRETION BY P116RIP VIA MYOSIN AND CREB PHOSPHORYLATION IN HUMAN LUNG FIBROBLASTS

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Background and Aims: p116Rip binds to cytoskeletal components such as myosin, actin, and myosin phosphatase. Although p116Rip is expressed in the lungs, its role in pulmonary disorders has never been investigated. Fibroblasts, in particular, affect pulmonary airway remodeling in asthmatic disease caused by the release of pro-inflammatory cytokines due to eosinophilic inflammation. Among them, GM-CSF contributes to lifetime extension and maintenance of eosinophils causing airway remodeling. We previously observed that CREB phosphorylation in the p38MAP kinase signaling plays an important role in TNF- α -induced GM-CSF secretion (Koga et al. Allergol. Int. 2016;65:406-413).

Here, we investigated the effects of p116Rip on TNF- α -induced GM-CSF secretion, CREB phosphorylation, and cell motility in human lung fibroblasts.

Methods: TNF- α -induced GM-CSF secretion, phosphorylation of CREB and myosin light chain, and cell motility were each evaluated using ELISA, western blot, and wound healing and migration analysis, respectively.

Results: CREB knockdown in fibroblasts decreased TNF- α -induced GM-CSF secretion. p116Rip knockdown in fibroblasts, using p116Rip-specific siRNA, enhanced TNF- α -induced GM-CSF secretion and CREB phosphorylation. Furthermore, p116Rip knockdown increased myosin light chain phosphorylation and enhanced cell motility after PDGF stimulation.

Conclusion: p116Rip regulates TNF- α -induced GM-CSF secretion by modulating CREB phosphorylation. p116Rip also controls cell motility by regulating myosin light chain phosphorylation. Taken together, the results suggest that p116Rip may play an important role in eosinophilic pulmonary disorders by regulating GM-CSF secretion and cell motility.

A NOVEL PEPTIDE WKYMVM HAS THERAPEUTIC EFFECT VIA IRF7/STAT1 PATHWAY AGAINST ENDOTOXIN-INDUCED ARDS

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Background and Aims: There is no obvious treatment for acute respiratory distress syndrome (ARDS), although ARDS is a severe, acute inflammatory response within the lung, characterized by diffuse damage to alveolar-capillary barrier and crawling with protein-rich oedema fluid in airspaces resulting in serious gas-exchange abnormalities. In this study, we investigate whether the administration of novel peptide WKYMVM (Trp-Lys-Met-Val-D-Met), with immune-stimulating properties, protects against oedematous lung inflammation in endotoxin-induced acute lung injury (ALI) mice via activation of interferon-induced transcription factor and signal transducer and activator of transcription (STAT) signalling.

Methods: The WKYMVM peptide was intraperitoneally injected (2.5 and 5 mg/kg) daily for 4 days and then intratracheally injected lipopoly-saccharides from *E. coli* O26:B6 (1 mg/kg). The After 24 h, the mice was sacrificed and the oedematous lung was analysed. Infiltrated inflammatory cells in bronchoalveolar fluid (BALF) was validated using Wright-Giemsa method and H&E staining. The expression of pro-inflammatory cytokines, myeloperoxidase (MPO) activity expressed by neutrophil and nitric oxide (NO) level were measured with ELISA, MPO assay and Griess assay, respectively in BALF or serum. The protein levels of IRF/STAT were determined by Western blot analysis in lung tissues.

Results: After instillation of LPS with WKYMVM, the alveolar congestion, haemorrhage, neutrophil infiltration and alveolar wall thickness were mildly reversed compared with LPS group. The cytokine release and MPO activity were decreased in LPS with WKYMVM treated mice, but not NO production. Moreover, we verified that the WKYMVM reduced the increased protein level of IRF7 and phosphorylation of STAT1 in LPS group, but increased IRF1 was not regulated by WKYMVM.

Conclusion: We have shown the therapeutic ability of novel peptide WKYMVM and IRF7 and STAT1 are able to a critical signalling intermediate for endotoxin-induced ARDS mice.

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AO161

BIOLOGICAL EFFECTS OF PRETERM BIRTH ON AIRWAY DEVELOPMENT

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Background and Aims: Using a clinically relevant newborn sheep model, we aimed to separate the two strongly related conditions and to evaluate their biological effects/mechanisms independently on/in development of airway injuries.

Methods: For ontogenic study, the lambs were surgically delivered and euthanized either at 128 d gestational age (GA) ($n = 7$), 150 d full term ($n = 9$) or sacrificed 1 month after term delivery ($n = 9$). For infection study, pregnant ewes received ultrasound guided intra-amniotic injections of *U. parvum* serovar 6 ($n = 15$) or medium/untreated ($n = 8$) as controls at 55 d GA. Subsequently the lambs were delivered at 138 d GA. We

analysed the expression of three groups of genes in airway tissue, including genes associated with innate immunity (*CD14*, *TLR2*, *TLR4*, *TLR6*, *TLR10*, *NOD1*, *NOD2*); Th2-cell differentiation (*GATA3*, *FOXP3*, *TBX21*, *IL4*, *STAT6*, *IL12B*); epithelial biology (*CCL24*, *CCL26*). The specific genes with abnormal expression were further studied for functional expression and promoter methylation status.

Results: Out of 15 genes examined, six gene expression levels were changed with development. Specifically, *NOD1* was down-regulated from 128 d GA to postnatal 1 month, while *TLR2*, *TLR4*, *NOD2*, *FOXP3*, and *IL12B* tended to increase toward term, followed by a significant reduction at postnatal 1 month. Conversely, intra-amniotic infection did not alter the expression in these genes. Similarly, a consistent change of *NOD1*, *TLR4* and *FOXP3* protein expression was found in the developmental groups, and these protein contents remained similar between infection and control groups. Additionally, the CpG methylation in the promoter of *NOD1* and *TLR4* was significantly affected by development, negatively correlating with its mRNA level for *TLR4* ($r = -.416$, $P = 0.043$).

Conclusion: The increased risk of airway injuries in later life of pre-term infants is likely due to prematurity per se, rather than the infectious factors associated with preterm delivery. The underlying mechanisms are related to developmental regulation of innate immunity genes, partially through DNA methylation.

AO162

THE EFFECT OF OBESITY ON THE EXPRESSION OF $\alpha 7$ NICOTINIC ACETYLCHOLINE RECEPTOR IN LPS-INDUCED LUNG INFLAMMATION

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Background and Aims: Obesity is a metabolic disease that increases the risk of multiple lung disorders. It is well-known that chronic inflammation plays an important role in the pathogenesis of obesity. Particularly, $\alpha 7$ nicotinic acetylcholine receptor ($\alpha 7$ nAChR) mediates cholinergic anti-inflammatory signaling pathways that inhibit synthesis of cytokines and control inflammatory responses. However, it remains unclear whether and how the expression levels of $\alpha 7$ nAChR in lung are affected in the obesity model mouse.

Methods: Here we developed a mouse model of diet-induced obesity with high-fat diet (HFD), and we investigated the morphological changes of lung and measured the proportion of related cells and $\alpha 7$ nAChR+ cell population in these subpopulations, the expression levels of $\alpha 7$ nAChR simultaneously in normal condition and LPS-induced lung inflammation by using multicolour flow cytometry approached.

Results: We found that the subpopulation of $\alpha 7$ nAChR+ cells existed in neutrophils, monocytes, alveolar macrophages and pulmonary interstitial macrophages. The proportion of CD45+ cells in the lung of obese mice without LPS stimulation is higher than that in normal mice. The proportion of alveolar macrophage subpopulation in obese mice without LPS stimulation is higher than normal mice. The expression level of $\alpha 7$ nAChR in $\alpha 7$ nAChR+ pulmonary interstitial macrophages was increased in obese mice that were stimulated with LPS compared with normal mice.

Conclusion: Such findings indicate that the cholinergic anti-inflammatory pathway status is different between obese and normal mice, the difference is pronounced after LPS stimulation.

Respiratory Infections (Non-Tuberculous) 2

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CLINICAL CHARACTERISTICS OF COMMUNITY-ACQUIRED PNEUMONIA DUE TO *MORAXELLA CATARRHALIS* IN ADULTS: A RETROSPECTIVE SINGLE CENTER STUDY

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Background and Aims: Although *Moraxella catarrhalis* (*M. catarrhalis*) is one of the major pathogen in community-acquired pneumonia (CAP) in adult, clinical manifestation regarding CAP due to *M. catarrhalis* (MCAP) is still unknown. In fact, only a few case reports or investigations describing MCAP have been recorded in the past.

Methods: The aim of this study was to investigate the clinical comparison between MCAP and CAP due to *Streptococcus pneumoniae* (SCAP). Pneumonia patients with evidence of radiographic pulmonary infiltration and aged over 20 hospitalized between May 2014 and April 2018 were enrolled. All data were retrospectively collected from medical records. Patients with bed-ridden status, residents in nursing home, or more than two microorganisms were detected from sputum, were excluded.

Results: During the study period, 144 MCAP and 138 SCAP patients were identified. MCAP patients were more frequently admitted in the winter season compared with SCAP patients ($P < 0.01$). In addition, MCAP patients were significantly higher age (the mean age was 74.9 vs 66.4; $P < 0.01$), had higher pulmonary underlying diseases such as bronchiectasis ($P < 0.01$), asthma ($P < 0.01$), and interstitial pneumonia ($P < 0.05$), and also were under home oxygen therapy ($P < 0.01$). Diagnostic concordance rate between sputum smear on Gram-stain and bacterial cultivation was lower in MCAP patients compared with SCAP patients (78.5% vs 88.4%; $P < 0.05$). In radiological findings, bronchopneumonia pattern was predominant in MCAP than PCAP subjects (95.1% vs 65.2%; $P < 0.01$). On the other hand, developed a chill and co-infection with Flu were common in PCAP patients ($P < 0.01$). There was no statistical significant difference both length of treatment and hospital stay in these two groups ($P = 0.65$ and 0.94 , respectively). No patients died in both groups.

Conclusion: Compared with SCAP, MCAP were mainly occurred in elderly patients with pulmonary diseases particularly in winter season, and bronchopneumonia pattern was predominant in radiological findings.

AO165

RELATIONSHIP BETWEEN INITIAL ANTIBIOTIC THERAPY AND OUTCOMES IN HOSPITALIZED PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA AT DR. SOETOMO GENERAL HOSPITAL, SURABAYA

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Background and Aims: Pneumonia is still major cause of morbidity and mortality in worldwide resulting in 7% of the world's total death yearly. In Dr. Soetomo General Hospital, the mortality rate was high as 26.08% in 2015 despite the high rate of guideline concordancy. Failure of empirical therapy would increased the mortality risk by 11 times. It caused by either inappropriateness of antibiotic therapy or changes in the microbiological profile of pneumonia. This study aims to determine the bacterial profile and analyze the relationship between empirical therapy and outcomes in patient with pneumonia.

Methods: This was a retrospective observational study, which examined patient medical records with diagnosis of community acquired pneumonia (CAP) during hospitalization in the Pulmonary Ward Dr. Soetomo General Hospital from January to December 2016. Outcomes observed includes survival and mortality cases after therapy.

Results: There were 569 cases of CAP. Three most common bacteria found were *Streptococcus viridans* (20.2%), *Acinetobacter baumannii* (19.4%), and *Klebsiella pneumoniae* (14.8%). Amikacin, Cefoperazone-Sulbactam, and Meropenem were the most sensitive antibiotic with sensitivity of 87.8%, 81.9%, and 76.3% respectively. There were 79 cases of MDR pathogen involvement. Appropriateness of empirical therapy was found in 162 (41.1%) patients and Fluoroquinolone monotherapy has the highest appropriateness cases with 59.3% ($P < 0.001$). Survival outcomes was 278 (56.3%), while mortality outcomes was 216 (43.7%) and Fluoroquinolone monotherapy has the highest survival cases in all CAP cases with 90.1% ($P < 0.001$). In severe CAP cases, initial combination therapy with Betalactam+Aminoglycoside has a better outcomes compared to Betalactam+Fluoroquinolone with survival cases 50.9% vs 27.6% ($P = 0.001$).

Conclusion: There was a relationship between initial antibiotic therapy and therapy outcomes. Initial monotherapy with Fluoroquinolone has the highest survival cases in all patients with CAP. Initial combination therapy with Betalactam+Aminoglycoside has a better outcomes compared to Betalactam+Fluoroquinolone in patients with severe CAP.

AO166

IN VITRO ANTIMICROBIAL SUSCEPTIBILITY AND TREATMENT OUTCOMES OF MOLECULAR DIAGNOSED MYCOBACTERIUM KANSASII PULMONARY DISEASE

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Background and Aims: *Mycobacterium kansasii* (MK) is traditionally considered as the high virulent nontuberculous mycobacteria species. Anti-MK treatments including rifampicin, ethambutol and isoniazid or macrolides were usually effective for MK pulmonary disease (PD), but treatment failure did occur in our clinical practice. We aim to identify the possible association between drug resistance and treatment failure.

Methods: MK isolates from sputum were retrospectively collected at National Taiwan University Hospital from May 2013 to December 2014. MK isolates were identified from traditional biochemical method first, and then were confirmed based on the molecular method with 16S ribosomal RNA gene sequencing. The minimum inhibitory concentrations of several antibiotics for MK were determined by a microdilution assay. Clinical outcomes of MK-PD patients receiving anti-MK treatments were evaluated.

Results: 75 MK isolates from 75 patients were identified by the traditional biochemical method. Among them, the molecular method confirmed the MK identification in 56 isolates. For the antimicrobial susceptibility, the resistance rates of MK isolates were relatively low to rifampicin (2/56; 3.6%), clarithromycin (0/56; 0%) and ciprofloxacin (3/56; 5.4%). However, the MK isolates were highly resistant to ethambutol (44/56; 78.6%). Among 11 MK-PD patients have received anti-MK treatment including ethambutol, the treatment failure rates tended to be higher in ethambutol resistance group than without (42.9% vs 0%, $P = 0.236$). Kaplan-Meier curves also showed that the MK-PD patients with ethambutol resistance tended to have higher rates of radiographic progression ($P = 0.154$) and persistent MK isolation in sputum ($P = 0.127$) than those without.

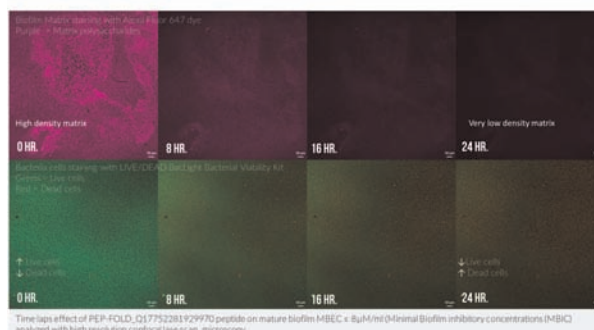
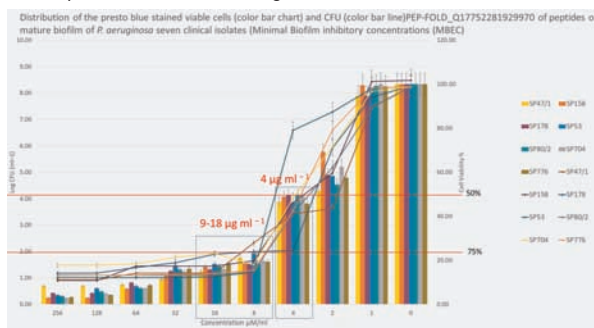
Conclusion: The MK isolates in our hospital were highly resistant to ethambutol and the resistance seemed to have an association with treatment failure to the traditional anti-MK regimen including ethambutol.

OVERCOMING BIOFILM MEDIATED RESPIRATORY INFECTIONS THROUGH EXPLOITATION OF PATHOGEN AND HOST-DIRECTED NOVEL PEPTIDES

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Background and Aims: The recurrent and chronic *P. aeruginosa*, biofilm colonization on the respiratory tract is the most prevalent cause of morbidity and mortality in patients with ventilator-associated pneumonia, cystic fibrosis (CF), chronic asthma and lung cancer. This situation has generated an urgent need for development of innovative, efficient and targeted treatments. Interest in host defence peptides (HDPs) has grown due to their potential therapeutic applications and their possible use against biofilm. This study, short, synthetic cationic novel peptides were tested for their anti-biofilm effectiveness as well as their ability to inhibit and disperse the mature *P. aeruginosa* biofilms.



Methods: The clinical isolates of *P. aeruginosa* from patients with chronic lung infections were used as a model to investigate inhibit and disperse of bacterial biofilms by synthetic short sequence novel host defence peptides (HDPs).

Results: The number of different novel anti-biofilm peptide candidates was tested against *P. aeruginosa*, and was found to exhibit an anti-microbial, anti-attachment as well as anti-biofilm activity at concentrations in the low µg/mL range compare with current conventional antibiotics. Confocal laser scanning microscopy and CFU count revealed that peptide treatment inhibited biofilm formation resulting in bio-volume reduction followed by induced disruption of mature biofilms and other chronic virulent factors. Further, peptides significantly reduce the extracellular matrix substance of mature biofilms.

Conclusion: These findings highlight the potential of novel peptides as a new group of antimicrobial weapons for disrupt biofilms and suggesting its potential use as a model for designing new treatment for chronic lung infections.

AO168

APPLICATION OF TRANSMISSION ELECTRON MICROSCOPY IN THE ETIOLOGIY DIAGNOSIS OF SEVERE PNEUMONIA VIA BALF: A RETROSPECTIVE STUDY

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Background and Aims: Severe pneumonia is responsible for great mortality and morbidity worldwide, and early-applied effective antibiotics are critical for good prognosis of patients. However, identification of infectious agents in severe pneumonia remains a major challenge. In this study, we aimed to evaluate the potential application of transmission electron microscopy (TEM) in etiologic diagnosis of severe pneumonia via BALF.

Methods: A total of 106 patients diagnosed with severe pneumonia at our hospital were included, and baseline characteristics of these patients were collected. Infectious agents detected by TEM in bronchoalveolar lavage fluid were summarized. Bacterial culture results of lower respiratory tract specimens and serological test results were also assessed.

Results: TEM revealed 74 bacteria, 24 viruses, 16 mycoplasmas and 10 chlamydia in 99 samples (61 samples were mixed infections), while pathogens in 7 samples were not detected, which supported that transmission electron microscopy had a good sensitivity in detecting infectious agents in bronchoalveolar lavage fluid. The detection rate of TEM was significantly higher when compared with bacterial culture or serological tests. Combined use of transmission electron microscopy with other diagnostic techniques significantly improved the detection rate of possible infectious agents in patients with severe pneumonia.

Conclusion: Our data support that TEM could facilitate the etiologic diagnosis of severe pneumonia via BALF and may consequently increase the opportunity of initial appropriate treatment.

AO169

SERUM IGA ANTIBODIES AGAINST GLYCOPEPTIDOLIPID CORE ANTIGEN WITH SMOOTH OR ROUGH MORPHOTYPES IN PATIENTS WITH MYCOBACTERIUM ABSCESSUS COMPLEX LUNG DISEASE

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Background and Aims: *Mycobacterium abscessus* complex (MABC) exhibits two distinct morphotypes, which are recognized by the

appearances of colonies: smooth morphotypes that express glycopeptidolipid (GPL) and rough morphotypes that exhibit diminished GPL expression on the cell wall. The advantage of testing serum immunoglobulin A (IgA) in the diagnosis of MAC (*Mycobacterium avium* complex) lung disease with smooth morphotypes has been well known, although the testing for GPL core antigen in patients with MABC lung disease is poorly documented. In this study, we focused on testing GPL core antigen in patients with MABC lung disease and confirmed the relationship between the co-infection in other non-tuberculous mycobacteria species and the colony morphology variant in MABC isolates.

Methods: Patients diagnosed with MABC lung disease between 2012 and 2017 at our hospital were enrolled and divided into group 1 (diagnosed with MABC lung disease with MAC co-infection) and group 2 (diagnosed with MABC lung disease without MAC co-infection).

Results: Of the 33 assessed patients with MABC, 13 were included in group 1 and 20 in group 2. The smooth colony variant was more frequently isolated from patients in group 1 than from patients in group 2 [group 1, 9 (69.2%) vs group 2, 4 (20.0%), $P = 0.01$]. The serum IgA antibody levels in patients in group 1 was higher than those in Group 2 [5.53 (0.07–17.48) U/ mL and 0.13 (0.00–8.32) U/ mL, respectively, $P = 0.02$].

Conclusion: Serum IgA antibodies against the GPL core antigens in patients with MABC are greatly affected by both MAC co-infection and colony morphology variant of the MABC isolate.

AO170

THE CORRELATION ANALYSIS BETWEEN VIRUS LOADING AND SHEDDING WITH THE CLINICAL FEATURE OF PATIENTS INFECTED BY INFLUENZA VIRUS IN ADULT

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Background and Aims: To study the clinical feature, viral load and shedding time of different influenza type infection of patients in adults, as well as analyze the correlation among them.

Methods: During 2016, the samples (nasopharyngeal swab) will be collected continuously in the influenza virus infection patients in adult; the virus load will be tested by RT-PCR method; and the clinical information of patients, which mainly is influenza symptom score, will be collected.

Results: A total of 160 influenza patients were recruited in 2016, including 70 cases of influenza A (H1N1) (65 cases were H1N1, 1 case was H3N2 and 4 cases were unclassified) and 90 cases of influenza B. The main clinical features were fever, cough, fatigue and headache. The clinical symptoms of influenza patients gradually decreased after reaching the peak on the second day of onset, while the viral load gradually decreased from the first day of onset, showing a positive correlation. Furthermore, on one hand, compare to influenza B infection, the age of patients in the influenza A infection group (45.5 ± 2.0 vs 40.4 ± 2.3 year, $P = 0.034$) was high, and the hospitalization rate (53.3% vs 33.0%) was significantly increased. Although the initial viral load of patients in the influenza A was significantly lower than that in the influenza B (3.4 ± 1.5 vs 4.5 ± 0.6 copies), yet the virus shedding time of influenza A patients was no difference. On the other hand, although the high-risk group of patients to begin with viral load was 3.4 ± 1.2 copies, lower than low-risk group (4.8 ± 0.7 copies), yet the high-risk group of virus shedding time (from onset to virus test negative) was 7.3 ± 2.3 days, significantly higher than it in the low-risk group (5.3 ± 0.7 days) (Figure 1).

Conclusion: There was significant correlation between the clinical symptoms score and viral load in influenza virus infection patients, however, the severity of clinical features depended on the shedding time of virus.

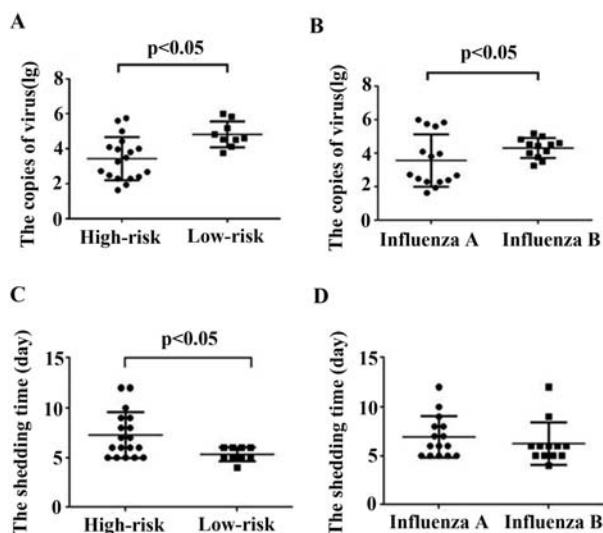


Figure 1. The copies and shedding time of virus in patients. A and B presents the copies of virus in different groups, including high-risk and low risk or influenza A and influenza B, respectively. C and D means the shedding time in different groups. P<0.05 indicates there were statistical differences between the two groups, high-risk and low-risk, or influenza A and influenza B.

Lung Cancer 2

AO171

TAIWAN LUNG CANCER SCREENING PROGRAM FOR NEVER SMOKERS

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Background and Aims: Lung cancer in never-smoker is a distinct disease and prevalent in East Asia. The study is aiming to perform low dose CT (LDCT) screening for lung cancer in never-smokers and validate the risk SNPs previously identified that associated with susceptibility to lung cancer in never-smokers (TALENT: Taiwan Lung Cancer Screening for Never-smoker Trial)

Methods: This is a prospective, nationwide, multicenter study sponsored by The Ministry of Health and Welfare, Taiwan. The inclusion criteria were age between 55–75 years, never-smokers with one of the following risk: family history of lung cancer within third-degree, passive smoking exposure, TB/COPD, cooking index ≥ 110 , and not using ventilator during cooking. The LDCT was conducted according to the ACR guideline. A solid or part-solid nodule 6 mm or pure ground glass nodule 5 mm in diameter was designated as positive on LDCT. The PBMC DNA was obtained for SNP typing (TERT, TP63, HLA-DRB1/HLA-DQA1, HLA-DRB9/HLA-DRB5, VT11A, BPTF and DCBLD1).

Results: This is the interim report. Till May 13, 2018, totally 10,397 subjects were enrolled, 329 underwent diagnostic procedures (31 by bronchoscopy or CT guided, 298 by surgery). The final diagnosis included 12 atypical adenomatous hyperplasia, 42 adenocarcinoma in situ, 46 minimally invasive adenocarcinoma, 152 invasive lung adenocarcinoma (stage IA 118, IB 23, IIA 2, IIB 1, IIIA 2, IV 5, and unknown 1), one

adenosquamous cell carcinoma, one squamous cell carcinoma, one small cell carcinoma, 66 benign lesions and 8 others. The lung cancer detection rate was 2.34% (243/10,397) and 94.7% stage I. The genotyping showed 3 SNPs (TERT, TP63, HLA-DRB1/HLA-DQA1) were significantly associated with the risk of lung cancer in never-smokers.

Conclusion: Our study revealed that the lung cancer detection rate by LDCT in high-risk never-smokers was even higher than that of the high-risk smoking group in NLST. We validated 3 SNPs that associated with susceptibility to lung cancer in never-smokers.

AO172

CLINICAL IMPLICATION OF DNA METHYLATION ANALYSIS IN THE ORAL EPITHELIUM FOR LUNG CANCER RISK STRATIFICATION

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Background and Aims: To improve the specificity of screening programs for the early detection of lung cancer, novel strategies for identifying individuals at high risk or extremely low risk of lung cancer should be investigated. Based on the hypothesis that similar molecular alterations may occur in the lungs and oral cavity because the entire airway is exposed to the same inhaled carcinogens, we analyzed DNA methylation profiles in the oral epithelium for lung cancer risk stratification.

Methods: Methylation-specific polymerase chain reaction (MS-PCR) was performed using the oral epithelium in 40 patients with lung cancer and 152 individuals without lung cancer (controls). As we have demonstrated that DNA methylation of GDNF, RARB, ProK, HOXD11, and PCDHGB6 in the oral epithelium might be promising biomarkers for lung cancer risk stratification in a pilot analysis using a small sample, MS-PCR was performed using the oral epithelium, and DNA methylation profiles were compared between patients and controls in the 192 enrolled participants.

Results: The MS-PCR analysis revealed that GDNF, RARB, and HOXD11 were more frequently methylated in patients than in controls ($P = 0.0026$, $P = 0.0170$ and $P = 0.0335$, respectively). Combined analyses indicated that 12 of 40 (30%) patients and 10 of 152 (6.6%) controls showed DNA methylation in 2–3 genes ($P < 0.0001$). In a subgroup analysis limited to non-smokers, 5 of 12 (41.7%) patients showed methylation in 2–3 genes, compared to 4 of 95 (4.2%) controls ($P < 0.0001$). Among the population aged >50 years, 12 of 40 (30%) patients and 9 of 63 (14.3%) controls showed methylation in both genes ($P = 0.0537$).

Conclusion: Results of this study demonstrate that risk stratification for lung cancer screening through DNA methylation analysis in the oral epithelium may be an ideal strategy, because it can be performed in a less-invasive manner.

Diagnostic value of the combined analysis

	Sensitivity	Specificity	PPV	NPV
Total participants	30.0%	93.4%	54.6%	83.5%
Never smokers	41.7%	95.8%	55.6%	92.9%
Age ≥ 50 years	30.0%	85.7%	57.1%	65.9%

PPV: positive predictive value, NPV: negative predictive value

AO173

METABOLIC PROFILING CLASSIFIES NON-SMALL CELL LUNG CANCER CELLS INTO DIFFERENT SUBTYPES WITH DISTINCT SENSITIVITIES TO METABOLIC INHIBITIONS

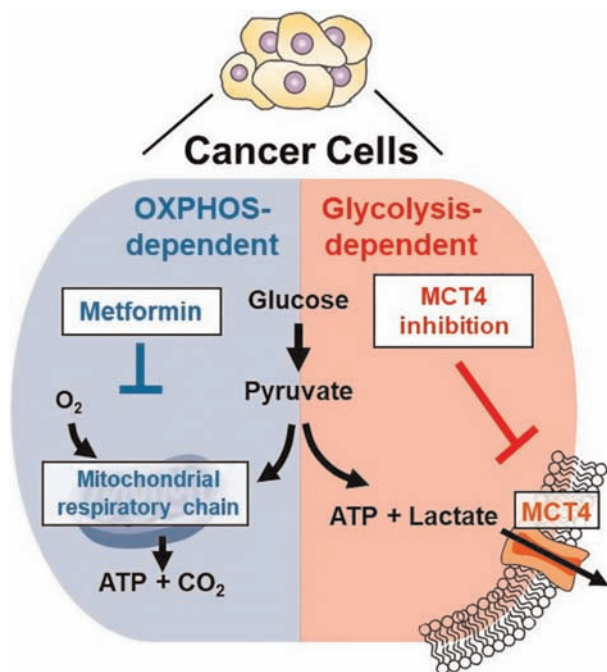
TING-CHUN KUO^{1*}, KUO-YEN HUANG², SHUENN-CHEN YANG², YIH-LEONG CHANG³, TSE-MING HONG⁴, HSUAN-YU CHEN⁵, TZU-HUNG HSIAO⁶, PAN-CHYR YANG¹

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Background and Aims: Lung cancer is the leading cause of cancer-related death in the world. Though many improvements in medical and surgical therapies have been done, the advancement in lung cancer mortality remains unsatisfactory. Targeting metabolic reprogramming in cancer has become an emerging strategy. For example, a widely used anti-diabetic drug, metformin, has been shown to have anti-cancer activities. However, the efficacy and safety of many of these metabolic-targeting drugs are unexpectedly inadequate.

Methods: Here, we tried to stratify non-small cell lung cancer (NSCLC) cells by their glycolytic dependency and increase anti-cancer activities of these metabolic-targeting drugs according to their metabolic subtypes.

Results: We found that NSCLC cells could be classified into oxidative phosphorylation-dependent and glycolysis-dependent subtypes. The former is sensitive to metformin but the latter is resistant. To target these metformin-resistant cells, monocarboxylate transporter 4 (MCT4), a lactate transporter, was identified. It was found to be overexpressed and regulated by Sp1 and p63 transcription factors in the glycolysis-dependent subtype of NSCLC cells. Besides, the lactate-transporting function of MCT4 was shown to play an important role in cancer cell proliferation. When we knockdown the expression of MCT4 by using shRNAs, the proliferation of these cells would be inhibited.



Conclusion: These results implied the potential of MCT4 as a drugable target against the glycolysis-dependent subtype of NSCLC. Here, a MCT4-neutralizing antibody has been developed with excellent anti-proliferation activity *in vitro* and *in vivo*. We strongly believe that after a series of optimizations this MCT4-neutralizing antibody will have great potential to become a novel anti-cancer reagent against the glycolysis-dependent subtype of NSCLC.

AO174

ANGIOTENSIN-(1-7) SUPPRESSES NSCLC ACQUIRED PLATINUM RESISTANCE-INDUCED TUMOR ANGIOGENESIS VIA PI3K/AKT AND MAPK SIGNALING PATHWAYS

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Background and Aims: Angiotensin II (Ang II) is the major effector peptide of the classical renin-angiotensin System (RAS) ACE/Ang II/AT1R axis. The new ACE2/Ang-(1-7)/Mas axis always plays a contrary role in many diseases. Ang-(1-7) reduced proliferation and angiogenesis in cancer. Our previous study found that Ang-(1-7) suppressed non-small cell lung cancer (NSCLC) migration and invasion. In this study, we investigated the effect of Ang-(1-7) on tumor-associated angiogenesis after the development of acquired platinum resistance in NSCLC.

Methods: qRT-PCR and western blot were carried out to detect the expression of ACE, AT1R, VEGFa, and signaling pathways productions. The proliferation-related gene Ki-67 and VEGFa was examined by immunohistochemistry. Microvessel density (MVD) were used to measure tumor-associated angiogenesis. Enzyme-linked immunosorbent assay (ELISA) were carried out to detect VEGFa expression levels.

Results: We found that ACE, AT1R and VEGFa productions decreased in the A549-DDP-Ang-(1-7) group than the A549-DDP group. The effects were blocked by the combination treatment of A779, the MAS receptor antagonist. The effect of Ang-(1-7) was partially mediated through inactivation of PI3K, P38 and ERK1/2 pathways. Additionally, we confirmed that Ang-(1-7) inhibited VEGFa production and microvessel density (MVD) development while simultaneously suppressed ACE and angiotensin II type 1 receptor (AT1R) expression *in vivo*.

Conclusion: Our results suggested Ang-(1-7) may potentially suppressed tumor associated angiogenesis induced by acquired platinum resistance in NSCLC.

AO175

THE ROLE OF THE GROUND-GLASS OPACITY RATIO IN RESECTED LUNG ADENOCARCINOMA

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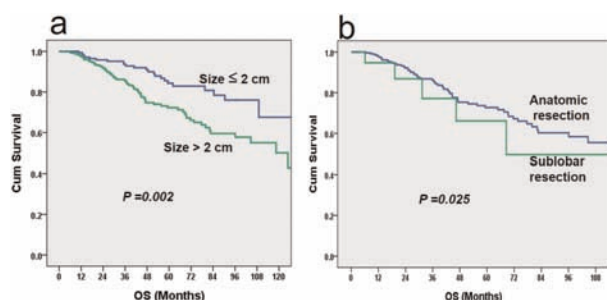
Background and Aims: The goal of this study was to investigate the role of the ground-glass opacity (GGO) ratio in lung adenocarcinoma in predicting surgical outcomes

Methods: Patients who underwent surgical resection for pulmonary adenocarcinoma between January 2004 and December 2013 were reviewed. The clinical data, imaging characteristics of nodules, surgical approaches and outcomes were analysed with a mean follow-up of 87 months.

Results: Of 789 enrolled patients, 267 cases were categorized as having a GGO ratio >0.75; 522 cases were categorized as having a GGO

ratio < 0.75. The gender, tumour differentiation, epidermal growth factor receptor mutation, smoking habits, lymphovascular space invasion, tumour size, maximum standard uptake value and carcinoembryonic antigen levels were significantly different in the 2 groups. In the group with a GGO ratio >0.75, 63.3% of the patients underwent sublobar resection (18.8% with a GGO ratio < 0.75, $P < 0.001$). These patients had fewer relapses (2.2% for GGO ratio >0.75, 26.8% for GGO ratio < 0.75, $P < 0.001$) and a better 5-year survival rate (95.5% for GGO ratio >0.75, 77.4% for GGO ratio < 0.75, $P < 0.001$). None of the patients with a GGO ratio >0.75 had lymph node involvement. The multivariable Cox regression analysis revealed that a GGO ratio < 0.75 was an independent factor for postoperative relapse with a hazard ratio of 3.96.

Conclusion: A GGO ratio >0.75 provided a favourable prognostic prediction in patients with resected lung adenocarcinoma. Sublobar resection and lymph node sampling revealed a fair outcome regardless of tumour size. However, anatomical resection is still the standard approach for patients with tumours with a GGO ratio < 0.75, size >2 cm.



AO176

DIFFERENTIAL C-TERMINAL PROTEIN FRAGMENTS OF α -1-MICROGLOBULIN/BIKUNIN PRECURSOR AS POTENTIAL MAKER FOR EARLY DETECTION OF LUNG ADENOCARCINOMA

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Background and Aims: Lung cancer is the world's leading cause of cancer death. Early detection of lung cancer is quite limited because of the lack of sensitive and specific biomarkers. Lung cancer conducts cell proliferation and invasion through aberrant protease activity. The aberrant protease activity induces protein fragments from cancer tissues and the fragments have potential as detection markers of lung cancer. In the present study, we focused on the exploration of lung adenocarcinoma specific C-terminal protein fragment in urine by using iTRAQ method and multiple reaction monitoring (MRM) method which are methods used in tandem mass spectrometry.

Methods: We comprehensively analyzed the structure of C-terminal protein fragments in the urine from 24 patients with early stage lung adenocarcinoma and 25 healthy controls by iTRAQ method. We quantified the amount of the C-terminal protein fragments in the urine from 26 patients with stage I lung adenocarcinoma and 40 healthy controls by MRM method. We investigated the amount of C-terminal protein fragments in lung cancer tissues and lung adenocarcinoma cell lines (HLC-1, A549 and PC-9) by western blotting and evaluated the diagnosis capability of the fragments in serum by ELISA.

Results: In iTRAQ analyses, we discovered a fragment of α -1-microglobulin/bikunin precursor (AMBP) as an early diagnostic marker of lung

adenocarcinoma. The expression levels of the AMBP fragment in lung adenocarcinoma tissues and lung cancer cell lines are higher than those of levels in normal lung tissues and BEAS-2B cells. The AUC value of the AMBP fragment levels in urine determined by MRM method for detection of stage I adenocarcinoma was higher than that of the serum CEA. The AUC for C-terminal AMBP levels determined by ELISA is also higher than that of CEA.

Conclusion: Identification of C-terminal protein fragment of AMBP in the urine and plasma may have potential as an early detection marker of lung adenocarcinoma.

AO177

PHOSPHORYLATION OF THE CYTOSKELETAL PROTEIN CAP1 REGULATES NON-SMALL CELL LUNG CANCER SURVIVAL AND PROLIFERATION BY GSK3 β

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Background and Aims: Adenylate Cyclase-associated protein 1 (CAP1) is an evolutionarily conserved protein that regulates actin dynamics.

Methods: Our previous study indicates that CAP1 is overexpressed in NSCLC tissues and correlated with poor clinical outcomes. Further establishing the role and dissecting underlying mechanisms are imperative before targeting CAP1 can become a possibility for cancer treatment.

Results: Here we report our findings that knockdown of CAP1 inhibited cell proliferation and induced apoptosis in vitro and in vivo. Moreover, Phosphor mutants of CAP1 at the S307/S309 regulatory site had compromised rescue effects for both the invasiveness and proliferation in CAP1-knockdown cells and GSK3 β kinase inhibitor LiCl inhibits cell phosphorylation site S307/S309 by up-regulating the expression of p53, BAK, Bad and cleaved PARP induced ROS production, decreased lung cancer cell viability, adhesion, proliferation, migration and Invasion, induction of apoptosis.

Conclusion: These novel mechanistic insights may ultimately open up avenues for strategies targeting CAP1 in the treatment of lung cancer, tailored for specific types of the highly diverse disease.

AO178

EPIGENETIC THERAPY MODULATES POLYFUNCTIONALITY OF TUMOR-REACTIVE T CELLS IN NON-SMALL CELL LUNG CANCER

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Background and Aims: Cytotoxic T cells in patients with advanced tumours are often dysfunctional due to continuous cancer antigen stimulations. Dysfunctional T cells are less proliferative, express more inhibitory receptors, and produce less effector cytokines. Recent studies have found that immune checkpoint blockade therapy did not completely reverse the 'exhausted' phenotype of T cells, whose reprogrammability was also determined by epigenetic states. We hypothesized that epigenetic therapy may reprogram tumor-reactive T cells to enhance their effector function.

Methods: We isolated CD3 T cells from malignant pleural effusion or primary tumor tissues of 30 lung cancer patients, and examined their immunophenotypes including surface markers (CD4 and CD8), proliferative index (Ki67), as well as inhibitory receptors (PD-1, TIM3, and CTLA4). Tumor-reactive T cells were subject to *in vitro* daily treatment of a DNA methyltransferase inhibitor, decitabine, for 72 h. The percentages of polyfunctional T cells before and after treatment were determined by intracellular staining of TNF- α , IFN- γ , IL-2 and CD107a, followed by flow cytometric analysis.

Results: We discovered that malignant pleural effusion is an abundant source of tumor-reactive T cells. T cells in the malignant pleural effusion or primary lung cancer tissues have higher CD4/CD8 ratios, as compared with peripheral blood mononuclear cells from healthy volunteers. Notably, around 60% (range 20–90%) of T cells exhibited the exhausted phenotype and expressed at least one inhibitory receptors. Decitabine treatment significantly increased polyfunctionality of PD1+ T cells in certain patients.

Conclusion: T cells from malignant pleural effusion could potentially reflect dysfunctional immune states in lung cancer patients when tumor tissues are not available. Epigenetic therapy may enhance polyfunctionality of tumor-reactive T cells, and has potentials for combinational uses with immune checkpoint blockade therapy.

AOL003

PROGRESSION-FREE SURVIVAL AMONG PROGRESSED NON-SMALL CELL LUNG CANCER (NSCLC) WITH T790M MUTATION AS GUIDED BY LIQUID BIOPSY IS SHORTER THAN THOSE BASED ON TISSUE RE-BIOPSY

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Background and Aims: Osimertinib has been approved by the US Food and Drug Administration (FDA) for non-small lung cancer (NSCLC) harboring acquired T790M mutation that have progressed while on other EGFR (Epidermal growth factor inhibitor)-inhibiting therapy. We compare the progression-free survival of patients whose T790M mutation was identified by liquid biopsy as compared with those by tissue sampling.

Methods: This is a retrospective cohort study conducted in Hong Kong that included 139 Chinese patients with advanced NSCLC who have disease progression after first line EGFR tyrosine kinase inhibitor and received osimertinib upon detection of T790M mutation, either by liquid biopsy (by identification of circulating tumor DNA) or by tissue re-biopsy. The primary end point is progression-free survival.

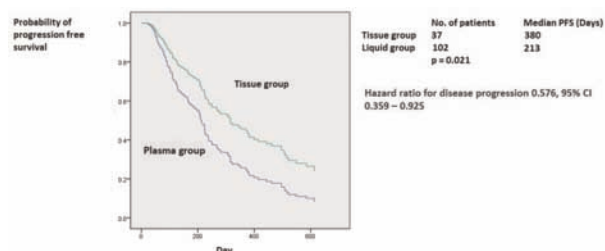
Results: Patients with EGFR T790M mutation detected by tissue sampling ($n = 37$) have significantly better progression free survival than those by peripheral blood liquid biopsy ($n = 102$) (PFS 380 vs 213 days, hazard ratio 0.576, 95% CI 0.359 – 0.925, P value = 0.021). A small subgroup with positive liquid biopsy but concomitant negative tissue result ($n = 6$) have the lowest PFS among the different cohort (Median PFS = 57 days).

Conclusion: Tissue re-biopsy for T790M mutation is preferred for patients who have NSCLC that progressed after first-line tyrosine kinase inhibitor. For cases that only have confirmatory liquid biopsy results, clinician should inform their patient that the expected PFS may be significantly shorter than those previously reported in literature.

Table 1

Demographic and Clinical Characteristics of the Patients at Baseline

	Plasma group (PC)	Tissue group (TC)	p value
Age (Mean)	65.5 (45-92)	63.6 (45-95)	0.412
Sex			0.662
Male	24 (23%)	10 (27%)	
Female	78 (77%)	27 (73%)	
Smoking status			1.0
Ever-smoker	10 (10%)	3 (8%)	
Non-smoker	92 (90%)	34 (92%)	
Primary mutation			0.253
Exon 19 deletion	50 (49%)	19 (50%)	
L858R mutation	48 (47%)	15 (40%)	
Rare EGFR mutation	2 (2%)	0 (0%)	
Complex mutation	1 (1%)	2 (5%)	
Prior tyrosine kinase inhibitor			0.527
Gefitinib	73 (72%)	30 (81%)	
Erlotinib	21 (21%)	5 (13.5%)	
Afatinib	8 (7%)	2 (5.5%)	
Brain metastasis prior to the initiation of osimertinib			0.96
No	74 (73%)	27 (73%)	
Yes	28 (27%)	10 (27%)	
Prior chemotherapy			1.0
No	73 (72%)	26 (70%)	
Yes	29 (28%)	11 (30%)	



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ADVERSE REACTIONS AMONG PATIENTS BEING TREATED WITH SHORTER MULTI-DRUG RESISTANT TUBERCULOSIS REGIMEN AT PERSAHABATAN HOSPITAL, INDONESIA

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Background and Aims: A shorter multidrug-resistant tuberculosis (MDR-TB) regimen refers to a course of treatment for MDR-TB lasting 9–12 months. A shorter, cheaper, and well-tolerated MDR-TB regimen will impact the number of patients treated and improve adherence. However, medications used to treat MDR-TB have many known side effects. The aim of this study was to assess adverse reactions of TB drugs in patients

treated with shorter MDR-TB regimen at Persahabatan Hospital from August 2017 to March 2018.

Methods: Retrospective observational study of MDR-TB patients with shorter regimen. Samples were obtained from medical record of MDR-TB patients who underwent outpatient treatment in Persahabatan Hospital.

Results: A total of 52 patients included in the study, 61.5% were males and 38.5% were females. The majority of MDR-TB patients belonged to the 41–50 years old group. The most common co-morbidities associated with MDR-TB were malnutrition (32.7%) and diabetes (30.8%). There was no significant relationship between adverse reactions and risk factors. The incidence of mild and moderate adverse drug reaction occurred in 96% patients and severe adverse drug reaction in 29% patients. Side effects of drugs were; 82.6% GIT manifestations, 26.9% hyperuricemia, 26.9% electrolyte imbalance, 26.9%, central nervous systems, 23% skin reaction, 11.5% vertigo 11.5% arthritis, 9.6% optic neuropathy, 9.6% ototoxicity, 9.6% drug eruption, 7.9% psychiatric problem, 7.6% nephrotoxicity and 1.9% hepatotoxicity. Most of the side effects started to appear within the first 2 months of treatment. Nine patients (17.3%) was excluded, related to adverse drug reaction and treated with longer regimen.

Conclusion: The adverse reactions in shorter MDR-TB regimen treatment not much different with the study in Persahabatan Hospital before, that most adverse reactions complained due to MDR standard treatment are nausea and arthralgia. There was no significance of relationship between adverse reactions and risk factors.

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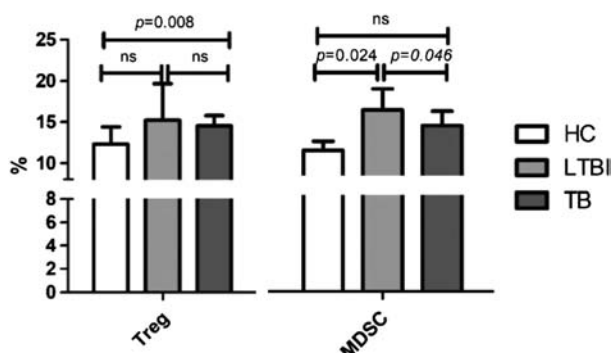
THE MYELOID DERIVED SUPPRESSOR CELLS INCREASED PREDOMINANTLY IN LATENT TUBERCULOSIS INFECTION WHILE REGULATORY T CELLS ELEVATED IN TB REACTIVATION

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Background and Aims: Tuberculosis (TB) is the most important infectious disease worldwide. However, there are poor understanding for host factors prone to have *Mycobacterium tuberculosis* infection or the reactivation from latent TB infection (LTBI). In this study, we therefore surveyed the myeloid derived suppressor cells (MDSC) and regulatory T cells (Treg) during LTBI and active TB and aimed to investigate the association.

Methods: We recruited patients with active TB or LTBI and healthy controls. The blood MDSCs (CD11b+/CD33+ cells in CD3-/CD14-/HLA-DR- population) and Treg cells (positive CD4, CD25, and Foxp3) were measured using flow cytometry and analyzed.



Results: We have enrolled 26 healthy controls, 6 participants with LTBI, and 29 patients with active TB. The age and sex were comparable among the three groups. We measured the MDSCs and Treg cells in peripheral blood mononuclear cells and found that MDSCs was higher in LTBI subjects than that in active TB or controls (Fig 1). In contrary, Treg cells increased in patients with active TB, higher than that in the other two groups.

Conclusion: We preliminarily found that the MDSCs proportion was increasing during LTBI status and by contrast, Treg cells elevated in TB reactivation. We suggest that the immune modulation pathways of MDSCs and Treg cells influence different stage of *M. tuberculosis* infection and needs further investigation for the application in treatment.

AO181

HOW EFFECTIVE IS THE SYSTEMIC INTEGRATION OF SMOKING CESSATION INTO TUBERCULOSIS CONTROL PROGRAMME IN CREATING SMOKE-FREE ENVIRONMENTS IN THE PHILIPPINES?

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Background and Aims: Tuberculosis (TB) is still one of the most significant health burdens in the Philippines. Health hazards by cigarette smoking have further put loads on the people in this country. TB patient care potentially offers a valuable opportunity for health workers to help smokers to quit smoking and to expand smoke-free home environments. This study aims to assess the effectiveness of the systematic integration of smoking control and TB control programmes at health center level in creating smoke-free environments in the Philippines.

Methods: The design of this study is prospective and observational, setting the intervention group composed of TB patients who receive the modified ABC Smoking Cessation approach by the UNION using modified recording forms, and the control group consisting of TB patients who receive only regular health education at health centers. Nurses-in-charge at each of the health centers interviewed to all TB patients registered on smoking status, then repeated interviews monthly afterward.

Results: 1,140 TB patients as an intervention group and 762 as a control group have been enrolled as of February 2018. There were no significant differences in smoking rate and smoke-free-home rate upon initial interviews in these groups. Both the smoking quit rate and the smoke-free-home rate at the 6th month of TB treatment among the TB patients registered by August 2017 indicated higher in the intervention group than those in the control group (71.9% vs 47.7%, $P < 0.001$; 66.9% vs 54.0%, $P < 0.001$, respectively). While, so far many of the TB patients were successfully treated (84.7% vs 86.2%, $P = 0.738$).

Conclusion: The preliminary data indicated that the interventions using the modified ABC Smoking Cessation approach by the UNION worked well both to reduce the smoking rate and to keep the smoke-free environment at home without adverse effect to TB patient care even in the urban setting in the Philippines.

AO182

CORRELATION BETWEEN CLINICAL MANIFESTATION AND SEVERITY OF TUBERCULOSIS DISEASE (A MULTI-CENTRE STUDY IN INDONESIA)

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Background and Aims: Tuberculosis (TB) remains a worldwide health problems with high morbidity and mortality. The pattern of clinical presentations of TB is reflected in the radiological and microbiological of the disease. Both of radiological and microbiological aspect can represent the severity of TB disease. This study was aimed to assess the correlation between clinical manifestation and severity of TB disease.

Methods: This study was an observational with cross sectional approach, data derived from multicentre study consist of 7 hospitals in Indonesia which has been starting from February 2017.

Results: From 248 subjects, 60% were male, 48% underweight, 90% denied contact with active TB patients, 11% smoker, and 29% also have diabetes mellitus. Clinical manifestation were cough (93%), hemoptysis (31%), dyspnea (61%), chest pain (38%), body weight loss (75%), and night sweating (53%). From radiology finding, mean of total lung damage was 44.5% (SD 24.6%). While from microbiology finding before treatment was started, positive acid fast bacilli (AFB) in 64% cases, positive molecular rapid test in 72% cases, and positive culture of *M. tuberculosis* in 64% cases. From clinical manifestation, dyspnea, body weight loss and night sweat were significantly correlated with radiological lung damage with $P = 0.02$, $P = 0.006$, $P = 0.01$ respectively. Yet only body weight loss was significantly correlated with microbiological AFB finding ($P = 0.007$).

Conclusion: There is correlation between clinical manifestation and severity of TB disease but only body weight loss correlated to both of radiologic and microbiologic finding whereas dyspnea and night sweating correlated to radiologic severity.

AO183

ENDOBRONCHIAL LESION IN PATIENTS WITH SMEAR-NEGATIVE PULMONARY TUBERCULOSIS

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Background and Aims: Endobronchial lesion (EL) in pulmonary tuberculosis directly contributes to the sequelae of bronchostenosis. Suspecting the presence of EL is helpful in comprehensively approaching patients with smear-negative pulmonary tuberculosis (SNPT), especially in contexts where bronchoscopy is not widely available and therapeutic decision of SNPT usually bases on clinical and radiologic features without microbiologic evidence. This study aims to evaluate clinical and radiologic findings which are useful to identify EL in patients with SNPT.

Methods: A retrospective descriptive study was performed at an out-patient pulmonary clinic from October 2015 to February 2018. Patients with complete medical records undertaken bronchoscopy to determine SNPT were included.

Table 1: Logistic regression analysis for factors associated to endobronchial lesion

Variables	Univariate		
	Odds ratio	95% confidence interval	P-value
Age < 40	4.20	1.08-16.32	0.038
Gender, female	1.68	0.47-5.96	0.422
Cough, present	2.06	0.57-7.47	0.270
Symptom duration	0.21	0.04-1.14	0.072
Consolidation and infiltration, absent	12.37	2.21-69.21	0.004
Abnormality at upper lobe, absent	4.53	0.97-21.14	0.054

Results: We found 39 cases with SNPT in which there are 19 cases with EL. The mean age was 40.77 years, male to female ratio # 1:1. Patterns of EL included active caseous lesion (36.8%), fibrostenotic lesion (31.6%), tumorous lesion (21.1%), and edematous-hyperemic lesion (10.5%). Univariate logistic regression analysis revealed that age < 40 (odds ratio (OR) 4.20, 95% confidence interval (CI) 1.08–16.32) and absence of consolidation and infiltration on chest X-ray (atelectasis, hilar widening, pleural effusion, and normal) (OR 12.37, 95% CI 2.21–69.21) were significantly associated to presence of EL.

Conclusion: EL should be considered in young patients suspecting SNPT without consolidation and infiltration on chest X-ray.

AO184

PROLONGED QT AND TORSADE DE POINTES IN PATIENT WITH XDR TUBERCULOSIS TREATED WITH BEDAQUILLINE

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Background and Aims: Extensively drug-resistant tuberculosis (XDR-TB) is a global problem due to the high morbidity and mortality. Difficult to treat XDR Tuberculosis can caused by severe side effect.

Methods: We observed 2 patient diagnosed with XDR tuberculosis treated with Bedaquiline (BDQ) regimen at Dr M Goenawan Partowidigdo Lung Hospital Indonesia who underwent treatment in 2017. Two patients received BDQ regimen after drug susceptibility test result show resistant to Rifampicin, Isoniazid, Streptomycin, Amikacin, Kanamycin and Ofloxacin and have allergy reaction to Capreomycin. We monitor ECG of patient routinely.

Results: We present two case of 32 years old (patient no 1) and 19 years old female (No 2) diagnosed with XDR Pulmonary Tuberculosis and have allergy with capreomycin. We use Bedaquiline regimen based on World Health Organization (WHO) recommendation with Bedaquiline (Bdq) for total use of Bdq maximum 24 weeks. After 8 weeks treatment, patient no 1 have severe fatigue, dizziness and vomit that need hospitalization and stop Bdq. ECG monitoring show normal sinus rhythm with prolonged QT corrected with Fridericia 472 ms. A day after, ECG monitoring show Torsades de pointes and patient complain nausea, dizziness and weakness but still have normal vital sign. Patient treated with Magnesium sulphate 2 g iv initially in 60 second, followed by maintenance dose. Until now patient have negative smear and culture after 6 month stop Bdq regimen and only have mild side effect with individual regimen treatment. Patient No. 2 complain atypical chest pain and discomfort after treatment with Bdq for about 2 months and ECG show QTcF 490 ms and QTcF 535 ms two weeks later, we stop Bdq. After we stop Bdq for 3 weeks, ECG show QTcF decrease to 438 ms. We continue XDR treatment with individual treatment and have culture conversion

Conclusion: The use of Bdq should carefully and closed monitored to reduce risk of mortality

AO185

CD8 RESPONSE MEASURED BY QUANTIFERON-TB GOLD PLUS AND TUBERCULOSIS DISEASE STATUS

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Background and Aims: Clinical application of CD8 response measured by the newer interferon gamma release assay, QuantiFERON-TB Gold-Plus (QFT-Plus), remained to be investigated.

Methods: We performed this prospective study and recruited active TB patients, contacts with latent tuberculosis infection (LTBI) and healthy contacts in two centers in northern Taiwan in 2017. QuantiFERON-TB Gold In-Tube (QFT-GIT) and QFT-Plus were both tested. LTBI was defined by QFT-Plus positivity and exclusion of active TB.

Results: A total of 314 participants (107 healthy contacts, 90 LTBI, 107 active TB) were included. The concordance rate of QFT-GIT and QFT-Plus was high ($n = 278$, 88.5%). While TB1 and TB2 response were not different between active TB and LTBI (TB1, active TB vs LTBI: 1.79 ± 2.80 IU/ml vs 1.99 ± 2.26 IU/ml, $P = 0.581$; TB2, active TB vs LTBI: 2.29 ± 3.15 IU/ml vs 2.03 ± 2.25 IU/ml, $P = 0.507$), CD8 response was higher in active TB than LTBI (active TB vs LTBI: 0.49 ± 1.57 IU/ml vs 0.04 ± 1.53 IU/ml, $P = 0.041$). CD8 response was also higher in active TB than healthy contacts (active TB vs healthy contacts: 0.49 ± 1.57 IU/ml vs 0.01 ± 0.19 IU/ml, $P = 0.002$). For CD8 response >2 IU/ml ($n = 12$), 9 (75%) were active TB and 3 (25%) were LTBI. The results were also similar if the diagnosis LTBI was made by positivity of QFT-GIT rather than QFT-Plus.

Conclusion: This study revealed CD8 response by QFT-Plus was different between healthy contacts, LTBI as well as active TB and holds potential as a novel biomarker.

AOL004

A RARE ENTITY: DISSEMINATED TUBERCULOSIS WITH EVANS SYNDROME

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Background and Aims: We are presenting a case of 65-year-old man with complains of shortness of breath, fever, red black patches, blood tinged sputum, weight loss. He had history of blood transfusion for recurrent anaemia. Patient was known case of diabetes mellitus type-2, hypertension, coronary artery disease and seizures.

Methods: We investigate patient as per presenting complaints. Haemogram and peripheral blood film shows pancytopenia, high LDH level and negative for ANA, Anti DS DNA antibody, G6PD. Serology for HIV was non-reactive. Coombs test was positive for auto immune haemolytic anemia.

Computed tomography of chest and abdomen reveal multiple enlarged mediastinal, pre & para aortic lymphnodes, tiny discrete nodule in bilateral lung fields and left pleural effusion, splenomegaly with microabscesses. Cardiac echo demonstrated LVEF 35%, severe MR.

Bone marrow aspiration suggestive of mildly hypercellular marrow, normoblastic erythropoiesis, normal myelopoiesis and adequate megakaryocytes consistent with platelet destruction.

Bone marrow biopsy confirmed necrotizing granulomatous inflammation consistent with tuberculosis, positive acid fast bacilli stain. Patient was put on antitubercular drugs, corticosteroid along with continuing treatment for diabetes mellitus, hypertension, coronary artery disease and seizures.

Results: Patient was diagnosed a case of disseminated tuberculosis with auto immune haemolytic anemia as Evans syndrome.

Conclusion: Tuberculosis had a wide spectrum of haematological manifestation. We describe this case who presented with haemolytic anemia turn out as Evans syndrome as a part of rare complications of disseminated tuberculosis.

Clinical Allergy and Immunology

AO186

AN EVIDENCE-BASED MEDICINE FOLLOW-UP AND COMPARISON STUDY ON ATOPIC UPPER AND LOWER AIRWAY DISORDER

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Background and Aims: Stable COPD had variety of inflammatory markers (Núñez B 2016; LoE[3]). The intrinsic hypercontractility in asthmatic ASM correlated to TGF β -1 (Tatler 2011; LoE [5]). TGF β -1, as a pro-fibrotic cytokine, up-regulates collagen deposition while down-regulates its catabolism. The base exchange at -09 in the TGF β promoter linked to IgE ($P < 0.01$) (Hobbs 1998; LoE [4]). The risk of asthma associated with -509T allele elevated among Asians (OR 1.50, 95% CI: 1.04–2.17) but not Caucasians (Yong-Gang Zhang 2010; LoE[1]).

Methods: EBM research were undertaken on PubMed using the search terms fibrinogen, remodeling, TGF β -1, AE-COPD, airway hyperresponsiveness, chronic rhinosinusitis (CRS) and peripheral eosinophil. Meta-analysis and systematic review or RCT were initiated and also limit papers published between Jul 2012 to May 2018. Oxford center for EBM 2011 edition was referenced for level of evidence (LoE).

Results: TGF β 1 polymorphism rs1982073 was associated with decreased risk of COPD in Caucasians (OR 0.79) ($P = 0.038$) but not in Asians (Liao N 2017; LoE [1]). COPD markers such as soluble urokinase-type plasminogen activator receptor, CRP and fibrinogen decreased after treatment, and only suPAR ($P = 0.002$) and fibrinogen ($P = 0.014$) predicted AE-COPD (Gumus A 2015;LoE[3]). COPD associated bronchiectasis showed significantly more severe in w/CRS than in s/CRS ($P = 0.034$) and the eosinophils% and the levels of IL-6 and MMP-9 in sputum were increased (Yang X 2017; LoE [3]). CRP elevated in AE-COPD compared to the control but IL-6, TNF- α still variated (Chen YW 2016; LoE [1]). The use of Anti- IgE, anti-IL-5 and anti-IL-4/anti-IL-13 therapy in CRS with nasal polyp (CRSwNP) were effective in reducing total nasal endoscopic polyp score, nasal airflow, olfaction and Th-2 associated biomarkers (Tsetsos N. 2018; LoE[1]).

Conclusion: Our study highlights on difference of the roles of ethnicity, TGF β -1 and fibrinogen. Therapeutic interest by monoclonal antibody is arising soon.

AO187

INCREASED NUMBERS OF GROUP 2 INNATE LYMPHOID CELLS IN THE AIRWAYS OF PATIENTS WITH EOSINOPHILIC BRONCHITIS

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Background and Aims: Previous studies demonstrated that the newly group 2 innate lymphoid cell (ILC2) can quickly induce airway eosinophilic inflammation by releasing Th2 cytokines when activated by the epithelium-producing alarmins in asthma. However, whether ILC2 also plays a role in the airway inflammation of eosinophilic bronchitis (EB) remains unclear.

Methods: In a follow-up study, we enumerated blood and sputum ILC2 (CD45⁺Lin⁺CRTh2⁺CD127⁺) in subjects with EB, eosinophilic asthma and healthy control in baseline and after one-month ICS therapy.

Results: The sputum ILC2 level in EB subjects [98(189) cells/g], EA subjects [174(333) cells/g] were both significantly higher than that in the healthy control subjects [3(13) cells/g] ($P < 0.05$, $P < 0.01$, respectively). No significant difference in sputum ILC2 level was found between EB subjects and EA subjects ($P > 0.05$). No significant difference in blood ILC2 level was found in three groups (all $P > 0.05$). After one-month ICS therapy, the sputum ILC2 level in EB subjects [7.5(33) cells/g] decreased significantly as compared with the baseline [101(164) cells/g] ($P < 0.05$). The sputum ILC2 level in EA subjects [37(74) cells/g] decreased significantly as compared with the baseline [159(328) cells/g] ($P < 0.05$). No significant difference in blood ILC2 level was found in EB subjects or EA subjects as compared with the baseline (all $P > 0.05$).

Conclusion: In EB subjects, the ILC2 level is increased in airway but not in circulation and decreased after ICS therapy suggesting local innate immunity might play a potential role in the pathogenesis of eosinophilic bronchitis.

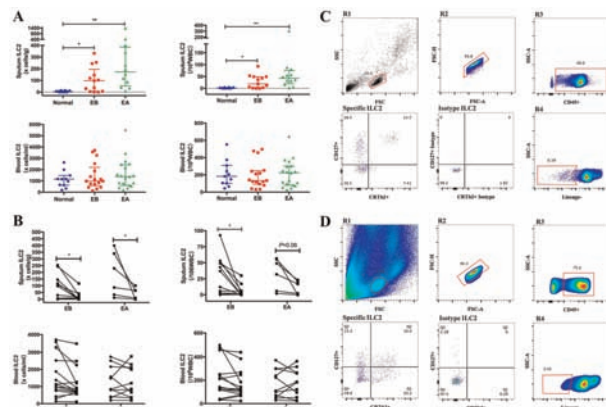


Fig 1A. Baseline sputum and blood ILC2 level in three groups. Significantly increased absolutely number and percentage of ILC2 in sputum was found in patients with EB and EA compared to the healthy control. No significant difference in blood ILC2 level was found in three groups. Fig 1B. The change of sputum and blood ILC2 level after ICS treatment. Absolutely number and percentage of ILC2 in sputum in patients with EB decreased significantly as compared with the baseline. The Absolutely number of ILC2 with EA decreased significantly as compared with the baseline. No significant difference in blood ILC2 level was found in EB subjects or EA subjects as compared with the baseline. Fig 1C&D. Multigating strategy for ILC2 enumeration from blood and sputum. Representative plots from a patient with asthma show sequential gating of blood and sputum cells to identified Lymphocyte (region R1), Singlets (region R2), CD45⁺ (region R3), Lineage⁻ (region R4), and CD127⁺CRTh2⁺ cells (region R4; C&D).

AO188

ASIA PACIFIC SURVEY OF PHYSICIANS ON ASTHMA AND ALLERGIC RHINITIS (ASPAIR): DATA FOR GENERAL PRACTITIONERS COMPARED TO PAEDIATRICIANS

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Background and Aims: The Asia-Pacific Survey of Physicians on Asthma and Allergic Rhinitis (ASPAIR) aimed to assess physicians' perceptions and management practices of patients with coexistent asthma and allergic rhinitis (AR).

Methods: General physicians (GPs, N = 603) and paediatricians (N = 601) treating at least 10 asthma patients/month were interviewed in six Asian countries. Physicians were questioned about their knowledge, beliefs and management of patients with coexistent disease.

Results: GPs saw fewer AR patients per month than paediatricians (mean 37 vs 56) but approximately the same number of asthma patients (mean 52 vs 56). Most GPs and paediatricians believed, respectively, that asthma and AR can coexist (82% for both), coexistent disease results in more burdensome symptoms than asthma (83% vs 87%) or AR alone (88% vs 91%), and that both conditions should be managed and treated (92% vs 90%). More paediatricians than GPs said they managed both diseases in patients with coexistent disease (81% vs 69%), and asked about AR symptoms in asthma patients (77% vs 64%) and about asthma symptoms in AR patients (74% vs 68%) at every clinic visit. Although >80% of both physician groups believed that guidelines are sufficient for treating coexistent disease and guideline-recommended inhaled and intranasal corticosteroids can be given concurrently, this combination was prescribed by less than half of all physicians (GPs: 44%, paediatricians: 50%); consistent with the belief that corticosteroids are associated with too many side-effects (41% vs 34% respectively) and that inhaled and intranasal corticosteroids should be delayed in children (29% vs 20% respectively).

Conclusion: Both GPs and paediatricians recognise the burden of coexistent asthma and AR. In this survey, paediatricians were more likely to treat both conditions separately and had fewer concerns regarding overall steroid used, with the primary aim to achieve disease control for both asthma and AR.

Funding: GSK (206753).

AO189

INCREASED NUMBERS OF CD4⁺CRTh2⁺ T CELLS IN THE AIRWAYS OF PATIENTS WITH EOSINOPHILIC BRONCHITIS

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Background and Aims: Chemoattractant receptor-homologous molecule expressed on Th2 cells

(CRTh2) is a receptor for PGD2 and expressed by T cells, eosinophils, basophils, and group 2 innate lymphoid cells. CRTh2 expression by CD4⁺ T cells identifies the Th2 subset, and these cells have been characterized as allergen-specific central memory Th2 cells. Recently, activation of the PGD2-CRTh2 pathway in the lungs was associated with asthma. Eosinophilic bronchitis (EB) has a similar eosinophilic inflammation with eosinophilic asthmatics, however whether CD4⁺CRTh2⁺ T cells plays a role in EB is unknown.

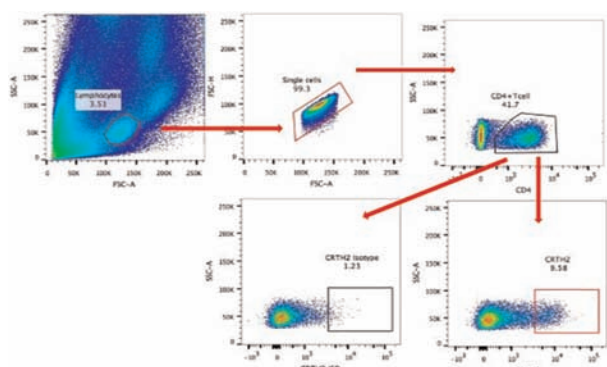
Methods: Peripheral blood cells and induced sputum cells expressing CRTh2 were detected by flow cytometry in patients with eosinophilic bronchitis (EB), eosinophilic asthmatics (EA) and healthy volunteers (HV).

Results: 14 patients with EB, 12 patients with EA and 8 healthy volunteers were enrolled in this study. EA had more circulating CD4⁺CRTh2⁺ T cells compared to HV but not EB [EA 22617(6857) vs HV 17003 (13439) cells/mL blood, $P < 0.05$]. No significant difference was observed

in circulating CD4⁺CRTh2⁺ between EB and HV, or between EB and EA. The Th2 cells in airway (induced sputum) in EB subjects, EA subjects were both significantly higher than that in HV. In the absolute number of Th2 cells: [EB 1651(6033) vs HV 450(439) cells/g sputum, EA 4665 (6314) vs HV 450(439) cells/g sputum, all $P < 0.01$]. In the percentage of Th2 cells: [EB 663(1687) vs N 174(299)/10⁶ WBC, $P < 0.05$], [EA 870 (1339) vs HV 174(299) /10⁶ WBC, $P < 0.01$].

No significant difference in sputum Th2 cell level was found between EB and EA ($P > 0.05$).

Conclusion: Compared with EA subjects, EB subjects only has an increased level of Th2 cells in airway, indicating adaptive immunity might play a role in the pathogenesis of eosinophilic bronchitis. However, unlike eosinophilic asthma, the eosinophilic inflammation may be predominantly localized in airway but not circulation in EB.



Interstitial Lung Disease 2

AO190

IMPAIRMENT OF LUNG DIFFUSE FUNCTION IN PATIENTS WITH PULMONARY LYMPHANGIOMYOMATOSIS (LAM)

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Background and Aims: Pulmonary lymphangiomyomatosis (LAM) is a rare pulmonary disease that mainly affects the lungs, kidneys, and retroperitoneum, with typical manifestations include dyspnea, pneumothorax, diffuse cystic changes in the lungs, which severely affect lung function, especially diffuse function.

Methods: We retrospectively collect data of lung function tests of LAM patients consulted in Guangzhou Institute of Respiratory Disease from 2014 to 2018, and analyzed the characteristics of pulmonary function.

Results: A total of 69 LAM patients were included, and the data were analyzed. The patients were females with mean age 37.6 ± 9.4 years old.

For the results of spirometry, 9 cases (13%) were normal, 5 (7%) restrictive, and 55(80%) obstructive. The mean value of FEV₁ was 59.6 ± 22.2 , FVC 82.4 ± 19.4 , FEV₁/FVC 74.3 ± 20.8 ; RV 143.8 ± 41.5 , TLC 104.7 ± 15.6 , RV /TLC 136.5 ± 30.9 ; DLCO 46.9 ± 19.5 , DLCO/VA 53.4 ± 22.6 .

According to results of spirometry, LAM patients were divided into normal group ($n = 9$), restrictive group ($n = 5$), light-moderate obstructive

group ($n = 33$), and severe-very severe obstructive group ($n = 22$), and the diffusion function were DLCO 67.6 ± 21.9 , 66.2 ± 11.8 , 47.0 ± 17.5 , 34.1 ± 10.4 , DLCO/VA 70.2 ± 17.8 , 88.0 ± 15.7 , 52.3 ± 21.0 , 40.4 ± 15.0 , respectively.

Conclusion: The pulmonary function of LAM patients is mainly obstructive (gas traps exist in some patients), and the diffusion function is significantly reduced. Even in some patients with normal pulmonary function of spirometry, the diffusion function has been mild to moderate impaired, suggesting that the diffusion function was significantly impaired and it happened earlier than the impairment of spirometry in LAM.

AO191

LONG-TERM TREATMENT WITH NINTEDANIB IN ASIAN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS: RESULTS FROM INPULSIS-ON

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Background and Aims: The efficacy and safety of nintedanib 150 mg twice daily (bid) in patients with IPF were investigated in the two placebo-controlled INPULSIS trials. Patients who completed an INPULSIS trial could receive open-label nintedanib in the extension trial INPULSIS-ON.

Methods: The long-term efficacy and safety of nintedanib were assessed in the subgroup of Asian patients treated in INPULSIS-ON. Analyses were descriptive and based on final data (from September 2017).

	Asian patients treated with nintedanib in INPULSIS-ON (n=215)	Asian patients treated in INPULSIS	
		Nintedanib (n=194)	Placebo (n=128)
Diarrhoea	68.8	88.5	21.6
Nasopharyngitis	23.9	28.9	29.6
Progression of IPF*	14.6	14.5	21.6
Upper respiratory tract infection	14.2	19.7	19.2
Lung infection	12.3	5.8	4.8
Decreased appetite	9.9	17.4	9.6
Nausea	8.3	24.3	1.6
Bronchitis	6.7	13.3	6.4
Adverse events with rate >12 per 100 patient exposure-years in any group are shown.			
*Corresponds to MedDRA term 'IPF', which included disease worsening and IPF exacerbations.			

Results: Of 734 patients treated in INPULSIS-ON, 215 were Asian (of whom 121 continued nintedanib in INPULSIS-ON and 94 initiated nintedanib in INPULSIS-ON having received placebo in INPULSIS). In the Asian subgroup, at baseline of INPULSIS-ON, mean age was 66.3 years, 80.5% were male, and mean FVC % predicted was 78.9. Mean (SD) exposure to nintedanib in INPULSIS-ON was 27.5 (15.4) months. Mean (SD) total exposure for Asian patients treated with nintedanib in both INPULSIS and INPULSIS-ON was 40.1 (15.1) months (maximum: 64.1 months). In INPULSIS, the annual rate (SE) of decline in FVC over 52 weeks in Asian patients was -124 (20) mL/year in the nintedanib group and -218 (24) mL/year in the placebo group. In INPULSIS-ON, the

annual rate (SE) of decline in FVC over 192 weeks in Asian patients was -127 (11) mL/year. Diarrhoea was the most common adverse event in Asian patients treated with nintedanib in INPULSIS and INPULSIS-ON (88.5 and 68.8 events per 100 patient-exposure years, respectively) (table). The event rate of serious adverse events in Asian patients treated with nintedanib in INPULSIS and INPULSIS-ON was 71.1 and 80.9 events per 100 patient-exposure years, respectively.

Conclusion: Data from INPULSIS-ON indicate that the effect of nintedanib on reducing disease progression in Asian patients with IPF is maintained over the long term. Treatment with nintedanib, up to 64 months, had an acceptable safety and tolerability profile.

AO192

NON-INTERVENTIONAL STUDY COLLECTING EXPERIENCES FOR IPF IN TAIWAN (NICEFIT STUDY): INTERIM REPORT

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Background and Aims: The prevalence and incidence of IPF from 1997 to 2007 in Taiwan is 0.7–6.4 cases/100,000 and 0.6–1.4/100,000 respectively, which is relatively low compared to western countries (Raghu, G., et al. *Am J Respir Crit Care Med*, 2006. 174: P. 810-6.). The mean survival in Taiwan is only 0.9 year after IPF diagnosis.

There are two anti-fibrotic drugs conditionally recommended in 2015 IPF treatment guidance: Nintedanib and Pirfenidone. Nintedanib (OFEV[®]) is on the market in Taiwan since September 2015 and Pirfenidone (Pirespa[®]) will be on market in the first half of 2017.

Data on characteristics and management of IPF patients are still scarce in Taiwan. An IPF non-intervention study would help to gain a better understanding of the epidemiology of the disease and how it is currently managed.

The objective of this non-interventional study is to characterize the IPF population in Taiwan with regard to their demographic, clinical characteristics and treatment.

Methods: IPF patients will be enrolled in a consecutive manner and data will be collected in accordance with real-world clinical practice (baseline, and planned at 1st month and every 3 months afterward, and visits will be in accordance with clinical needs judged by physicians).

The enrolment period for the study will be one year and each patient will be followed-up for 2 years.

Results:

- d. Enrolment period: 2017 Aug.–2018 Feb.
- e. Total enrolment: 101
- f. Excerpted baseline characteristics (until abstract submission):

Conclusion:

- g. NICEFIT study is the first IPF registry in Taiwan and documents real world epidemiology of IPF in Taiwan.
- h. NICEFIT study shows similar patient characteristics as other published registries.
- i. Most of enrolled patients are under anti-fibrotic drug treatment which is reimbursed before NICEFIT study enrolment. No unexpected adverse effect is observed for anti-fibrotic drug.

- j. Further analysis will be posted after 90 patients completing at least 4 months follow up.

AO193

EFFECT OF TOCILIZUMAB ON INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background and Aims: Interstitial lung disease (ILD) is the most common pulmonary complication in patients with rheumatoid arthritis (RA). Certain drugs used to treat RA, such as methotrexate or anti-tumor necrosis factor- α antibodies, have been associated with the development or progression of ILD. Therefore, drugs used for treating RA with ILD should be administered carefully. This study aimed to evaluate the safety of tocilizumab on ILD in patients with RA.

Methods: Subjects were 12 patients (6 men, 6 women, mean age 74.5 years) with both RA and ILD. Types of ILD were idiopathic pulmonary fibrosis pattern 11 and nonspecific interstitial pneumonia pattern 1. The effect of tocilizumab was evaluated before, 1 month after, and 6 months after administration.

Results: Mean levels of matrix metalloproteinase-3 (MMP-3), which is a biomarker of RA disease activity, were 296 ± 319 , 200 ± 266 , and 202 ± 270 ng/mL, respectively. Significant differences were observed between before and after administration of tocilizumab (before vs 1 month: $P < 0.05$, before vs 6 months: $P < 0.05$). Mean levels of Krebs von den Lungen-6 (KL-6) were 718 ± 323 , 720 ± 210 , and 594 ± 276 U/mL, respectively. No significant differences were observed between before and after administration. Mean levels of lactate dehydrogenase (LDH) were 236 ± 37 , 241 ± 44 , and 248 ± 51 U/mL, respectively. No significant differences were observed between before and after administration. Chest computed tomography (CT) revealed no differences between before and 1 year after administration.

Conclusion: The disease activity of RA was significantly improved by administration of tocilizumab, and ILD did not progress. In patients with both RA and ILD, tocilizumab could be administered safely without progression of ILD. We have analyzed other markers and will present our final results at the APSR 2018 Congress.

AO194

DOES FEF₂₅₋₇₅ DISTINGUISH BETWEEN AIRWAY OBSTRUCTION AND RESTRICTION IN DPLD?

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Background and Aims: The diagnosis of restriction from low FVC with or without $\geq$ FEV₁% cannot effectively predict or distinguish between obstruction and restriction according to literature. We perceive and postulate that FEF₂₅₋₇₅ remains relatively unaffected or paradoxically increased in parenchyma restrictions as Diffused parenchyma lung disease (DPLD).

Methods: We selected 140 spirometry belonging to obstructive lung disease (OLD) patients (including COPD and asthma) and 134 spirometry belonging to DPLD patients from the archive of different research protocols. These patients were diagnosed according to the standard evaluation of diagnosis of the disease. We compared the predicted percentage value of FEF₂₅₋₇₅ values between the two groups and tried to analyze the capacity of FEF₂₅₋₇₅ to differentiate OLD from DPLD.

Results: The predicted percentage value of FEF_{25-75} remains significantly higher in DPLD patients [78.0(54.2-109.0)] compared to OLD [25.0 (15.0–36.5)] patients. We tried to look for the diagnostic ability of the parameter and found that it distinguishes between DPLD and OLD by a cut off value of 54.45 which has 90.3% sensitivity, 94.0% specificity, 75.6% positive predictive value, 93.8% negative predictive value and the area under the curve for ROC analysis for the parameter being 0.91.

Conclusion: FEF_{25-75} can be regarded as the marker to identify DPLD in situations in situations of clinical and radiological suspicions. Further evaluations are being conducted for validation of the result.

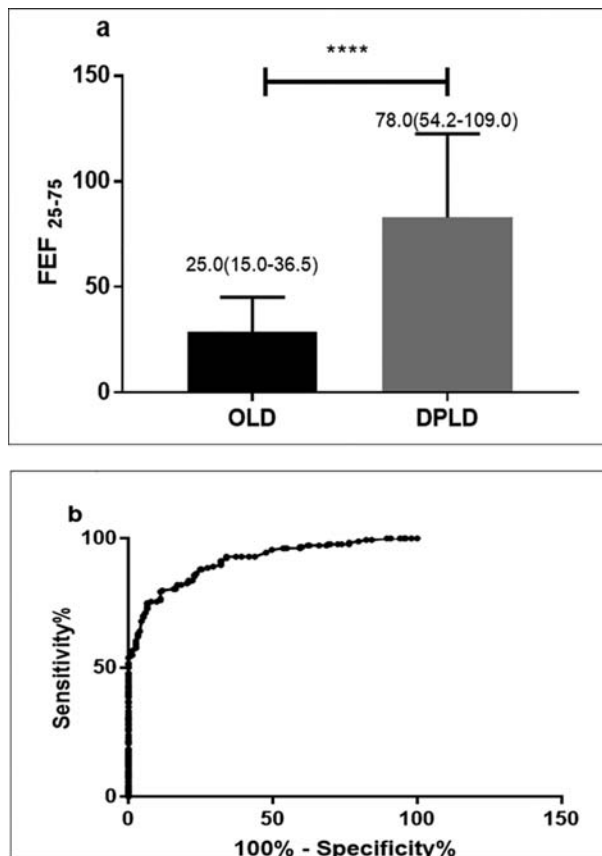


Figure 1: (a) The difference in the percentage predicted values FEF_{25-75} between OLD and DPLD. (b) The ROC curve between OLD and DPLD has 0.91 area under the curve.

AO195

CIGARETTE SMOKING CAN AGGRAVATE PULMONARY FIBROSIS BY INDUCING ALVEOLAR EPITHELIAL CELL II SENESCENCE

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Background and Aims: In vivo, we aimed to determine whether cigarette smoking can promote ACEII senescence and aggravate bleomycin (BLM) induced pulmonary fibrosis in mice; in vitro, to explore the mechanisms underlying ACEII senescence following cigarette smoke extract (CSE) treatment.

Methods: In vivo, 60 male C57 mice were randomly divided into three groups: control, BLM and BLM+cigarette smoking. In control and BLM group, 100 μ L sterile saline and equivalent sterile saline containing BLM at a single dose of 5 mg/kg were administered, respectively; in BLM+cigarette smoking group, following treated with BLM, mice were exposed to 5 commercial filtered cigarettes for 1 h each time, 2 times a day (respectively in the morning and afternoon) for 4 weeks. 4 weeks later, lung tissues were harvest and H&E, Masson's trichrome were performed and Ashcroft score were assessed. The expression of SPC, p16 and p21 were detected by immunohistochemistry. In vitro, mouse AECII strain MLE-12 were stimulated respectively with 0.05%, 0.1%, 0.25%, 0.5%, 1% CSE for 36 h and H_2O_2 stimulation as positive control. The cellular senescence were evaluated with β -galactosidase staining and western blot analysis of p16 and p21. The protein level of p62 and LC3 were also detected. The cells were treated with or without 3-methyladenine (3-MA), bafilomycin (BA) and rapamycin (RAPA) following CSE stimulation and senescence rate were evaluated.

Results: Compared with BLM group, the masson staining and Ashcroft score were upregulated significantly in BLM+cigarette smoking group, accompanied with elevation expression of p16 and p21 in SPC-positive cells. The senescence markers including β -galactosidase, p16 and p21 were increased after CSE stimulation at a concentration of 0.5% and the conversion of LC3I to LC3II were blocked. 3-MA, BA and RAPA had no significant impact on senescence rate.

Conclusion: Cigarette can aggravate pulmonary fibrosis by inducing alveolar epithelial cell II senescence, which may be mediated by abnormal autophagy flux.

COPD 3

AO196

HEART RATE VARIABILITIES BIOFEEDBACK AS AN ADJUNCT TO PULMONARY REHABILITATIVE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: To test the effectiveness of combined a heart rate variability biofeedback (HRVBF) with PR on improving physiological and psychological well-being, adherence to regular exercise, and further improving the quality of life in patients with COPD.

Methods: This was a randomized controlled trial. Subjects were recruited from a Medical Center in Taiwan, and randomly divided into usual care (sham group), PR alone (PR group), or combined PR and HRVBF group (PR-HRVBF group). All subjects received twice a week supervised hospital training and a weekly unsupervised home training for four weeks. We compared pre-, post-training, 12-week and 24-week follow-ups of psychophysiological indices among three groups

Results: Thirty-six subjects completed the participation. The PR-HRVBF groups had significantly higher adherence to regular exercise at 12-week follow-up than the other two groups ($\chi^2 = 12.6$, $P = 0.01$). Both PR and PR-HRVBF groups had higher quality of life in physical component than usual care group ($P = 0.05$) at 12-week follow-up. The PR-HRVBF group showed significantly decreasing depression, improving SF12-MCS ($P < .05$), 6MWD ($P < 0.05$), HRV ($P < 0.05$), and 6MWD after 4 weeks training and 12-week follow-up. The PR group presented significantly decreasing dyspnea ($P < 0.05$), improving SF12-PCS ($P < .01$), and HRV-TP ($P < 0.05$) after 4 weeks training, but decreasing dyspnea ($P < 0.05$), anxiety ($P < 0.05$), and depression, improving SF12-PCS ($P < .01$), and HRV ($P < 0.01$) significantly changed at 12-week follow-up. In sham group, all psychophysiological indices did not significantly change at any time

point. In 24-week follow-up, there were only combined PR and HRV group presented, significantly improved SF12-MCS, 6MWT, and the changed of HRV-SDNN In, LF, and TP ($P < 0.05$).

Conclusion: PR exercise can improve the physiological component of quality of life for COPD patients. However, HRVBF as an adjunct to PR exercise can further improve adherence to regular exercise, 6MWT, HRV, and mental component of quality of life for COPD patients.

AO197

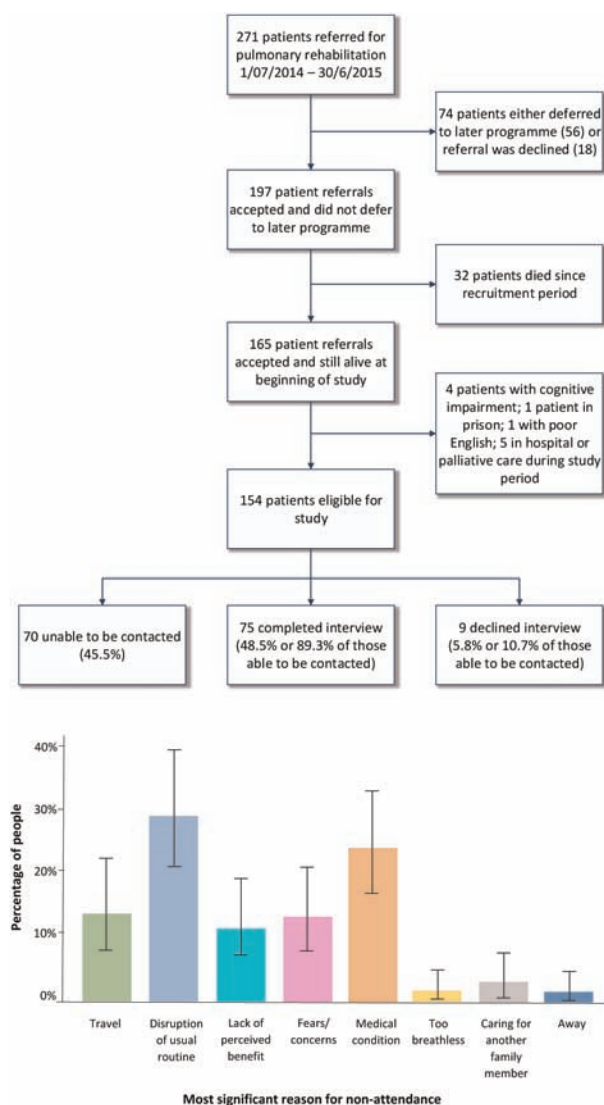
FACTORS ASSOCIATED WITH NON-ATTENDANCE TO PULMONARY REHABILITATION IN CANTERBURY, NEW ZEALAND

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Background and Aims: Despite the evidence of the benefits that PR can have, only a minority of COPD patients are being referred for this service, and, more worryingly, very few of those referred actually enter and complete a PR programme for various reasons.

This project aims to explore the non-attendance factors using a semi-structured interview questionnaire with a cohort of patients who have previously not attended PR after being referred by their doctor.



Methods: A mixed-methods cohort study of patients referred for Pulmonary Rehabilitation to the Canterbury Clinical Network was performed.

Patient electronic records were examined and the exclusion criteria were applied. The final eligible population consisted of 154 patients.

A telephone-based interview tool was developed that utilized a mixed-methods design where a series of quantitative questions were included to measure themes identified from a review of the relevant literature.

Results: Non-attendees at PR were on average younger than attendees. Those participants unable to be contacted were younger still.

The five most significant reasons reported were disruption of usual routine (32.3%), current medical condition (24.6%), issues with travel (13.8%), fears or concerns about aspects of the PR programme (12.4%), and lack of perceived benefit (10.8%).

There appeared to be a relationship between the amount of information given to patient at the time of referral, and subsequent non-attendance.

Conclusion: Practical factors like work, competing interests, and transport all play a significant role in non-attendance to PR programmes. In addition to this, the patient's attitude also contributes, where factors like a lack of perceived benefit, poor understanding, or the perception that one is unsuitable for the programme all result in lowered engagement in the programme. Major contributing factors are the information and communication delivered to patients at the time of initial referral.

AO198

IMPACT OF MUSIC THERAPY ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS

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Background and Aims: The debilitating symptom of breathlessness often limited chronic obstructive pulmonary disease (COPD) patients' participation in social activities. Consequently, many became socially isolated and prone to developing depression. Singing requires a high degree of breathing control as it involves strong and fast inspiration, followed by extended and regulated expiration. Group music therapy (MT) could provide breathing training while increasing COPD patients' social well-being.

Objective: Evaluate the effect of MT on COPD patients' well-being.

Methods: MT was offered to members of a COPD self-help group 'BreatheStrong' in 2017 by certified music therapists. An initial nine-session class was conducted to experiment with different training modes including vocal exercise, singing and playing simple instruments. A second nine-session class was held from August to December with the aim of performing on World COPD Day. Participants completed the Hospital Anxiety and Depression (HAD) questionnaire before and after MT.

Results: Twenty-seven 'BreatheStrong' group members participated in the second MT class. Fourteen patients were female (mean age: 77 years) and 13 were male (mean age: 73 years). Mean forced expiratory volume at one second (FEV1) was 1.04 L with 37% patients having advanced COPD (Global Obstructive Lung Disease GOLD stage III-IV). Ten participants were on long-term oxygen therapy. Mean HAD depression score improved by 1.8 (4.5 > 2.7) while mean HAD anxiety score improved by 1.6 (4.8 > 3.2). Many patients reported that singing facilitated breathing control and helped in dyspnoea relief. Other comments included 'My breathing becomes more sustained', 'I can speak loudly', 'I feel full of energy when singing', 'Playing instruments is like doing exercise' and 'Singing is so relaxing that I forget my suffering'. 'BreatheStrong' choir performed three songs, including one with self-written lyrics unique to COPD, on World COPD Day.

Conclusion: MT succeeded in engaging a group of elderly COPD patients while reducing their feelings of anxiety and depression.

AO199

**EFFICACY AND SAFETY OF GLYCOPYRRONIUM/
FORMOTEROL FUMARATE DIHYDRATE METERED DOSE
INHALER (GFF MDI) DELIVERED USING CO-SUSPENSION
DELIVERY TECHNOLOGY IN CHINESE PATIENTS
WITH COPD**

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Background and Aims: COPD is a major public health concern in China. We assessed the efficacy and safety of GFF MDI vs placebo MDI and monocomponents in patients with moderate-to-very severe COPD in the China subpopulation of the PINNACLE-4 study (NCT02343458).

Table. Primary and secondary efficacy endpoints (China ITT population*)

	GFF MDI 14.4/10 µg ^b vs placebo MDI	GFF MDI 14.4/10 µg ^b vs GP MDI 14.4 µg	GFF MDI 14.4/10 µg ^b vs FF MDI 10 µg
Primary endpoint			
Change from baseline in morning pre-dose trough FEV₁ at Week 24, mL			
LSM difference	173 [†]	98***	104 [†]
95% CI	110, 235	48, 148	55, 153
Secondary endpoints			
Change from baseline in morning pre-dose trough FEV₁ over 24 weeks, mL			
LSM difference	163 [†]	79 [†]	93 [†]
95% CI	115, 212	40, 118	55, 131
Peak change from baseline in FEV₁ within 2 hours post-dosing at Week 24, mL			
LSM difference	305 [†]	182 [†]	151 [†]
95% CI	234, 376	125, 239	95, 207
TDI focal score over 24 weeks			
LSM difference	1.11***	0.42	0.20
95% CI	0.52, 1.69	-0.05, 0.89	-0.26, 0.66
Change from baseline in SGRQ total score at Week 24			
LSM difference	-3.24	-1.21	0.87
95% CI	-6.76, 0.28	-4.02, 1.61	-1.90, 3.64
Change from baseline in average daily rescue medication use over 24 weeks, puffs/day^c			
LSM difference	-1.11	-1.42**	-0.63
95% CI	-2.24, 0.02	-2.26, -0.59	-1.45, 0.19
Onset of action on Day 1, mL^d			
LSM difference at 5 mins	184 [†]	34	169 [†]
95% CI	(150, 219)	(-1, 70)	(135, 204)
LSM difference at 15 mins	225 [†]	76 [†]	193 [†]
95% CI	(189, 262)	(38, 113)	(156, 230)

p<0.01, *p<0.001, [†]p<0.0001; Results were not Type I error controlled and are considered exploratory rather than inferential.

*The China ITT population included all patients enrolled in China who were randomized and received any study treatment (excluding patients from Site 174); GFF MDI n=146, GP MDI n=122, FF MDI n=135, placebo MDI n=63. Data are shown for patients with evaluable data for each endpoint.

^bDoses are expressed as glycopyrronium 14.4 µg and formoterol fumarate dihydrate 10 µg, equivalent to glycopyrrolate 18 µg and formoterol fumarate 9.6 µg, respectively.

^cAssessed in the China rescue medication population: all patients in the ITT population with average baseline rescue medication use of ≥1 puff/day (GFF MDI n=45, GP MDI n=39, FF MDI n=44, placebo MDI n=16).

^dChange from baseline in FEV₁ at specified time post-dose on Day 1 vs placebo MDI.

CI, confidence interval; FEV₁, forced expiratory volume in 1 second; FF, formoterol fumarate dihydrate; GFF, glycopyrronium/formoterol fumarate dihydrate; GP, glycopyrronium; ITT, intent-to-treat; LSM, least squares mean; MDI, metered dose inhaler; SGRQ, St George's Respiratory Questionnaire; TDI, transition dyspnoea index.

Methods: In this 24-week, randomized, double-blind, parallel-group, Phase III study, patients received twice-daily GFF MDI 14.4/10 µg, formoterol fumarate dihydrate (FF) MDI 10 µg, glycopyrronium (GP) MDI 14.4 µg, or placebo MDI. Efficacy endpoints are shown in the Table.

Results: The intent-to-treat population in China included 466 patients (96% male; 33% current smokers; mean post-bronchodilator FEV₁, 54% predicted). GFF MDI improved the change from baseline in morning pre-dose trough FEV₁ at Week 24 (primary endpoint; China approach) vs placebo MDI (least squares mean difference 173 mL), GP MDI (98 mL), and FF MDI (104 mL, all $P \leq 0.0001$). Improvements in secondary lung function and symptomatic endpoints were also observed for GFF MDI vs comparators (Table). Adverse event frequency was similar across treatments.

Conclusion: GFF MDI improved lung function and symptoms in the PINNACLE-4 China subpopulation. Efficacy and safety results were consistent with the total patient population and support the use of GFF MDI in Chinese patients with moderate-to-very severe COPD.

AO200

**BENEFITS AND RISKS OF INHALED CORTICOSTEROID
TREATMENT IN PATIENTS WITH COPD CLASSIFIED BY
BLOOD EOSINOPHIL COUNTS**

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Background and Aims: Chronic obstructive pulmonary disease (COPD) generally includes neutrophilic airway inflammation, but some cases demonstrate eosinophilic inflammation. Inhaled corticosteroid (ICS) for patients with COPD suppresses eosinophilic inflammation of the airway, and may possibly reduce acute exacerbation. On the other hand, however, ICS may raise the risk of pneumonia. We classified patients with COPD by blood eosinophil counts and retrospectively evaluated the benefit and risk of ICS treatment.

Methods: A total of 244 patients with COPD enrolled between 2014 and 2017 were assigned to groups with blood eosinophil counts of ≥300/µL and < 300/µL, respectively. Moreover, we divided these groups into subgroups with and without ICS treatment, and statistically compared the incident rate of acute exacerbation and merger of pneumonia in each group.

Results: Of the 244 patients with COPD, 97 (39.8%; 33 with and 64 without ICS) and 147 (46 with and 101 without ICS) had blood eosinophil counts of ≥300/µL (group 1) and < 300/µL (group 2), respectively. In group 1, a significantly lower incidence rate of acute exacerbation was noted in the ICS than in the non-ICS groups ($P = 0.023$), while there was no difference in group 2. Regarding merger of pneumonia on acute exacerbation, there was no significant difference between the ICS groups in group 1, while in group 2 the ICS group had a higher incidence ($P = 0.009$).

Conclusion: We concluded that the blood eosinophil count was a useful marker for suppression of acute exacerbation by ICS treatment. Also, ICS treatment did not increase the risk of pneumonia in patients with blood eosinophil counts of ≥300/µL, but the risk was increased in patients with < 300/µL. To identify the presence of eosinophilic inflammation by checking blood eosinophil counts may lead to obtain a long-term prognosis in patients with COPD.

AO201

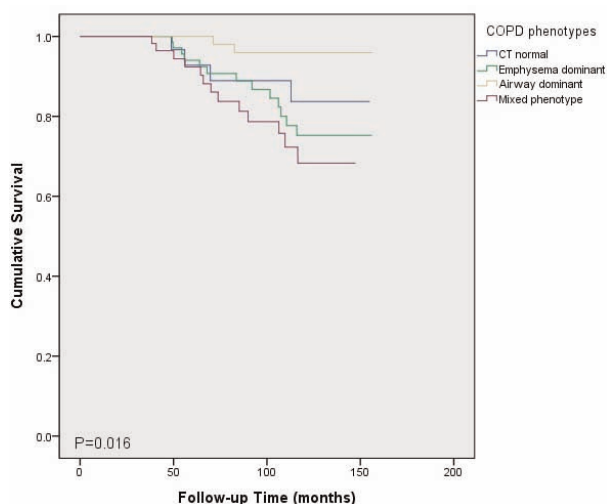
CLINICAL COURSE OF COPD PATIENTS WITH BOTH EMPHYSEMA AND AIRWAY WALL THICKENING ON CT COMPARED TO OTHER PHENOTYPES

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Background and Aims: Volumetric CT has been widely used to phenotype COPD patients. A mixed phenotype is defined as the presence of both emphysema and airway wall thickening on volumetric CT. Long-term clinical courses of this phenotype has not been studied in depth. This study aimed to compare baseline clinical characteristics and clinical course of the mixed phenotype to other phenotypes of COPD patients.

Methods: Patients enrolled in the Korean Obstructive Lung Disease (KOLD) study from June 2005 to October 2015 were evaluated for this study. The patients were spirometrically diagnosed with COPD and had a smoking history of more than 10 pack-years. Volumetric CT scans were performed for each patient upon enrolment in the cohort and annual follow up pulmonary function tests were performed for at least 3 years. The emphysema index and the percentage of bronchial mean wall area percentage were calculated from the volumetric CT. Patients with COPD were classified into four distinct phenotypes using two cutoffs: emphysema index of 15% and median value of mean wall area (%) (MWA%).



Results: Of 261 patients with COPD, 51 (19.5%) were classified as CT-normal phenotype, 71 (27.2%) as airway-dominant phenotype, 80 (30.7%) as emphysema dominant phenotype and 59 (22.6%) as mixed phenotype. The patients in the mixed phenotype showed the highest baseline SGRQ-score among the four phenotypes with significant difference ($P < 0.001$). Overall survival of the four phenotypes were evaluated using Kaplan-Meier curve analysis, showing significantly shorter survival

time in patients in the mixed phenotype (Figure, $P < 0.01$). There was no significant difference in frequency of COPD exacerbations between the phenotypes ($P = 0.157$). FEV1 (%) decline over 3 years was most prominent in the mixed phenotype (-9.9%+-10.4) compared to the other phenotypes ($P = 0.032$).

Conclusion: The patients in the mixed phenotype showed relatively higher SGRQ score, and shorter survival when compared to other phenotypes.

AO202

FOUR-WEEKS REMOTE PULMONARY REHABILITATION PROTOCOL WITH MOBILE APPS OF REAL-TIME HEART RATE MONITORING FOR GOLD CATEGORY B/C/D- A STUDY DESIGN

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Background and Aims: Recently before 2015, a health system that provides better care, spends dollars more wisely, and has healthier people was mentioned (Burwell SM NEJM 2015/Jan/26). One of the three major aspects (incentives, care delivery and information) suggested 'bring electronic health information to the point of care for meaningful use'. Another systematic review article concluded 'strongly support pulmonary rehabilitation, including at least four weeks of exercise training, as part of the spectrum of treatment for patients with COPD.' (McCarthy B et al Cochrane Reviews 2015). Therefore, we propose a protocol for PR on COPD GOLD B/C/D with mobile apps.

Methods: A randomized controlled trial named 'BIG-apps' study (Breathing Is Getting apps) was designed. Enrolment: out-patient-department patients with GOLD category B, C to D since 2018/July/1 to 2020/June/30. BIG-apps includes an online social society discussion group via line, facebook WeChat or twitter. A mobile app named 'instant heart rate' designed by azumio™ was installed initially to mobile phone for real-time heart rate monitoring. Randomization is on a 2:1 ratio for intervention-to-control. The intervention arm had well-organized PR information by education of deep-inspiration, pursed lip breathing, diaphragmatic breathing, individualized goals on nutrition, daily step-counts, predicted step-up and step-down heart rate on exercise, motivational and emotional attention, notification of inhaler dose/frequency, particle matters density, life-style modification, tobacco smoking cessation and daily-offered pulmonary medical information on website/health blog. PR is offered 30 min per day, 3 days per week, targeting on 70% maximum heart rate (70MHR) in interventional arm. The control is only referral to web-based information offered at social society. Cases numbers: Intervention group is 300, the control is 150 cases (each group has equal ratio in different GOLD B/C/D categories).

Results: Primary endpoint: 6-min walk distance. 2nd outcome: mMRC, CAT and length of stay in hospital admission if any severe acute exacerbation develops.

Conclusion: to be initiated.

Lung Cancer 3

AO203

IMMUNOLOGICAL ANALYSIS OF PLEURAL EFFUSION IN CANCER PATIENTS WHO RECEIVED IMMUNE CHECKPOINT INHIBITORS (ICI) FOR THE DEVELOPMENT OF BIOMARKERS

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Background and Aims: Malignant pleural effusion of cancer patients has been well known to be correlated with worse outcome and sign of progression disease after chemotherapy. However, we previously reported a case in which a cancer patient treated with immune checkpoint inhibitor (ICI) developed massive pleural effusion followed by remarkable tumor shrinkage. This finding suggested to us a hypothesis that pleural effusion in patients treated with ICI holds distinct immunological characteristics to enable to predict response to ICI treatment and no such analysis had been done before. Therefore, we currently have performed a multi-institutional, prospective observational study in patients who developed pleural effusion after the initiation of ICI for the development of novel therapeutic biomarkers of ICI.

Methods: We analyzed lymphocytes in pleural effusion by flow cytometry immunologically to understand the expression of immune checkpoints and comprehensive cytokine profiles. As a control, we also analyzed pleural effusions of patients by cancer treatments other than ICIs (cytotoxic agents and TKIs). Primary objective was to reveal immunological characteristics of lymphocytes in pleural effusion of patients treated with ICI. This study was approved by each institutional review board.

RESULT

Median of days when patients developed pleural effusion		22.5 days (7-44)
*Response to ICI after developing pleural effusion		Patients (n=8)
Objective Response (Complete response and Partial response)		2
Disease Control (Complete response, Partial response and stable disease)		5
Progression Disease		3
Need to pleurodesis		Patients (n=8)
yes		3
No		5

Expression of immune checkpoints on T lymphocytes and IL-17A producing CD4+T cells in pleural effusion.

		ICI	control	P value	responders of ICI	non-responders of ICI	P value
PD-1	CD4+T cells (%)	20.7	10.1	0.26	21.9	19.97	0.76
	CD8+T cells (%)	13.4	7.7	0.37	16.4	10.3	0.55
TIM-3	CD4+T cells (%)	7.1	4.1	0.058	11.3	5.7	0.55
	CD8+T cells (%)	13.9	4.3	0.0062**	14.1	6.6	0.23
TIGIT	CD4+T cells (%)	34.7	19.9	0.0018**	43.3	28.5	0.37
	CD8+T cells (%)	53.1	38.3	0.04*	57.1	49	0.76
LAG-3	CD4+T cells (%)	16.9	18.6	0.33	10.4	21.03	0.13
	CD8+T cells (%)	14.6	10.9	0.97	18.7	10.6	0.37
PD-L1	CD4+T cells (%)	44.1	40.8	0.65	44.1	40.8	0.65
	CD8+T cells (%)	67.7	43.5	0.076	67.4	74.2	0.55
IL-17A	CD4+T cells (%)	1.89	2.3	0.93	1.1	4.03	0.037*

*:P<0.05, **:P<0.01

Results: Total 20 patients (eight patients treated with ICI and 12 patients with other anticancer agents) were analyzed at the time of abstract registration. Our study demonstrated that anti-PD-1 therapy upregulated expression of TIM-3 on CD8-positive T cells ($P = 0.0062$) as well as TIGIT on both

CD4-positive T cells ($P = 0.018$) and CD8-positive T cells ($P = 0.04$) in comparison to other anticancer agents. Among patients treated with ICI, CD4-positive T cells of pleural effusion produced significantly less IL-17 in patients who responded to ICI than those who did not respond ($P = 0.037$).

Conclusion: Our result demonstrated that the emergence of IL-17-producing CD4-positive T cells in pleural effusions after the onset of ICI could be a potential biomarker for ICI treatment.

AO204

STUDY OF SYNERGISTIC EFFECT OF METFORMIN WITH PEMETREXED IN LUNG CANCER THERAPY VIA ORTHOTOPIC LUNG INJECTION FLUORESCENT MICE TUMOR MODEL

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Background and Aims: Cancer acts as the first ranking for cause of death in Taiwan. As for lung cancer, it calls for cancer related mortality for both men and women. For advanced disease, poor prognosis was anticipated. The scope of therapy was based on chemotherapy for wild type lung adenocarcinoma. In this study, we try to show the synergistic effect of **Metformin** combined with **Pemetrexed (Alimta®)** based on orthotopic lung injection fluorescent mice tumor model.

Methods: First, we set up the Near-Infrared Fluorescent Protein (iRFP) Image System and construction the dual fluorescence-expression vector pCAG-iRFP-2A-Venus and transfection the lung adenocarcinoma A549 cell line. Then, Xenografts model was created by orthotopic trans-pleural (lung) injection. We applied IVIS to observe the effect of Metformin combination with Pemetrexed in lung cancer therapy. Finally, we tried to explore the angiogenesis associated pathway involved in the therapy process under Metformin combined with Pemetrexed.

Results: 1. The IVIS study and Total Radiant Efficiency (By ROI analysis) showed decreased tumor formation in Pemetrexed (Alimta®) with Metformin (A+M) Group compared with other groups. 2. The detection of mouse CD105 and VEGF expression in Mouse Serum by ELISA method indicated reduced expression level in (A+M) Group compared with Mock group (without treatment). 3. mRNA expression level of hVEGFα and hCEACAM5 in (A+M) Group showed decreased compared with Mock Group and some other treatment groups. 4. The H&E morphology and IHC analysis of LDH expression in each group showed tumor size decreased after Alimta combined with metformin (A+M) treatment.

Conclusion: In our orthotopic lung injection fluorescent tumor model, we explored and found preliminary anti-tumorigenesis effect of combination of **Metformin** with **Pemetrexed (Alimta®)** in lung cancer treatment. Further prospective and clinical trials are needed to further elucidate the synergistic effect of Metformin Combined with Pemetrexed (Alimta®) in real life lung cancer patients.

AO205

ADENYLATE CYCLASE-ASSOCIATED PROTEIN 1-TARGETED NANOPARTICLES AS A NOVEL STRATEGY FOR THE TREATMENT OF METASTATIC NON-SMALL CELL LUNG CANCER

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Background and Aims: Non-small cell lung cancer (NSCLC) is the most common cause of cancer death in the world.

Methods: Adenylate cyclase-associated protein 1 (CAP1) is a member of the cyclase-associated proteins contributing to tumor progression. Our previous study has confirmed that CAP1 is associated with lung cancer and cancer cell metastasis.

Results: In the present research, PLGA/CAP1-siRNA nanoparticles were prepared and used to deliver CAP1-siRNA to A549 cells and down regulate CAP1 expression both *in vitro* and *in vivo*. The attractive performance of PLGA/CAP1-siRNA nanoparticles for delivering siRNA was confirmed by transwell assay, scratch assay and animal experiments.

Conclusion: The results demonstrated that the multifunctional nanoparticles interfered with the expression of CAP1 and reduced NSCLC metastasis both *in vitro* and *in vivo*, suggesting that PLGA/CAP1-siRNA nanoparticles may become a new strategy of the treatment for metastatic NSCLC.

AO206

INCIDENCE OF BRAIN METASTASIS IN PATIENT WITH NEWLY DIAGNOSED LUNG ADENOCARCINOMA

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Background and Aims: Routine brain magnetic resonance imaging (MRI) is still controversial in patients with non-small cell lung cancer (NSCLC) even among major clinical guidelines. While National Comprehensive Cancer Network (NCCN) guidelines do not recommend routine brain MRI screening in stage I NSCLC patients who are asymptomatic, the European Society for Medical Oncology (ESMO) guideline suggests that screening for brain metastases (BM) with MRI might be useful in patients considering for curative therapy. While the prevalence of brain metastasis (BM) is known to be very low in patients with stage I squamous cell carcinoma, that of patients with adenocarcinoma is not well studied. In the present study, we aimed to evaluate the prevalence of brain metastasis across the stages and clinical factors associated with BM.

TABLE 1. Clinical Factors Associated With Brain Metastasis

	Any brain metastases					
	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	Adjusted OR	95% CI	P value
Age, years	1.01	0.98-1.03	0.637	1.01	0.99-1.03	0.467
Sex, female	1.47	0.95-2.29	0.089	2.61	1.28-5.52	0.010
Smoking history						
Nonsmoker		Ref			Ref	
Current or ex-smoker	1.06	0.78-1.41	0.723	1.49	0.93-2.41	0.098
T staging						
T1		Ref			Ref	
T2	2.29	1.31-4.03	0.004	1.38	0.73-2.63	0.325
T3	2.25	1.10-4.46	0.022	1.02	0.45-2.27	0.959
T4	6.34	3.29-12.29	< 0.001	2.04	0.94-4.45	0.071
N staging						
N0		Ref			Ref	
N1	7.25	2.88-17.88	< 0.001	4.66	1.71-12.39	0.002
N2	6.42	3.22-13.38	< 0.001	3.07	1.39-6.94	0.006
N3	12.39	6.60-24.83	< 0.001	5.15	2.47-11.23	< 0.001
M staging*						
M0		Ref			Ref	
M1a	14.65	4.63-47.90	< 0.001	10.53	3.02-37.75	< 0.001
M1b	10.34	6.33-17.15	< 0.001	5.85	3.38-10.27	< 0.001

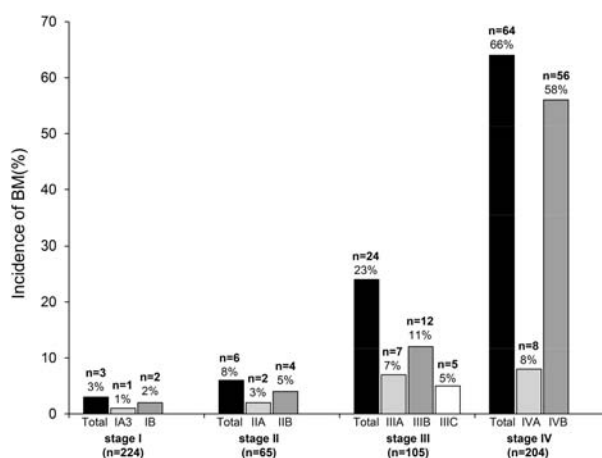
* Brain metastasis was not included in the staging.

OR = odds ratio; CI = confidence interval; Ref = reference value.

Methods: Patients who were diagnosed with lung adenocarcinoma at Samsung Medical Center in 2014 were retrospectively identified and reviewed comprehensively for TNM staging by 8th edition of AJCC. All brain metastasis were confirmed by gadolinium-enhanced magnetic resonance image and invasive nodal staging were performed in all patients with equivocal nodal metastasis in CT/PET.

Results: Among 598 included patients, 97 (16%) had BM. BM occurred in patients with all stage disease and increased as the disease progressed (3 [1%], 6 [9%], 24 [23%], and 12 [31%] in stage I, II, III, and IV, respectively, *P*-for trend < 0.001). All three patients with BM in stage I showed epidermal growth factor receptor (EGFR) mutations. Multivariate analysis showed that T4 versus T0, any N stages versus N0, distant metastasis other than BM (M1 vs M0) and EGFR mutation versus no EGFR mutation, were independently associated with the development of BM.

Conclusion: Routine brain MRI screening in patients with newly diagnosed lung adenocarcinoma can help to identify BM across all stages, especially in stage I patients with EGFR mutation.



AO207

ASSOCIATION BETWEEN LIQUID BIOPSY AND TISSUE BIOPSY FOR EGFR MUTATION IN LUNG ADENOCARCINOMA

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Background and Aims: The identification of EGFR mutation is very important for advanced NSCLC been diagnosed. The traditional method is gene analysis from biopsied tissue. The procedures for tissue biopsy are usually invasive. Liquid biopsy is less invasive and can identify circulating tumor DNA from patients' blood. However, the association between tissue biopsy and liquid biopsy for EGFR mutation in adenocarcinoma before treatment remains unclear. Our study aimed to evaluate the association between the results from liquid biopsy and tissue biopsy in advanced NSCLC patients before treatment.

Methods: Our retrospective study enrolled 76 naïve stages III or IV lung adenocarcinoma patients in Kaohsiung Medical University Hospital between June 2016 and April 2018. The tumor stage was defined according to AJCC 7th Edition. Tumor tissue was analyzed by Qiagen EGFR RQ-PCR kit to identify EGFR mutation. Liquid biopsy was performed by cobas®EGFR Mutation Test v2 to confirm EGFR mutation in the

circulating tumor DNA. The association of liquid biopsy and tissue biopsy is analyzed in multivariate models.

Results: In our study, the concordant rate of EGFR mutation detected from tissue biopsy and liquid biopsy was 75%. There were 48 patients with tissue EGFR mutation positive (tissue (+)), in which 32 patients had circulation DNA EGFR mutation positive (liquid (+)). The sensitivity rate was 66.67%. If the group of tissue (+) was taken as gold standard, the rate of liquid (+) was higher in the patients with lymph node and extrathoracic metastasis. Multivariate analysis showed that the patients with brain and bone metastasis had higher rate of liquid (+).

Conclusion: Liquid biopsy for EGFR mutation revealed higher positive rate in the patients with lymph node or extrathoracic metastasis, such as brain and bone metastasis. Our study suggest that liquid biopsy may be considered first if the patient have NSCLC with lymph node, brain and bone metastasis.

AO208

MIR-126* AND MIR-145 AS POTENTIAL BIOMARKERS FOR NON-SMALL CELL LUNG CANCER

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Background and Aims: This study aimed to examine the role of microRNAs (miRNAs) as potential biomarkers for non-small cell lung cancer (NSCLC). Our previous miRNA microarray profiling study in paired NSCLC tissues found that miR-126* and miR-145 were down-regulated in the tumor tissues. Restoration of miR-145 inhibited cancer cell growth in lung adenocarcinoma with epidermal growth factor receptor mutation. This study further investigate their diagnostic values in NSCLC patients.

Methods: The expression levels of miR-126* and miR-145 were detected by real-time RT-PCR in the paired frozen lung cancer tissues with adjacent normal lung parenchyma and in the plasma of 20 NSCLC patients compared to normal controls using the locked nucleic acid miRNA PCR system. RNU6 and miR-16 were employed as endogenous reference genes. The diagnostic values of these miRNA markers were analyzed using receiver-operating characteristic (ROC) curve.

Results: The expressions of miR-126* and miR-145 were found to be significantly down-regulated in both tumor tissues and plasma compared to normal controls ($P \leq 0.03$). For the diagnostic values of miR-126* and miR-145 in tissue samples, the area under the ROC curve (AUC) were 0.867 (95% CI: 0.75–0.984) and 0.83 (95% CI: 0.698–0.963), respectively. These results were in line with the findings in plasma samples, in which the AUC of miR-126* and miR-145 were 0.82 (95% CI: 0.637–1) and 0.95 (95% CI: 0.849–1), respectively.

Conclusion: Our results confirmed the diagnostic values of miR-126* and miR-145 in NSCLC patients. These data suggested that plasma miR-126* and miR-145 may be useful non-invasive biomarkers for the clinical diagnosis of NSCLC. To further explore the clinical significance of these miRNAs, larger sample size is being retrieved for validation. Droplet digital PCR may be used for the sensitive absolute quantification of miRNAs. Bioinformatics and luciferase reporter assay can also be employed to identify the gene targets of these miRNAs.

MIR-204 RESTORES THE EGFR TYROSINE KINASE INHIBITOR-SENSITIVITY THROUGH ATTENUATING EPITHELIAL TO MESENCHYMAL TRANSITION AND CANCER STEMNESS

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Background and Aims: MicroRNAs (miRNAs) regulate cellular homeostasis and cancer progression. Studies have demonstrated that miR-204 has a opposite function as a tumor-suppressive gene or an oncomiR in different cancers. We explored whether miR-204 controlled tumor progression and regulated EGFR-tyrosine kinase inhibitor (TKI) treatment response in lung cancer cells.

Methods: The Cancer Genome Atlas (TCGA) dataset was used to evaluate the relationship between miR-204 level and overall survival in early lung cancer patients. The miR-204 expression was examined by RT-PCR in EGFR TKI-sensitive and TKI-resistance cell lines. The serum miR-204 expression was analyzed and correlated with the treatment efficacy of EGFR TKIs in the EGFR-mutant patients. Molecular manipulations (silencing or overexpression) were performed to investigate the effects of miR-204 on migration, invasion, cell survival under EGFR TKI treatment, expressions of epithelial to mesenchymal transition (EMT) markers and cancer stemness markers, in vitro.

Results: The Cancer Genome Atlas (TCGA) dataset was used to evaluate the relationship between miR-204 level and overall survival in early lung cancer patients. The miR-204 expression was examined by RT-PCR in EGFR TKI-sensitive and TKI-resistance cell lines. The serum miR-204 expression was analyzed and correlated with the treatment efficacy of EGFR TKIs in the EGFR-mutant patients. Molecular manipulations (silencing or overexpression) were performed to investigate the effects of miR-204 on migration, invasion, cell survival under EGFR TKI treatment, expressions of epithelial to mesenchymal transition (EMT) markers and cancer stemness markers, in vitro.

Conclusion: MiR-204 reverts TKI-sensitivity in TKI resistant cells through attenuating EMT and cancer stemness.

AO210

EVALUATION OF THE EFFICACY AND SAFETY OF INTRAPLEURAL INJECTION OF BEVACIZUMAB TREATMENT OF MALIGNANT PLEURAL EFFUSION CAUSED BY LUNG ADENOCARCINOMA

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Background and Aims: Evaluation of the mechanism and the efficacy of Bevacizumab in the management of malignant pleural effusion (MPE) in lung adenocarcinoma.

Methods: Between Dec 2014 to Dec 2016, 60 untreated patients with MPE in lung adenocarcinoma were randomly assigned to one of two groups: intrapleural injection of Bevacizumab (5 mg/kg) ($n = 30$) and intrapleural injection of OK432 (5ke) once every 3 days ($n = 30$). Recorded and assessed adverse events. ELISA was applied to detect the vascular endothelial growth factor (VEGF) level in serum.

Results: The Bevacizumab group: Fifteen (50%) and eleven (37%) patients achieved CR and PR, 1 case of stable (3%), 3 cases of progress (10%). The OK432 group: Thirteen (43%) and twelve (40%) patients achieved CR and PR, 2 cases of stable (7%), 4 cases of progress (13%). There was no statistically significant difference between the effective rate of the two groups ($P > 0.05$). The Bevacizumab group: only 1 case with

fever. But OK432 group, chest pain, fever, dyspnea, fatigue, nausea, anorexia were occurred 16 (53%), 21 (70%), 5 (16.67%), 5 (16.67%), 1 (3.33%), 7 (23.3%). The adverse reactions of the patients in the OK432 group were significantly higher than those in the bevacizumab group ($P < 0.05$). The Bevacizumab group: The serum VEGF concentration was 246.79 ± 179.51 PG / ml before treatment, 129.85 ± 113.09 PG / ml after treatment, and VEGF decreased ($P < 0.001$).

Conclusion: Intrapleural injection of Bevacizumab is efficacious and safe for MPE. The expression of VEGF in pleural effusion and serum plays a guiding role in the treatment of MPE.

Table 1 Patient characteristics

Characteristics	Bevacizumab Group (n=30)	OK432 Group (n=30)	P value
Age (mean±sd, year)	64.33±8.872	62.50±9.062	P=0.432
Gender			P=0.438
Male	14	17	
Female	16	13	
Pretreatment ZPS score			P=0.125
0	2	5	
1	2	7	
2	14	11	
3	12	7	
Smoker			P=0.301
Yes	12	16	
No	18	14	

Award Session

AO211

CLINICAL SIGNIFICANCE OF *ASPERGILLUS* SPECIES ISOLATED FROM RESPIRATORY SPECIMENS IN PATIENTS WITH *MYCOBACTERIUM AVIUM* COMPLEX LUNG DISEASE

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Background and Aims: Chronic pulmonary aspergillosis (CPA) is associated with mortality in patients with *Mycobacterium avium* complex lung disease (MAC-LD). An *Aspergillus*-positive respiratory specimen often reflects colonization, and thus the clinical significance of *Aspergillus* isolation in MAC-LD patients is not well understood. The objective of this study was to investigate the clinical characteristics and outcomes of MAC-LD patients in whom *Aspergillus* was isolated from respiratory specimens.

Methods: We performed a retrospective review of the medical records of 329 MAC-LD patients. We compared the characteristics and mortality rates between patients with *Aspergillus* isolation and those without. All *Aspergillus* species detected from respiratory specimens within the follow-up period were reviewed.

Results: *Aspergillus* was detected in 40 (12.2%) of the 329 patients. There were no significant differences in the clinical characteristics and mortality rates between patients with and without *Aspergillus* isolation. Among the 40 patients with *Aspergillus* isolation, 9 (22.5%) developed CPA. CPA was most often caused by *A. fumigatus*. In the 40 *Aspergillus*-positive patients, patients with *A. fumigatus* isolation had a significantly higher mortality rate than those without ($P < 0.001$). The multivariate Cox proportional hazard model showed older age ($P = 0.050$), presence of respiratory comorbidities ($P = 0.008$), hypoalbuminemia ($P < 0.001$), and isolation of *A. fumigatus* ($P = 0.005$) to be prognostic factors for mortality in MAC-LD patients.

Conclusion: There were no significant difference in the mortality rates between patients with *Aspergillus* isolation and those without. However, isolation of *A. fumigatus* may be associated with poor prognosis in MAC-LD patients.

AO212

COMBINATION THERAPY WITH NINTEDANIB AND PREDNISOLONE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: Nintedanib was reported to reduce the change in forced vital capacity (FVC) in patients with idiopathic pulmonary fibrosis (IPF) in the INPULSIS trial. In contrast, combination therapy with prednisolone, azathioprine, and N-acetylcysteine was reported to increase the risk of early hospitalization and death in the PANTHER trial. Therefore, clinicians cannot use this combination immunosuppressant therapy for IPF. However, there has been no research regarding combination therapy with nintedanib and prednisolone for IPF. Our aim is to investigate the efficacy and toxicity of combination therapy with nintedanib and prednisolone for IPF.

Methods: Sixty-four IPF patients who received nintedanib between October 2015 and April 2018 were enrolled in this study. The diagnosis of IPF was based on the ATS/ERS/JRS/ALAT IPF statement in 2011. They were classified into two groups: patients treated with both nintedanib and prednisolone (NP group, $n = 21$) and patients treated with nintedanib only (N group, $n = 43$). Efficacy and toxicity were retrospectively compared between the two groups.

Results: Mean FVC before nintedanib initiation was 2195 ± 729 mL among all patients. Moreover, the mean annual decline in FVC was -15 mL. There were no significant differences in annual change in FVC between the two groups. Weight loss and diarrhoea occurred in 12 (18.5%) and 19 patients (26.7%), among all patients who received nintedanib. The incidence of weight loss and diarrhoea in the N group was significantly higher than in the NP group. However, there were no significant differences in the incidences of other adverse events, including nausea and liver dysfunction between the two groups. Although the incidence of acute exacerbation in the NP group was significantly higher than in the N group, there was no significant difference in survival time between the two groups.

Conclusion: The addition of prednisolone therapy may prevent digestive adverse events for IPF patients who are treated with nintedanib.

AO213

A QUALITATIVE STUDY EXPLORING THE BARRIERS AND CHALLENGES TO ASTHMA MANAGEMENT AS PERCEIVED BY MALAYSIAN ASTHMATIC PATIENTS

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Background and Aims: In the light of growing burden of asthma, there is increasing focus on addressing the barriers and challenges as perceived by asthmatic patients in asthma management. Currently, these barriers and challenges vary widely based on the provision of quality healthcare services. This study was conducted to explore the barriers and challenges faced in asthma management among Malaysian adult asthmatic patients.

Methods: A qualitative study utilizing face-to-face interviews was conducted with a convenience sample of 17 adult asthmatic patients at two respiratory specialist clinics in Selangor, Malaysia. The socio-demographic characteristics, and medical data were recorded and patients were interviewed using a semi-structured interview guide exploring the barriers and challenges faced by asthmatic patients in asthma management. The transcripts of all the interviews were generated from audio tapes. The tapes were verified for accuracy of transcription and appropriate measures were taken to ensure study rigor and validity. Data obtained were coded independently for the relevant themes and verified by two researchers.

Results: Three main themes of the barriers were identified. These themes were named as patient-related, disease and treatment-related, and healthcare-related barriers. The most frequent types of identified patient-related barriers included: forgetfulness to take controller medicine, feeling stigmatized to use inhaler in public, lack of knowledge regarding asthma management, and limited physical activity because of asthma. The difficult access to healthcare facility and continuity of care were the most cited healthcare-related barriers; whereas, in disease and treatment-related theme the frequently reported barriers included: the inability to avoid allergens, perceived side effects of medicines, and financial limitations. The financial limitations and unavoidable exposure to allergens were two distinct themes identified in the challenges faced by asthmatic patients.

Conclusion: To improve asthma management and health outcomes, it is critical to identify and address the barriers and challenges as perceived by asthmatic patients.

AO214

EVALUATION OF UPPER AIRWAY (UA) ANTHROPOMETRY USING MAGNETIC RESONANCE IMAGING (MRI) AND LATERAL CEPHALOMETRY IN PATIENTS OF OBSTRUCTIVE SLEEP APNEA (OSA) IN NORTH INDIAN POPULATION.

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Background and Aims: Anatomical and nonanatomical factors are implicated in OSA in which repetitive collapse of UA occurs. Scarcity of data regarding UA anthropometry in OSA exist especially in Indian population.

Methods: A prospective observational case control study was carried in which 60 OSA (mild:n=20, moderate:n=20, severe:n=20) and control group (n=20) underwent MRI and lateral cephalometry of UA. Linear Regression analysis (univariate and multivariate linear regression) of various parameters was done to find out the factors correlated with OSA.

Results: In MRI, distance between hyoid bone and posterior nasal spine (H-PNS) and hyoid and posterior pharynx wall near vertebral column (H-COL) was found to be statistically significant (mild= 60.23mm, moderate=68.72mm, severe= 77.26mm: control=60.23mm:p=0.001) and (mild=14.8mm, mod=15.2mm, severe=19.09mm: control=11.5mm: p<0.001). Laterolateral dimension of tongue and lateral pharyngeal wall thickness were found to be statistically significant and increases with severity of OSA. Significant narrowing was found at level 1 i.e. rhinopharynx level and low retropalatal oropharynx level i.e. level 3(p<0.001). In lateral cephalometry, distance between hyoid bone and mandibular plane increase with severity of OSA and was found to be statistically significant among all groups (mild=16.68mm,mod=25.25mm,severe=28.1mm:control=16.15mm:p-value <0.001). In univariate analysis, Epworth sleepiness scale (ESS), neck circumference, Modified Mallampati Score, anteroposterior and laterolateral dimension at level 3 and 4, hyoid bone position and laterolateral length of tongue were associated with severity of OSA. In multivariate analysis, the following parameters remained significant: anteroposterior and laterolateral dimensions at level3, hyoid bone position, ESS and neck circumference.

Conclusion: In OSA, significant alteration of anthropometry of upper airway occurs and is associated with severity of OSA.

AO215

IDENTIFICATION OF A NEW TARGET FOR DIAGNOSING IDIOPATHIC PULMONARY FIBROSIS WITH AUTOIMMUNE FEATURES

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Background and Aims: The aetiology of idiopathic pulmonary fibrosis (IPF) remains unclear though some studies refer similar autoimmunity to collagen tissue disease associating interstitial lung disease (CTD-ILD). The aim of our study is to detect the profiles of circulating auto-antibodies and establish a biomarker for IPF with autoimmune features.

Methods: To identify circulating auto-antibodies in IPF, we first performed microarray system constructed by 9,480 human proteins. For this analysis, we used serum samples from five healthy subjects and nine interstitial lung disease (ILD) patients. The most strongly positive auto-antibody in the ILD group was chosen to compare the concentration among various ILDs by performing enzyme-linked immunosorbent assay (ELISA). For ELISA, 13 CTD-ILD samples, 29 IPF samples, 29 NSIP samples, six chronic hypersensitive pneumonia (CHP) samples and 61 healthy subjects were included.

Results: In the microarray analysis, 3971 types of positive auto-antibodies on average were detected in the ILD group. Among them, the most strongly positive auto-antibody was against ubiquitin-conjugating enzyme 2T (UBE2T). We performed ELISA for anti-UBE2T antibody (aUBE2Tab) and detected its presence in 92% of CVD-ILD patients (median value: 460.1 ng/ml), 76% of IPF patients (344.1 ng/ml) and 55% of NSIP patients (251.3 ng/ml) while only 17% of CHP patients (166.9 ng/ml) and 16% of healthy control subjects (170.7ng/ml) had a positive result. The area under the curve in ROC for diagnosing CTD-ILD was 87% indicating the spectrum of aUBE2Tab is inclining towards the presence of autoimmunity. However, the association of commercial auto-antibodies did not correlate with aUBE2Tab, suggesting the independent ability of aUBE2Tab in detecting autoimmune conditions. In addition, immunohistochemistry observation demonstrated high expression of UBE2T in alveolar epithelial cells from IPF lung tissues.

Conclusion: In this study, we comprehensively analyzed the various profiles of circulating auto-antibodies in ILDs and detected aUBE2Tab has a possibility to become a biomarker for IPF with autoimmune features.

AO216

ENDOSOMAL NOX2 OXIDASE INHIBITOR PROTECTS AGAINST HIGHLY PATHOGENIC INFLUENZA VIRUS MORBIDITY

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Background and Aim: Influenza A viruses have the ability to cause severe respiratory tract infections that can be lethal when the virus spreads to the alveolar space, which is more commonly observed with high pathogenic influenza virus strains. The excessive generation of reactive oxygen species (ROS), regardless of the subcellular source can indiscriminately exacerbate lung inflammation and injury during influenza virus infections. Our previous work demonstrates that influenza A viruses, irrespective of strain, causes a substantial burst of ROS production via NOX2 oxidase that occurs in endosomes. Evidently, targeting this process with an endosomal NOX2 oxidase inhibitor (cholesterol conjugated gp91ds-TAT (Cgp91)) improved overall morbidity in mice infected with a low pathogenic strain of influenza A virus (IAV) (1). The aim of this present study was to determine the effect of Cgp91 treatment on the lung pathology induced by a highly pathogenic strain of IAV.

Methods: Male C57Bl/6J mice were treated daily via intranasal administration with Cgp91 (0.2mg/kg) or DMSO (2%; control) over a 4-day period. Mice were infected with the PR8 (H1N1; 500 PFUs) strain of IAV or PBS control, one-day post initial drug treatment and analysed at day 3 post-infection. Bronchoalveolar lavage (BAL) fluid collected from mice was used to assess airway inflammation. Histopathological analysis of lung was assessed using H&E stain and scored for alveolitis, inflammatory cell infiltrate and peribronchiolar inflammation. Superoxide generation in the BAL was measured using L-012 enhanced chemiluminescence and changes in cytokine and viral mRNA expression in the lung were quantified using real-time QPCR.

Results: Cgp91 treatment significantly ($P < 0.05$) reduced airway inflammation, neutrophil extravasation, and pulmonary inflammation as measured by the degree of alveolitis, inflammatory cell infiltrate and peribronchiolar inflammation. Furthermore, Cgp91 attenuated ROS production in inflammatory cells isolated from the BAL and influenza viral mRNA expression in the lung of PR8-infected mice.

Conclusion: The spatial targeting of this pathogenic process by inhibiting NOX2 in endosomal compartments with Cgp91 could be used as a potential treatment strategy against highly pathogenic IAV strains.

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AO217

EPIGENETIC REGULATION OF FZD9 AND ILOPROST LUNG CANCER CHEMOPREVENTION

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Background and Aims: Lung cancer continues to be the leading cause of cancer death in the United States, with most cancers diagnosed in former smokers. While avoidance of tobacco abuse is clearly the strongest deterrent of lung cancer, chemoprevention in former smokers may be a more effective intervention than treatment of established lung cancers. A phase II trial found that the oral prostacyclin analogue iloprost improves endobronchial dysplasia in former smokers but not current smokers. We hypothesize that epigenetic mechanisms mediate the chemopreventive effects of iloprost and could be markers of iloprost activity. Frizzled 9 (Fzd9) is required for iloprost activity *in vitro* and has reduced expression with cigarette smoke exposure and in NSCLC.

Results: We detected increased promoter hypermethylation of Fzd9 in lung cancer cell lines, suggesting a role for cigarette smoke induced methylation in the effectiveness of iloprost. We identified reduced Fzd9 3'UTR-luciferase activity *in vitro* with exposure to cigarette smoke. Iloprost reduces the expression of several miRNA that are increased by cigarette smoke in bronchial epithelial cells, pointing to a role for miRNA in regulation of Fzd9 expression and iloprost activity. We identified a panel of lncRNA with altered expression induced by cigarette smoke exposure and reversed by iloprost *in vitro*. In particular, the conserved lncRNA GAS5 is similarly altered *in vitro*, in mice exposed to tobacco carcinogens or increased levels of prostacyclin, and in progressive and regressive primary bronchial dysplastic cells.

Conclusions: This work characterizes epigenetic regulation in smoke and iloprost exposed lung epithelial cells, offering potential mechanisms for iloprost action and markers to monitor response during iloprost chemoprevention. These studies are an important step toward precision lung cancer chemoprevention in high-risk populations and they are on the leading edge of chemoprevention research.

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AO218

A MULTI-LEVEL APPROACH TO ASTHMA HEALTH DISPARITIES: FROM BIOMARKERS TO GEOCODED DATA

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Background and Aims: Minority youth of low socioeconomic status (SES) have a disproportionate burden of environmental exposures. Allergen sensitization to these exposures is a strong determinant of childhood asthma. However, research examining SES and atopy has been inconsistent. A multi-level approach to evaluating intrinsic and extrinsic factors may allow for better understanding of this complex relationship. We aimed to determine 1) allergen sensitization patterns according to SES and 2) how asthma characteristics and early-life environmental exposures may relate to these identified sensitization patterns.

Methods: African American and Latino youth (age 8–21 years) with asthma ($n = 1782$) were recruited from five urban study centers across the mainland United States and Puerto Rico. A composite SES index was derived from reported maternal education, annual household income, and

insurance type and was categorized into tertiles (low, medium and high SES). Skin prick test (SPT) response was assessed for a panel of 13 aeroallergens. Geocoded residential addresses from the first year of life were linked to the 2000 Census and air quality data from the U.S. Environmental Protection Agency to estimate population density (urbanized area ≥ 1000 people per square mile) and nitrogen dioxide (NO₂) exposure in the first year of life. We performed latent class analysis (LCA) of SPT results with SES as a covariate to identify sensitization patterns. We then examined class membership with asthma outcomes (rescue medication use, spirometry measures), SES, and environmental factors.

Results: LCA identified four sensitization patterns (Figure): indoor allergens (atopic-indoor, 19.6%); outdoor allergens (atopic-outdoor, 14.4%); high probability of sensitization to almost all allergens (atopic-all, 8.5%) and low probability of sensitization to any allergen (non-atopic, 57.5%). Only 7.4% of children in the atopic-outdoor class had a FEV1 percent predicted $< 80\%$ compared with 21.1% in atopic-all class and 18.6% in atopic-indoor class ($P < 0.001$). Albuterol rescue medication use was highest among atopic-all class members, followed by atopic-indoor class members ($P < 0.001$). Participants of low SES composed more of the atopic-indoor and atopic-all class (67 and 61%, respectively), whereas the atopic-outdoor class consisted of those with medium to high SES (55.3%). Non-atopic class members were more likely to have lived their first year of life in non-urbanized areas (34.8%), whereas 96–98% of atopic-outdoor and atopic-all were from urbanized areas ($P < 0.001$). Atopic-all had the highest first year NO₂ exposure across all classes, whereas the non-atopic class had the lowest (26.7 vs 17.5 ppb, $P < 0.001$).

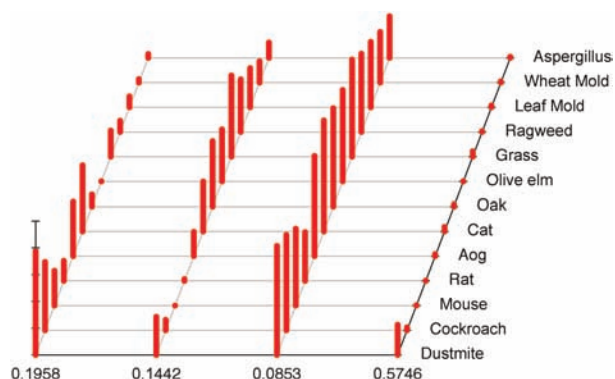


Figure Allergen Sensitization Patterns determined through Latent Class Analysis

Conclusion: SES status predicts allergy sensitization patterns, and these patterns are associated with specific asthma outcomes and early life environmental exposures. Better defining sensitization patterns

associated with SES and neighbourhood factors will allow for identification of at-risk populations and modifiable exposures for intervention.

AO221

PULMONARY HYPERTENSION IN CPFE (COMBINED PULMONARY FIBROSIS AND EMPHYSEMA)

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Background and Aims: Previous studies reported that CPFE patients with pulmonary hypertension (PH) showed shorter survival than patients without PH. We tried to clarify the effect of PH, diagnosed by non-invasive means on their exercise performance.

Methods: We selected twenty-nine patients who were diagnosed as COPD with interstitial pneumonia from medical records. Seven cases were excluded as they did not fulfil the criteria or lack the records of echocardiogram and/or 6MWT (six minutes walk test). The breathlessness and tiring of legs were shown in modified Borg scale. We divided the patients into two groups, i.e., PH and non-PH according to TR-PG (tricuspid regurgitation pressure gradient). Patients with TR-PG > 25 mmHg were PH (nine patients) and TR-PG < 25 mmHg were non-PH group (thirteen patients). We compared pulmonary function including diffusing capacity, chest CT (computed tomogram) pattern, blood KL-6 and 6MWT results between these two groups.

Results: In patients with CPFE, there were no significant differences in age, FEV1, %VC, DLco and breathlessness and tiring of legs in 6MWT, between subjects with PH and without PH. Size of pulmonary artery was significantly larger and walk distance in 6MWT was significantly shorter in subjects with PH than in subjects without PH. KL6 was significantly lower in subjects with PH than in subjects without PH. (table)

Conclusion: In patients with CPFE, presence of PH was a sign of poor exercise performance. Activity of interstitial pneumonitis did not affect PH.

	TR-PG ≥ 25 mmHg (n=9)	TR-PG < 25 mmHg (n=13)	P value
Age	77.3 $\pm$ 4.8	73.4 $\pm$ 5.5	0.10
FEV1	2.2 $\pm$ 0.4	2.1 $\pm$ 0.2	0.65
%FVC	79.1 $\pm$ 8.2	82.8 $\pm$ 14.3	0.49
%DLCO	43.4 $\pm$ 14.1	56.9 $\pm$ 24.3	0.17
Borg (chest,leg)	3.8,3.0	3.3,1.5	(0.69,0.17)
6MWD	209.4 $\pm$ 97.4	334.6 $\pm$ 125.0	0.02
KL-6	688.1 $\pm$ 182.5	1342.3 $\pm$ 870.0	0.03
PA/Ao	0.95 $\pm$ 0.08	0.80 $\pm$ 0.08	0.0005

ABSTRACT

Asthma 1

AP001

CHANGES IN FRACTIONAL NITRIC OXIDE CONCENTRATION IN EXHALED BREATH WITH THE USE OF ICS/LABA INHALERS

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Background and Aims: Fractional nitric oxide concentration in exhaled breath (FeNO) has been used by several facilities since the Japanese National Health Insurance accepted it as an index of asthma control. FeNO reportedly reflects eosinophilic inflammation in the respiratory tract as it correlates with the eosinophil number in the sputum, bronchoalveolar lavage fluid, and tissues and reflects the improvement in bronchial hypersensitivity and forced expiratory volume in 1 second (FEV1) levels before and after treatment for asthma. By contrast, choosing among inhaled corticosteroid (ICS), long-acting β 2-agonist (LABA), long-acting muscarinic antagonist (LAMA), and a combination of these as the most suitable inhaler is difficult. This study aimed to compare changes in FeNO before and after the use of each targeted inhaler in asthma, chronic obstructive pulmonary disease (COPD), asthma-COPD overlap syndrome (ACOS), and cough-variant asthma (CVA).

Methods: FeNO was measured for 474 outpatients with asthma, COPD, ACOS, or CVA treated at our hospital between April 2014 and March 2015 at the time of inhaler introduction and after switching to another inhaler.

Results: The pathological conditions of the 474 patients were: asthma ($n = 230$), COPD ($n = 106$), ACOS ($n = 30$), and CVA ($n = 108$). A significant decrease in FeNO was observed in 30 patients who switched from the fluticasone propionate/salmeterol (FP/SA) to the fluticasone furoate/vilanterol (FF/VI). A decreasing trend in FeNO was observed in 26 patients who switched from budesonide/formoterol (BUD/Fo) to FF/VI, although not statistically significant.

Conclusion: Compared to FP/SA inhaler, FF/VI inhaler significantly decreased FeNO. FF/VI inhaler

AP002

FEF₂₅₋₇₅ IS THE BETTER DIAGNOSTIC TOOL FOR IDENTIFYING ASTHMA PATIENTS

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Background and Aims: Airflow obstruction is diagnosed by an FEV1/FVC ratio <0.7 . However, the criteria have severe limitations and a good number of asthma patients, despite having symptoms and documented reversibility (200 mL and 20%) to bronchodilators have the aforesaid ratios above 0.7. Hence it becomes necessary to look for a test that does not miss the asthmatic patients at a screening diagnosis of obstructive lung disease (OLD). Thus we decided to look for changes in FEF₂₅₋₇₅ in these patients as a diagnostic clue since this value is a marker for small airway obstruction.

Methods: We selected 92 patients with asthma from our achieves randomly and classified them into two groups (a) FEV₁/FVC <0.7 ($n = 45$) and (b) FEV₁/FVC > 0.7 ($n = 47$). We analyzed the predicted percentages of FEF₂₅₋₇₅ between these two groups and tried to analyze the

distinguishing capacity of the parameter to identify asthma having FEF₂₅₋₇₅ <0.7 and >0.7 . Our study included a group of normal patients ($n = 64$) who are asymptomatic and have normal chest X-ray and spirometry values.

Results: The FEF₂₅₋₇₅ remained significantly low (24.48 ± 9.19) and (47.47 ± 13.00) in asthmatics with FEV₁% < 0.7 and >0.7 respectively than normal patients ($83.3 \pm .37$). The cut off value 35.5 (for predicted percentage FEF₂₅₋₇₅) shows a good distinguishing capacity between the two groups of asthmatics (with FEV₁ percentage <0.7 and >0.7) with sensitivity, specificity, positive predictive value and negative predictive value being 87.67%, 89.36%, 84.67% and 90.6%, respectively. The same parameter can also distinguish these two subsets of asthma with from normal people with very high efficiency with cut off value of FEF₂₅₋₇₅ predicted percentage being 44.5 and 64.5 respectively.

Conclusion: FEF₂₅₋₇₅ is a better marker of airflow obstruction than FEV₁% in OLD as asthma.

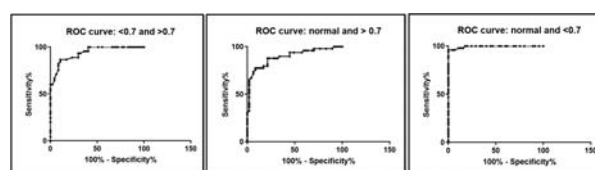


Fig 1: The ROC curves between asthma patients with FEV1/FVC ratio <0.7 , >0.7 and normal group were analysed.

AP003

HEALTHY LUNG ASIA INITIATIVE

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Background and Aims: Healthy Lung is a partnership between AstraZeneca and clinicians, public officials, and other stakeholders to ensure that people with respiratory disease have access to the care they need. Launched in 2017, Healthy Lung is a unique region-wide initiative, with programs being tailored and developed in Asia, all focused on the same overall health objectives.

Objectives: Raise profile of respiratory disease with policy makers and build health system capacity to support improved care through a three-pillar approach:

- Partnerships and awareness: Convene National taskforces raising awareness, addressing health system changes needed to improve outcomes
- Understanding and skills: Develop medical education with clear objective of spreading an evidence-based practice at scale
- Capacity and access: Holistic, partnership-driven interventions in selected countries to resolve issues of infrastructure, education or access

Methods: Data collected through key stakeholders and collated, according to the individual country objectives

Results: See Table Below

Conclusion: Through collaboration, Healthy Lung Asia is improving respiratory management and capability in the nine Asian countries: India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam. We look forward to publishing impact of Healthy Lung project as the initiative evolves.

Type of Initiative	Gov. MOU	External Societies/NGO partnerships	National Healthy Lung Initiatives created	Healthy Lung training and education programmes	Update of National Guidelines	Development of Care Pathways	People reached through education, diagnosis and/or treatment for COPD or asthma	Establishment of new respiratory centres, encouragement of respiratory disease screening
1	2	3	4	5	6	7	8	9
Country	Taiwan, Indonesia, Vietnam	Philippines: UP-PGH Department of Pediatrics, Lung Center of the Philippines Vietnam: Medical Service of Administration, Ministry of Health, Respiratory Society, Vietnam Association Against Tuberculosis and Lung Disease and HCM Asthma- Allergy and Clinical Immunology Association Indonesia: MARI, Project Hope Taiwan: TSPCCM Thailand: AAAT, Pediatric Respiratory and Critical Care Medicine Society India: Indian Chest Society, St John's, ES Dehi, ES Bangalore, AIMS Korea: KAMAC, KAPARD		5,000+ HCPs	Taiwan, Indonesia, Thailand	Singapore, Malaysia	1,34,000	Malaysia, India, Thailand, Taiwan, Philippines, Indonesia, Vietnam

AP004

ANCA NEGATIVE EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: 4 CASES REPORT AND LITERATURE REVIEW

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Background and Aims: To improve the understanding of antineutrophil cytoplasmic antibody (ANCA) negative eosinophilic granulomatosis with polyangiitis (EGPA) which primary manifestations were respiratory involved.

Methods: The clinical data of 4 cases of ANCA negative EGPA from February 2017 to April 2017 in our hospital was analyzed, including clinical features, procedure of diagnosis and treatment options. Relevant literatures of EGPA were reviewed.

Results: 3 cases were diagnosed as EGPA and 1 was EGPA combined with allergic bronchopulmonary aspergillosis (ABPA). The age of onset was 28 to 59 years, with the average age of 44 years, and the course of disease was ranged from 1 month to 3 years. ANCA was negative of all those 4 patients. Airway hyperresponsiveness (AHR) of these patients varied from cough variant asthma (CVA) to refractory asthma. Patients were confirmed with chronic sinusitis by computer tomography (CT) scan, whereas clinical symptoms were nearly absent. Gastrointestinal, skin and neurological system were involved as extra-pulmonary manifestations. Eosinophilia of peripheral blood and induced sputum, pulmonary infiltration and peripheral neuropathy were found in 3 patients. 3 cases with elevated serum total IgE before using systemic glucocorticoid. Eosinophilic infiltration in extravascular and intravascular space was verified by tissue biopsy in 3 cases with chronic inflammation in 1 case.

Conclusion: EGPA patients who first suffered from respiratory symptoms are tend to have the negative result of ANCA. The degree of AHR is associated with the course of the disease. Patients with asthma complicated with eosinophilia and sinusitis should be aware of ruling out of EGPA.

AP005

COMMON MICRORNA CHANGES IN BRONCHIAL EPITHELIAL CELLS OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASES

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Background and Aims: Asthma and chronic obstructive pulmonary disease (COPD) are chronic airway inflammatory diseases. Although some differences exist in terms of aetiologies, clinical features, and

treatment policies, these two diseases still share some common features. Bronchial epithelial cells play important roles in the pathogenesis of both asthma and COPD. MicroRNAs are important regulators of gene expression. The aim of this study is to investigate the common microRNA changes in bronchial epithelial cells of asthma and COPD.

Methods: Primary bronchial epithelial cells from asthma (aHBE) and COPD (cHBE) patients and healthy subjects (nHBE) were cultured, and the RNAs were extracted for small RNA sequencing using next generation sequencing (NGS). The miRNA expression levels in aHBE and cHBE were compared to nHBE. We took a 2-fold change in the expression level as a significant change (up-regulation or down-regulation).

Results: Using NGS, we identified 28 up-regulated miRNAs and 17 down-regulated miRNAs in aHBE and 45 up-regulated miRNAs and 38 down-regulated miRNAs in cHBE. The common up-regulated miRNAs in both aHBE and cHBE were hsa-miR-10a-3p, hsa-miR-10a-5p, hsa-miR-146a-5p, hsa-miR-203a, hsa-miR-3130-5p, hsa-miR-365a-5p, and hsa-miR-548d-5p, while hsa-miR-487a and hsa-miR-873-5p were down-regulated in both aHBE and cHBE.

Conclusion: These common microRNA changes might play important roles in the pathogenesis of asthma and COPD. Further study is warranted to understand their targets and regulatory mechanisms, which might provide scientific basis for further treatment development.

AP006

S1P/S1PR3 PATHWAY HAS THE ROLE IN EOSINOPHILIC AIRWAY INFLAMMATION VIA RELEASE OF CCL20 FROM BRONCHIAL EPITHELIAL CELLS

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Background and Aims: Sphingosine 1 phosphate (S1P) regulates diverse biological responses. The aim of this study is to reveal the relationship between S1P and S1P receptors (S1PR) using human bronchial epithelial cells (BECs) and asthma model.

Methods: Transcriptome analysis was performed for total RNA from BEAS-2B and Calu-3 cells stimulated with S1P, and asthma-related genes expression were identified. CCL 20 expression was evaluated using siRNAs for S1PR knockdown. The effect of anti-CCL20 antibody and VPC23019, S1PR1/3 antagonist on eosinophilic airway inflammation, was examined in the ovalbumin (OVA)-induced murine asthma model.

Results: S1P upregulated asthma-related genes, including ADRB2, PTGER4, and CCL20 in BECs. The knockdown of S1PR3 reduced CCL20 expression. In the asthma model, anti-CCL20 antibody and VPC23019 significantly reduced the number of eosinophils in bronchoalveolar lavage fluid.

Conclusion: S1P/S1PR3 is shown to induce CCL20 expression and eosinophilic airway inflammation, suggesting their potential roles in asthma pathogenesis.

AP007

ALLERGIC SENSITIZATION PROFILE OF POLYSENSITIZED ASTHMATIC PATIENTS IN SOUTHERN CHINA USING MOLECULE-BASED IGE TECHNIQUE

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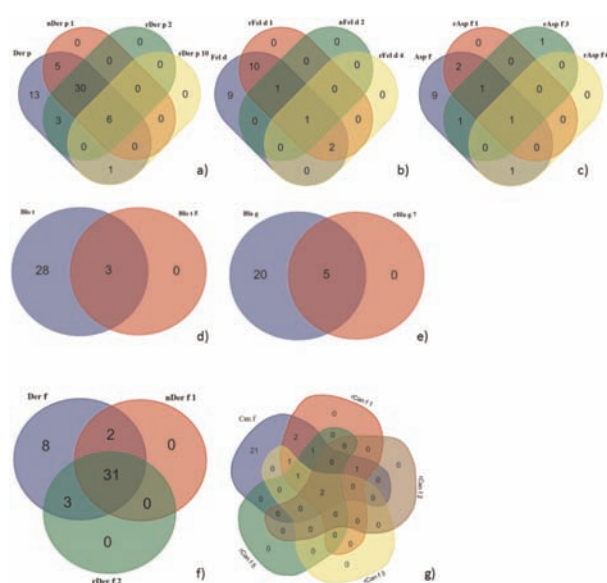
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Background and Aims: Data of allergic sensitization profile for polysensitized asthmatic patients in China are lacking. This cross-sectional study aimed to analyze the sensitization profiles of polysensitized asthmatic patients in southern China utilizing molecule-based IgE diagnostic technique.

Methods: Serum samples from 63 asthma patients in a tertiary referral centre of southern China were tested with ISAC for specific immunoglobulin E (sIgE) against 112 single allergen components.

Results: In this group of patients, 79.36% showed sIgE positive to more than three allergen components. Polysensitized asthmatic patients in southern China were mainly allergic to rDer f 2 (68.25%), nDer f 1 (66.67%), nDer p 1 (65.08%), rDer p 2 (61.90%), rFel d 1 (26.98%), nCyn d 1 (15.87%), nPhl p 4 (14.29%), rCanf 1 (12.70%), rDer p 10 (11.11%) and rLep d 2 (11.11%). Polysensitized asthma patients complicated with rhinitis showed higher positive rates of the allergen components Phl p 4 (19.05% vs 0.00%) and nCyn d 1 (26.19% vs 4.76%) than patients without rhinitis ($P < 0.001$). Among food allergen components, the walnut allergen component nJug r 2 showed the highest positive rate (9.52%). An optimal scaling analysis indicated that a positive test of rDer p 10 was associated with food allergy. (Cronbach's Alpha = 92.0%)

Conclusion: The sensitization profiles of polysensitized asthmatic patients in southern China were different from other countries. Polysensitized asthma patients complicated with rhinitis showed higher positive rates for nPhl p 4 and nCyn d 1 than without. Polysensitized asthmatic patients who positive for rDer p 10 were associated with food allergy.



AP008

PREDICTORS TO THE EXACERBATION OF BRONCHIAL ASTHMA AMONG CHILDREN BETWEEN 6–18 YEARS OLD AT CHONG HUA HOSPITAL

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Background and Aims Background: A well-controlled bronchial asthma is the ultimate goal of every healthcare provider. Knowledge of the profile of patients who frequently develop exacerbations of bronchial asthma within the community will help in the overall asthma control.

Aim: To determine the factors highly associated with the exacerbation of bronchial asthma among children between 6–18 years old

Methods Study Design: A case control study

Study Setting: Chong Hua Hospital, a private tertiary hospital in Cebu City, Philippines

Study Duration: October 15, 2016 to August 31, 2017

Population: A total of 104 asthmatic children between 6–18 years old with complaints of dyspnea and/or wheezing on chest auscultation were enrolled.

Methodology: Upon enrolment, subjects' peak expiratory flow rate (PEFR) were taken. The results categorized participants into Exacerbation (PEFR < 80%) and No Exacerbation group (PEFR > 80%). Age, sex, body mass index, average days of hospitalization, family history of atopy, exposure to indoor and outdoor allergen, second-hand smoking, comorbidities and non-compliance to medications were gathered from each group.

Statistical Analysis: Odds ratio with 95% confidence interval and logistic regression were used to identify high association and predictor variables. P value of < 0.05 was considered as significant.

Results: Among the factors under study, only 2 had significant association to the exacerbation of bronchial asthma: younger age between 6–10 years old (P value = 0.002) and exposure to indoor allergen (P value = 0.036).

Conclusion: This study hence shown that the profile of a child who will most likely develop an exacerbation of bronchial asthma is between 6–10 years old with indoor allergen exposure.

AP009

POST HOC ANALYSIS OF INITIAL TREATMENTS AND CONTROL STATUS USING DIFFERENT GINA CRITERIA IN INITIAL, AN OBSERVATIONAL STUDY OF NEWLY DIAGNOSED CHINESE PATIENTS WITH ASTHMA

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Background and Aims: INITIAL (NCT02143739) was a 12-week, multicentre, observational study of asthma severity in newly diagnosed Chinese patients.

Methods: This post hoc analysis investigated baseline medication combinations (prescribed per usual clinical practice) and the impact on control levels of using GINA 2012 vs 2018 criteria.

Results: At baseline, among 4491 patients, 3.9%, 12.0%, 22.6% and 61.6% had intermittent, mild-, moderate- and severe-persistent asthma, respectively. Inhaled corticosteroid/long-acting β_2 agonist (ICS/LABA) was prescribed to 90.2% patients. ICS/LABA plus ≥ 1 additional medication(s) was prescribed to 66.7% of patients. Leukotriene receptor antagonist (LTRA) was the most common additional medication in 54.7% of patients. ICS/LABA vs ICS/LABA+LTRA distribution was similar among intermittent,

mild-, moderate- and severe-persistent patients: 3.2% vs 3.0%, 11.5% vs 9.7%, 21.2% vs 19.9%, and 64.1% vs 67.4%, respectively. When LTRA was added to ICS/LABA, control levels were similar using GINA 2012 and lower using GINA 2018 criteria. The proportion of patients with intermittent, mild-, moderate- and severe-persistent asthma controlled at Week 12 (GINA 2012) using ICS/LABA with vs without LTRA was 78.1% vs 80.0%, 86.5% vs 85.8%, 78.5% vs 71.3%, and 59.6% vs 61.8%, respectively. Using GINA 2018 criteria, the proportion was 86.8% vs 95.9%, 86.1% vs 93.2%, 82.1% vs 85.3%, and 71.9% vs 77.6%, respectively.

Conclusion: In this Chinese non-interventional study, irrespective of the GINA criteria used and baseline severity, adding LTRA to ICS/LABA did not improve the level of asthma control and may have been unnecessary in some of these newly diagnosed patients.

AP010

SMALL AIRWAY DYSFUNCTION PREDICTED FIXED AIRFLOW OBSTRUCTION IN OLDER ASTHMA PATIENTS

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Background and Aims: Fixed airflow obstruction (FAO) is known as one of the poor prognostic factors in asthma. Little is known about the association between the small airway dysfunction and fixed airflow obstruction in aged asthma population.

Methods: Asthma patients 1) over the age of 40 years or more with a 2) diagnosis of asthma based on either positive bronchodilator test or provocation test and 3) post-bronchodilator (BDR) FEV1/FVC ratio < 70 were enrolled. FAO was defined as post-BDR FEV1/FVC ratio < 70 in at least 3 months follow up tests. Small airway dysfunction was assessed by RV/TLC ratio done at the initial examination. Retrospective chart review was done.

Results: Total 140 patients were included, 77 (55%) had FAO in subsequent PFT. 45 % were male, mean age was 60.2 (41–80). 26.7% were ever smokers and mean smoking history was 30.5 (3–90) pack-years. 25.7% had atopy, mean serum IgE was 205 (4–1000) and peripheral eosinophil counts were 411 (0–1651). The mean pre-BDR FEV1/FVC ratio was 57.3 (31–70), FEV1 (%) was 66.9% (28–110). Initial RV (%) was 108 (44–247) and RV/TLC (%) was 38 (21–74). Follow up PFT were done after mean 28 ± 22.6 months. In univariate analysis, male, old age, high smoking pack-years, low pre-FEV1/FVC ratio, high RV/TLC (41.4 ± 11.6 vs 34.3 ± 8.3, $P = 0.005$), high serum IgE were associated with the risk of FAO. Positive provocation test and bronchodilator responses were negatively correlated with the FAO.

Conclusion: The risk of FAO in asthma patients with airflow obstruction at initial evaluation was higher in patients who had air trapping by small airway dysfunction, assessed by high RV/TLC ratio. Although further prospective studies would be needed with long term observation periods, this study implies the positive correlation between the initial small airway dysfunction and progressive airflow limitation in aged asthma patients.

AP011

CHITIN INDUCED PRODUCTION OF PROSTAGLANDIN E₂ IN ALVEOLAR MACROPHAGES AND BRONCHIAL EPITHELIAL CELLS

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Background and Aims: Chitin, a polymer made up of repeating units of β -(1–4)-poly-N-acetyl-d-glucosamine, is a ubiquitous polysaccharide found in the walls of fungi and the exoskeleton of arthropods such as crabs, shrimp, and insects. As it does not have a mammalian counterpart, chitin could be important inhalant antigen for bronchial asthma. Chitin stimulates innate immune cells and regulates adaptive allergic immune responses. Previous studies have shown that as pathogen-associated patterns induced prostaglandin E₂ (PGE₂) production was independent of the NLRP3 inflammasome. In this study, we investigated whether chitin induces the PGE₂ production in alveolar macrophages and bronchial epithelial cells.

Methods: Mice were intranasally injected chitin on consecutive 3 days, and after 24 h from last injection bronchoalveolar lavage (BAL) fluids were collected. After alveolar macrophage preparation, total cellular RNA was isolated from alveolar macrophages and the supernates of the alveolar macrophage cultures were collected. The expression mRNA levels of PGE₂ synthases in mouse alveolar macrophages, MH-S cells (mouse alveolar macrophages cell line), and BEAS-2B cells (human bronchial epithelial cell line) after treatment with chitin were evaluated by quantitative real-time reverse transcription-PCR.

Results: The murine model of chitin-induced airway inflammation showed the inflammatory cell infiltration into BAL fluids and higher concentrations of PGE₂ in BAL fluids, as compared to control mice. Levels of cyclooxygenase (COX) 2 and microsomal PGE₂ synthase (mPGES)-2 mRNA expression and PGE₂ in culture supernatants of alveolar macrophages were significantly increased after the treatment with chitin. Moreover, we also showed that chitin induced mRNA expression levels of PGE₂ synthases in MH-S cells and BEAS-2B cells.

Conclusion: These results suggested that chitin has the potential to induce airway inflammation and PGE₂ production in alveolar macrophages and bronchial epithelial cells.

AP012

THE LEVEL OF PLASMINOGEN ACTIVATOR INHIBITORS 1 IN ASTHMA PATIENTS AND CORRELATION WITH LUNG FUNCTION AND DEGREE OF ASTHMA CONTROL

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Background and Aims: Chronic inflammation in asthma will cause healing processes and inflammation that may cause structural changes in the airways (remodelling). Tissue remodelling would cause severe airway limitation and worsen asthma. Plasminogen activator inhibitor-1 (PAI-1) considered to play an important role in the process of fibrosis after inflammation. The objectives of the study to assess the correlation between levels of PAI-1 and severity of asthma and lung function

Methods: This cross sectional study was conducted in the Wahidin Sudirohusodo and Hasanuddin University Hospital, Makassar, from April 2015 to June 2016. The subjects will be undertaken by history taking, physical examination, bronchodilator test (spirometry), x-ray, the degree of asthma control, and examination of PAI-1 levels.

Results: 47 patients became subject of research. Age range 20–74 years and FEV1% range of 31%–89%. Body mass index (BMI) research subject mostly in normal (61.7%). Subjects with a full degree of asthma control (48.9%) with a mild degree of obstruction is found most often

(55.3%). Levels of PAI-1 patients with asthma found most frequently in the range of 5.98 to 33.39 and 2.41 to 5.97 as much as 34%. There was a significant correlation between the levels of PAI-1 with the degree of obstruction ($P < 0.001$), where the percentage of obstruction was significantly increased in accordance with the value tertile 1, 2 and 3 (6.7%, 37.5% and 87.5 %) and there was correlation between the levels of PAI-1 with the degree of control ($P < 0.001$), where a significant percentage of uncontrolled asthma increased with the value tertile 1, 2 and 3 (26.7%, 43.8% and 81.3%).

Conclusion: There was significant correlation between the levels of PAI-1 in lung function and the degree of control in patients with asthma in which the higher levels of PAI-1, the more severe degree of obstruction and worse degree of control.

AP013

CORRELATION BETWEEN INHALED BETA-2 AGONIST AND CORTICOSTEROID WITH THE DEGREE OF ASTHMA CONTROL AND LUNG FUNCTION

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Background and Aims: Asthma is an important chronic airway disease and is still a serious and mass public health problem in many countries. Asthma control has been difficult to achieve using conventional therapies such as short-acting beta-2 agonists (SABAs), oral 2 oral agonists, oral corticosteroids and short-acting theophylline, leading to asthma difficult to control. Treatment of asthma based on GINA uses asthma control medications (controller) in the form of inhalation of beta 2 agonist combination with inhaled steroid/Inhaled Corticosteroids (ICS) and can be a combination of both. Classification of degree control based on GINA is considered more practical, easier to adapt, and more clinically valuable.

Objective: To know the relationship of type therapy with degree of control and lung function in asthma patient.

Methods: This study was a cross sectional study. The samples were patients with asthma diagnose both at outpatient and inpatient according to GINA criteria. The subjects of the study were collected according to the form of therapy method. Spirometry measurements determine FEV1% and asthma control degree according to GINA criteria. The study was conducted in February–May 2017 at Pulmonology Polyclinic RS Wahidin Sudirohusodo Makassar and hospital network of Internal Disease Section, Hasanuddin University Makassar Indonesia.

Results: The age of the subjects varied between 19 and 69 years old, the FEV1% score ranged from 18% to 98%, male subjects were 23 (33.8%) and 45 (66.2%). There was no significant association of therapeutic method with lung function ($P > 0.05$). There is a significant relationship between therapy method and degree of control ($P < 0.001$).

Conclusions: In patients with asthma who received combination therapy with controls such as combination budesonide and formoterol and salmeterol and fluticasone significantly more achieved a better degree of control than in patients who only received therapy agonist beta 2 inhalation or corticosteroid inhalation only.

AP014

THE ROLE OF APS F 6 THE COMPONENT OF ASPERGILLUS FUMIGATUS ON THE IDENTIFYING ABPA AND ASTHMA

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Background and Aims: *Aspergillus fumigatus* and total IgE are the main indicators for the diagnosis of ABPA, but it is difficult to identify ABPA and *A. fumigatus* sensitization asthma patients. In this study, we analyze the components of *A. fumigatus* of ABPA and asthma patients to find out the biomarkers that could help identify ABPA and asthma.

Methods: 18 ABPA and 30 asthma patients were chosen to detect sIgE of seven fungal allergens including *A. fumigatus* (m3), *Penicillium chrysogenum*, *Cladosporium herbarum*, *Mucor racemosus*, *Candida albicans*, *Alternaria alternate*, *Helminthosporium halodes*, and the components of *A. fumigatus* Asp f 1, Asp f 2, Asp f 3, Asp f 4, and Asp f 6 and total IgE. ImmunoCAP (Pharmacia, Sweden) were used for serum allergen sIgE testing.

Results: Except for *M. racemosus*, the positivity rates of the other fungi were higher in ABPA than AS (all $P < 0.01$). The sIgE level of each fungus and total IgE levels were also higher in ABPA than in AS (all $P < 0.01$).

Each *A. fumigatus* component was positively correlated with the tIgE (all $P < 0.01$). The correlations in descending order were as follows: Asp f 6 ($r = 0.75$), Asp f 4 ($r = 0.63$), Asp f 2 ($r = 0.61$), Asp f 1 ($r = 0.52$), and Asp f 3 ($r = 0.51$).

The correlation between *A. fumigatus* and Asp f 2 was the strongest ($r = 0.73$); followed by Asp f 4 ($r = 0.67$), Asp f 6, and Asp f 1 (all $r = 0.58$).

The positivity rates of all *A. fumigatus* components and sIgE levels were higher in patients with ABPA than in patients with AS, but only the positivity rate and sIgE levels of Asp f 6 were significantly higher in ABPA than AS ($P < 0.05$), as shown in Table 1.

Conclusion: *A. fumigatus* have important sensitization effects in ABPA and asthma patients. Asp f 6 has a higher positive rate and concentration in ABPA patients, which can help identify ABPA and asthma.

Table Distribution of serum sIgE-positive of *Aspergillus fumigatus* components and sIgE levels in patients with ABPA and asthma

	ABPA (n=18)		AS (n=30)	
	Positive rate n (%)	sIgE level (kU/L), median (interquartile)	Positive rate n (%)	sIgE level (kU/L), median (interquartile)
Asp f 1	16 (88.9)	7.93 (1.40-30.18)	22 (73.3)	1.21 (0.24-10.65)
Asp f 2	12 (66.7)	3.46 (0.08-9.10)	15 (50.0)	0.35 (0.03-3.00)
Asp f 3	12 (66.7)	0.83 (0.07-11.53)	18 (60.0)	1.03 (0.04-4.62)
Asp f 4	11 (61.1)	3.20 (0.10-17.65)	14 (46.7)	0.21 (0.02-12.93)
Asp f 6	12 (66.7)*	1.22 (0.07-5.70)†	8 (26.7)	0.03 (0.01-0.61)

Notes: * $P < 0.05$; † $P < 0.05$, the positive rates of all *Aspergillus fumigatus* components and sIgE levels were higher in patients with ABPA than in patients with asthma, but only the positivity rate and sIgE levels of Asp f 6 were significantly higher in patients with ABPA than in patients with asthma ($P < 0.05$).

AP015

ASSOCIATION OF PSORIASIS WITH ASTHMA: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

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Background and Aims: Psoriasis is a chronic inflammatory skin disease that has been associated various inflammatory comorbidities such as cardiovascular disease and uveitis. Asthma involves inflammation of the airway. The two diseases share inflammatory cytokine-mediated mechanisms.

Our aim is to examine the association of psoriasis with asthma.

Methods: We searched MEDLINE, Embase, and CENTRAL from inception to 22 January 2018 for case-control, cross-sectional, or cohort studies that examined the association of psoriasis with asthma. The risk of bias of included studies was assessed by using the Newcastle-Ottawa Scale. The random-effects model meta-analysis was used to calculate the odds ratio (OR) for case-control/cross-sectional studies and hazard ratio (HR) for cohort studies.

Results: We included 6 case-control/cross-sectional (1 case-control and 5 cross-sectional studies) and 1 cohort study. Three studies were rated with a high risk of bias in case definition, representativeness of the cases, selection of controls, definition of controls, and ascertainment of exposure. Psoriasis was associated with significantly increased odds (OR 1.29; 95% confidence interval (CI) 1.20–1.37) and risk (HR 1.38; 95% CI 1.23–1.54) for asthma. A subgroup analysis revealed no difference in the odds for asthma between patients with mild and severe psoriasis ($P = 0.29$), nor between paediatric and adult patients with psoriasis ($P = 0.56$).

Conclusion: The available limited evidence indicates a significant association of psoriasis with asthma.

Table 1 Characteristics of included studies.

First author, year, country	Study design	Case/Exposed group	Control group	Age of study subjects	Results
Augustin, 2015, Germany	Population-based cross-sectional study	1,313 children with psoriasis	291,868 children without psoriasis	<18 years	Calculated OR 1.34 (95% CI 1.14–1.59)
Gallil, 2017, Israel	Population-based cross-sectional study	3,122 adolescents with psoriasis	884,653 healthy adolescents	Between 16 and 18 years	All psoriasis: adjusted OR 1.18 (95% CI 1.04–1.34) Mild psoriasis: adjusted OR 0.95 (95% CI 0.79–1.15); Moderate-to-severe psoriasis: adjusted OR 1.83 (95% CI 1.20–2.81) Adjusted for age, sex, country of origin, socioeconomic status, and body mass index.
Andersen, 2017, Denmark	Population-based cross-sectional study	24,505 patients with diagnosed psoriasis	79,370 general population	≥ 18 years	Calculated OR 1.41 (95% CI 1.29–1.55)
Hajdarbegovic, 2013, Netherlands	Cross-sectional study	133 patients with psoriasis	147 patients with varicose veins but did not have psoriasis	All ages; mean age in the case: 49 ± 15.5 years; control: 54 ± 15.6 years	Adjusted OR (95% CI): 0.96 (0.43–2.15), after adjustment for age, sex, methotrexate use, and current smoking.
Lonnberg, 2015, Denmark	Population-based cross-sectional study	1,385 adults with psoriasis	31,993 adults without psoriasis	20–71 years	Adjusted OR 1.27 (95% CI 1.06–1.54), after adjustment for sex, age, smoking, body mass index, and hospital-diagnosed chronic obstructive pulmonary disease
Tsai, 2011, Taiwan	Population-based case-control study	51,800 patients with psoriasis	207,200 controls matched by age, gender, and urbanisation level of residential areas	Mean age 46.4 ± 18.6 years	Calculated OR 1.24 (95% CI 1.15–1.34)
Fang, 2015, Taiwan	Retrospective population-based cohort study	10,288 adults with psoriasis	41,152 adults without psoriasis matched by sex, age (within 5 years), and index year.	≥ 20 years	HR 1.38 (95% CI 1.23–1.54) after adjustment for age, sex and comorbidities

CI: confidence interval; OR: odds ratio; HR: hazard ratio.

PERCEPTION OF DOCTORS ABOUT DIAGNOSIS, MANAGEMENT AND FACING THE CHALLENGES WITH THEIR PATIENTS WITH ASTHMA: AN OBSERVATION-BASED SURVEY IN NEPAL

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Background and Aims: In 2017, 2.03% of total deaths in Nepal were asthma-related. There is a paucity of recent data about the prevalence and management methods for asthma.

Methods: We conducted an observation-based survey with 129 physicians and paediatricians from 135 locations in Nepal to understand practice patterns of doctors and challenges faced by them while treating asthma in Nepal.

Results: >44% doctors encountered at least 5 asthma patients daily. 37% doctors said most of their patients were under 12 years of age. 36.8% doctors always used spirometry for diagnosing asthma. Doctors asked for follow-up every 3 months, however, monthly follow-up was practiced for patients with uncontrolled asthma. Budesonide was doctors' most preferred inhaled corticosteroid followed by fluticasone. Salmeterol/fluticasone was the most preferred (69%) ICS/LABA combination followed by formoterol/budesonide (58%). Maximum doctors (84%) prescribed salbutamol as reliever and only 12% preferred SMART therapy with formoterol/budesonide. 1 in 5 doctors prescribed inhalation therapy to all patients. >60% doctors believed more than 40% patients were apprehensive to use inhalers. Doctors believed the most common reasons for patients not willing to use inhalation therapy were fear of addiction and lack of awareness. Both pMDI and DPI were equally preferred by doctors. Only 16% doctors perceived good adherence (>80%) to inhaled therapy in >70% of their patients. Almost all doctors checked inhalation technique either at every visit (40%) or on suspecting wrong technique (58%). Almost 80% doctors believed that incorrect inhaler technique was the most common reason for poor asthma control. Main reasons for non-adherence were skipping medication in absence of symptoms and wrong inhaler technique.

Conclusion: Use of spirometry can be increased for diagnosing asthma. Practice of inhalation therapy is limited for patients with asthma and can be encouraged. Incorrect technique and non-adherence were perceived as major factors responsible for poor asthma control.

AP017

ROUTINE BENZODIAZEPINE USE MAY NOT INCREASE THE FREQUENCY OF ASTHMA EXACERBATIONS RYUNOSUKE OOI^{1*}, KAZUNORI TOBINO¹

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Background and Aims: Benzodiazepines are thought as one of the risk factor of gastroesophageal reflux disease (GERD), and GERD is also known as one of the causative factor of asthma exacerbations. But the relationship between benzodiazepine and asthma exacerbations is uncertain. The aim of this study is to investigate the relationships between the routine use of benzodiazepines and the frequency of asthma exacerbations.

Methods: We included 135 asthma patients who have been followed-up for more than 1 year at our hospital between January 2013 and May 2018. Patients were classified into the following four groups: (a) non-users of sedative-hypnotic agents, (b) routine users of

benzodiazepines, (c) non-benzodiazepines, and (d) both agents. The frequency of asthma exacerbations and the time to first asthma exacerbation were compared.

Results: The number of patients in each group were as follows: (a) non-users, 103; (b) benzodiazepines, 12; (c) non-benzodiazepines, 7; and (d) both agents, 13. There was no significant difference in the frequency of asthma exacerbations among the four groups ($P = 0.528$). The routine use of benzodiazepines was not related with time to first asthma exacerbations (median time to first asthma attack was not available in both groups, $P = 0.844$).

Conclusion: This study suggested that there was no significant difference in the frequency of asthma exacerbations.

AP018

THE EFFECT OF USING MOBILE APP FOR TRAINING NURSES ON CORRECT USE OF INHALER DEVICES

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Background and Aims: An interactive mobile app was designed to provide nurses a tool to learn the different inhaler techniques. The aim of the study was to evaluate the effectiveness of using a mobile app as a teaching tool.

Methods: Participants were 30 newly recruited nurses. Prior to using the mobile app, participants completed a baseline inhaler technique assessment using standard checklists. A baseline self-efficacy survey on drug knowledge and inhaler technique was completed. Participants were given a mobile phone containing the app for a day to learn the usage of the different inhaler devices. There were a total of 6 devices i.e. metered dose inhaler, turbuhaler, accuhaler, respimat, breezhaler and ellipta. Following the usage of the mobile app, participants were asked to complete post self-efficacy surveys, questionnaires regarding the app, and were assessed for competency in using all 6 inhalers.

Results: There was an improvement in the competency and technique with the inhaler devices taught in the mobile app. The post-test scores improved significantly $Z = 4.744$ ($P < 0.001$) after the intervention compared to the pre-test scores. More participants scored well in demonstrating the correct use of accuhaler and ellipta inhaler. Overall, more than 90% of the participants agree that the app was useful with relevant content and it was easy to navigate. Majority of participants were comfortable and satisfied with the learning experience through the mobile app.

Conclusion: The study provided evidence on the effectiveness of learning inhaler techniques through a mobile app. This app provides a practical and accessible learning tool for nurses to acquire the knowledge and skills on inhalers. We propose that this may be a potential teaching tool for future trainees and patients.

AP019

A SURVEY ON THE MORBIDITY AND COST OF MULTIPLE CHRONIC CONDITIONS IN ASTHMA PATIENTS

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Background and Aims: The prevalence of patients with multiple chronic conditions (MCC) has been increasing with advances in treatment for diseases and aging. MCC is associated with poor outcomes in quality of life, high mortality, and high cost. The purpose of this study is to analyze the pattern of MCC and to estimate the cost and the utilization of medical care in asthma patients.

Methods: We analyzed the use of medical services in 2012 by individuals using the data from the National Health Insurance Corporation. MCC is characterized by 20 diseases (arthritis, asthma, autism spectrum disorder, cancer, cardiac arrhythmias, chronic kidney disease, chronic obstructive pulmonary disease (COPD), congestive heart failure, coronary artery disease, dementia, depression, diabetes, hepatitis, HIV infection, hyperlipidaemia, hypertension, osteoporosis, schizophrenia, stroke, and substance abuse disorders).

Results: The prevalence of treatment was in the order of hypertension (15.53%), diabetes (6.51%), dyslipidemia (5.70%), arthritis (3.81%) and COPD (3.41%). The prevalence of asthma treatment was 1.68% in males and 1.84% in females. As the age increased, the prevalence of MCC increased. In addition, 12% of men and 11% of women in 20 s asthma patients had MCC. As the number of chronic diseases increased, the cost of care and the frequency of use increased. The overall cost of medical care for asthma patients increased to 1.097 times as the number of chronic diseases increased. The lower the socioeconomic level, the higher the cost of medical treatment and the utilization of medical care.

Conclusion: Asthma patients with MCC have been reported at various ages. As the number of chronic diseases increases, the cost of medical care increased. Thus, the management of MCC is important.

AP020

DIFFERENT IMPACTS OF COMORBIDITY OF ALLERGIC RHINITIS ON OBESE AND NON-OBESE PATIENTS WITH ASTHMA

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Background and Aims: The association of asthma and obesity has been highlighted recently. Obesity reported to be associated with poor asthma control. Comorbidity of allergic rhinitis is also recognised to be a factor in poor asthma control. However, the precise associations among obesity, asthma and allergic rhinitis are unclear. The aim of this study was to investigate the impact of comorbidity of rhinitis on obese and non-obese patients with asthma.

Subjects and Methods: A total of 124 adult patients were enrolled in the study. A survey was performed using the Self-assessment of Allergic Rhinitis and Asthma (SACRA) questionnaire, as described in an article (Hojo M et al *Respirology* 2013, 18:1016-1021). The enrolled patients were divided into groups with obesity (OB, BMI ≥ 25 kg/m²) and without obesity (NOB, BMI < 25 kg/m²), using the criteria of the Japan Society for the Study of Obesity, and data were compared between the groups.

Results: There were no significant differences in age and spirometry data between the OB ($n = 32$) and NOB ($n = 92$) groups. The SACRA questionnaire revealed that a higher percentage of patients in the OB group felt limitation in daily activities by asthma symptoms ($P = 0.049$). There were no significant differences in the percentages of patients with rhinitis, perennial rhinitis, and severe rhinitis between the OB and NOB

groups. Asthma symptom VAS was positively correlated with Rhinitis symptom VAS in the NOB group ($r_s = 0.353$, $P = 0.008$), but not in the OB group ($r_s = -0.009$, $P = 0.971$). BMI and Asthma symptom VAS were not significantly correlated in the NOB group ($r_s = 0.076$, $P = 0.581$), but did show a trend for a positive correlation in the OB group ($r_s = 0.454$, $P = 0.050$). There was no significant correlation between BMI and Rhinitis symptom VAS in the NOB and OB groups.

Conclusions: Obesity-related factors may affect asthma symptoms and control more than rhinitis-related factors in adult obese asthmatic patients.

AP021

INHIBITION OF MAB ON PROLIFERATION AND MIGRATION OF ASMCs INDUCED BY PDGF-BB AND ITS EFFECTS ON MITOCHONDRIA

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Background and Aims: The purpose of this study was to investigate what is the effect of Mab on the proliferation and migration of ASMCs induced by PDGF-BB, and whether it is related to intracellular Ca^{2+} , mitochondrial fission, fusion, and ROS.

Methods: PDGF-BB was used to induce the migration and proliferation of ASMCs. Mdivi-1 was used to investigate the mechanism of Mab regulating the proliferation and migration of ASMCs. MTT and CCK-8 were used to detect ASMCs viability. Migration rate of ASMCs was detected by Transwell and scratch test. The intracellular Ca^{2+} immune fluorescence intensity was detected by inverted microscope, microplate reader and flow cytometry. Flow cytometry was used to analyze the effect of ASMCs cycle and MMP of Mab induced by PDGF-BB. The levels of ROS in ASMCs were measured by microplate reader and flow cytometry. In addition, Real-time PCR was used to detect Drp-1 and Mfn-2 mRNA in ASMCs. Western blot was used to detect the expression of Drp-1, Mfn-2, PCNA and CyclinD1 the key proteins of ASMCs proliferation.

Results: Mab could inhibit PDGF-BB induced proliferation, migration and the increased of the Ca^{2+} level of ASMCs in a dose-dependent manner. Mab could inhibit the increase of ROS and the S phase of ASMCs cycle, but promote the increase of MMP induced by PDGF-BB. Mab could inhibit the expression of mRNA and protein of Drp-1, promote the expression of mRNA and protein of Mfn-2, and inhibit PCNA and CyclinD1 proteins expression induced by PDGF-BB.

Conclusion: These findings suggested that Mab could inhibit the proliferation and migration of PDGF-BB-induced rat ASMCs and the mechanism was related to the inhibition of intracellular Ca^{2+} and mitochondrial fission, and the reduction of ROS level.

AP022

RETROSPECTIVE STUDY TOTAL SERUM IMMUNOGLOBULIN E, ALLERGEN-SPECIFIC IGE PROFILE AND PERIPHERAL BLOOD EOSINOPHILIA PERCENTAGE IN MODERATE TO SEVERE ASTHMATIC PATIENTS IN RESPIRATORY CLINIC, TAIPING HOSPITAL MANGAYARKARASI M. RAMANATHAN^{1*}, TENG T. TEE¹, UMADEVI A. MUTHUKUMARU¹

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Background and Aims: Serum immunoglobulin E (IgE) is one of the markers of atopy in bronchial asthma. The aim of this study is to determine total serum IgE levels, the distribution of allergen-specific IgE

by fluorescence enzyme immunoassay (FEIA) and peripheral eosinophil percentage in moderate to severe asthmatic patients.

Methods: Data was collected retrospectively from case notes of 148 asthmatic patients aged 17 to 82 whose outpatient total serum IgE was done from year 2011 to 2018 in Respiratory Clinic Hospital Taiping. Among these patients, only 137 had full blood count results and 86 had FEIA results. The diagnosis was confirmed via history, physical examination and spirometry with reversibility. Data collection also included demographics, smoking status, presence of allergic rhinitis, peripheral eosinophil percentage and age of onset of bronchial asthma.

Results: 89.9 % of the patients had elevated total serum IgE (>100 kU/mL) and 65.7% had raised peripheral eosinophil percentage ($\geq 3\%$). Mean total IgE and peripheral eosinophil percentage were 979 kU/mL and 5.0%. Males, early onset asthma and those with allergic rhinitis had higher average total IgE.

Among FEIA results, 80.3% were sensitized to at least one of the 3 house dust mites (HDM) species with 39.5% positive to all the three allergens. 33.7% were sensitized to grass pollen, followed by cockroach (29.1%), *Aspergillus fumigatus* (20.9%) and cat dander (10.4 %). 39.5% were sensitized to at least one of the seafood allergens but only 5 reported seafood allergy. Minority were sensitized to peanut and honey (4.6%).

Conclusion: Most asthmatic patients have elevated total IgE and peripheral eosinophil percentage. Sensitivity against HDM was the highest followed by seafood allergens, grass pollen, cockroach, *Aspergillus fumigatus* and cat dander. Hence we can advice patients with moderate to severe asthma to avoid these allergens especially HDM.

AP023

RESPONSE OF GOBLET CELLS OF BRONCHIAL EPITHELIUM IN PATIENTS WITH MILD ASTHMA AND COLD AIRWAY HYPERRESPONSIVENESS TO REGULAR CONTROLLER THERAPY WITH INHALED CORTICOSTEROIDS

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Background and Aims: The increase of efficiency of mucociliary clearance with corticosteroids in asthmatics is connected with the decrease of mucus secretion and correction of the contents of goblet epithelium in airways. We aimed to study the correlation between the number of cells of goblet epithelium of bronchi and the level of asthma control in patients against the therapy with inhaled corticosteroids (ICS).

Methods: There were examined 33 subjects with mild asthma (mean FEV₁ was 90. $\pm$.2%) with cold airway hyperresponsiveness that received a controller therapy with ICS/LABA in a low dose during 24 weeks. The patients were divided into two groups depending on the regularity of the using of ICS/LABA: 22 subjects received systematically controller therapy (1st group); 11 subjects received irregularly ICS/LABA (2nd group). The level of asthma control was assessed by Asthma Control Test (ACT, points). The content of the goblet cells was measured in the smears of the induced sputum (IS).

Results: The subjects of the 2nd group had a lower level of asthma control in comparison with the patients of the 1st group (15. $\pm$.2 vs 21. $\pm$.3 ACT points, respectively, $P = 0.03$) and lower FEV₁ (85. $\pm$.2 and 95. $\pm$.9%, respectively, $P = 0.03$). While studying IS, the contents of goblet cells in subjects of the 2nd group was higher than in the 1st group (0.3 $\pm$.05 and 0.1 $\pm$.4%, respectively, $P = 0.043$). According to the data of the correlation analysis a close correlation between the level of asthma control (ACT points) and the quantity of goblet cells in IS ($r = -0.30$; $P = 0.019$) was found out.

Conclusion: In the patients with mild asthma with cold airway hyper-responsiveness, a regular controller therapy with ICS/LABA in low doses leads to the increase of the number of goblet cells in IS, which reflects the recovery of the structure of bronchial epithelium and efficiency of mucociliary clearance.

The study was funded by RFBR (project 18-54-53019)

AP024

HEALTHY LUNG PROGRAMME: AN INITIATIVE FROM TSPCCM (TAIWAN SOCIETY OF PULMONARY AND CRITICAL CARE MEDICINE) AND ASTRAZENEC (AZ) TAIWAN TO IMPROVE TAIWAN ASTHMA MANAGEMENT

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Background and Aims: While Taiwan is a developed country in terms of protecting patients from respiratory diseases, there are opportunities for further improvement. With this context, Taiwan "Healthy Lung" (HL) Programme has been launched in November 2017. HL is a unique region-wide initiative from AZ, with programmes being tailored and developed in many Asia countries, all focused on the same overall health objectives to improve the management of respiratory diseases. HL is in collaboration between TSPCCM and AZ Taiwan that aims to address current gaps and improve the overall quality of asthma management.

Methods: Policy shaping: Asthma Pay for Performance (P4P) Programme has been implementing for 17 years. However, there are a few areas that might be improved, e.g. the participation of physicians and patients, and completion rate of enrolled patient are not satisfactory. One of HL's objectives is to develop asthma P4P improvement plan.

Education: HL aims to enhance GPs' capability in asthma management by working on standardising the training materials and providing certification courses.

Patient Care: To develop a patient "educational toolkit", which includes a variety of hardware and digital tools to meet the patient's needs. Asthma Centre of Excellence (ACE) programme has been established in primary medical unit that can bring high-quality care for patients.

Results: For policy shaping, a series of expert meetings has been held to create the "Asthma P4P Improvement Plan", which will be submitted to National Health Insurance Administration. Regarding education, the core materials have been completed to standardise the training for physicians. Asthma P4P Train the Trainer have been held. By 2018, 240 primary level continuing medical education courses will be accomplished. In terms of patient care, more than 100 ACEs have been successfully established.

Conclusion: The HL Programme is being rolled out in phases, and aims to create world-class asthma management and care quality in Taiwan.

AP025

THE RATIO OF NEURAL DRIVE TO TIDAL VOLUME MEASURED FROM SURFACE ELECTRODES CAN DETECT CLINICALLY SIGNIFICANT FALLS IN FEV₁ IN ASTHMATIC SUBJECTS DURING HISTAMINE CHALLENGE

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Background and Aims: A fall of $\geq 20\%$ in forced expiratory volume in the first second (FEV₁) with a cumulative dose of histamine $\leq 7.8 \mu\text{mol}$ is considered to indicate bronchial hyperactivity, but not all patients can perform spirometry properly. Here we hypothesized that increases in neural drive measured by chest wall electromyography expressed as a function of diaphragm EMG (EMG_{di}) to tidal volume (EMG_{di}-c/V_T) would have discriminative power to detect a 'positive' challenge test.

Methods: Forty-four patients with asthma and fifty-one healthy subjects were studied and all performed conventional histamine challenge tests. EMG_{di} was recorded either from chest wall surface electrodes (EMG_{di}-c). V_T was recorded from a digital flowmeter during study.

Results: With histamine challenge test EMG_{di}-c/V_T in patients with asthma was significantly higher than that in healthy subjects ($90.5 \pm 75.5\%$ vs $2.4 \pm 21.7\%$, $P < 0.001$). At the optimal cut-off point (29% increase in EMG_{di}-c/V_T), the area under the ROC curve (AUC) for detection of a positive test was 0.91 ($P < 0.001$) with sensitivity 86% and specificity 92%.

Conclusion: We conclude that the EMG_{di}-c/V_T increase during a histamine challenge provides a high discriminative for a positive result detected by spirometry.

AP026

RISK FACTORS AND MECHANISM FOR ANXIETY AND DEPRESSION IN CHINESE ADULTS WITH ASTHMA

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Background and Aims: To estimate the prevalence and risk factors for anxiety and depression in patients with asthma, and try to find out the possible mechanism of anxiety and depression in asthma.

Methods: A total of 120 asthma patients were recruited from the 2nd Clinical Medical College of Jinan University from April to December, 2017. The demographic and socio-economic data and the clinical data of the patients were collected. Patients were assessed for anxiety and depression using the Zung Self-Rating Anxiety Scale (SAS) and Zung Self-Rating Depression Scale (SDS). Logistic regression was used to analyze the risk factors for anxiety and depression in patients with asthma. And plasma cytokines IL-1, IL-6 and TNF- α were detected in patients and healthy controls.

Results: (1) 25 patients showed symptoms of anxiety. 16 were mild anxiety, 7 were moderate anxiety, and 2 were severe anxiety. 37 showed symptoms of depression. 29 were mild depression, 6 were moderate depression, and 2 were severe depression. 21 had both anxiety and depression. (2) Logistic regression showed that anxiety in asthma patients were associated with ACQ-7 score, financial stress, treatment compliance, FeNO level and religion. Depression in asthma patients was associated with ACQ-7 score, financial stress, treatment compliance and religion. (3) The concentrations of IL-1 were higher in the control group than that of the asthma anxiety/depression group ($P < 0.05$), and the asthma group had higher IL-1 concentrations than the asthma anxiety/depression group ($P < 0.05$). The concentrations of IL-6 in the control group were higher than that in the asthma anxiety/depression group ($P < 0.05$); No statistical significance was observed among groups for the concentrations of TNF- α ($P > 0.05$).

Conclusion: (1) Anxiety and depression is common in Chinese adults with asthma. (2) Anxiety and/or depression in patients with asthma were associated with ACQ-7 score, treatment compliance, religions, financial stress and FeNO. (3) Anxiety and Depression and asthma may interact through immune-inflammatory pathways.

Bronchoscopy and Interventional Techniques 1

AP028

AP027

USING GUIDING DEVICE AS ASSISTED TOOL WITH ENDOBRONCHIAL ULTRASOUND TRANSBRONCHIAL BIOPSY TO GET ADEQUATE REBIOPSY SAMPLE

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Background and Aims: Due to the mechanism of non-small cell lung cancer (NSCLC) treatment failure directs of the next step of management, rebiopsy in patients with NSCLC resistant to systemic chemotherapy or tyrosine-kinase inhibitors (TKI) became important. However, getting adequate rebiopsy sample for gene-mutation or other examination is difficult. We present a case who received Guiding device as assisted tool with endobronchial ultrasound transbronchial biopsy (EBUS-TBB) to get adequate rebiopsy sample.

Our case is a 64 y/o male patient with NSCLC, adenocarcinoma, diagnosed 4 years ago. The initial diagnosis was based on pathologic result from surgical sample from spinal metastasis. He received erlotinib and osimertinib treatment previously. Rebiopsy via EBUS-TBB was performed ever about 6 months before. However, the result of rebiopsy showed chronic inflammation and focal micro-calcification only. The current treatment regimen was pemetrexed with bevacizumab. However, the followed chest computed tomography showed disease progression again.

Methods: We used EBUS-TBB with Guide sheath (BF-1TQ290/ EU-ME2/ Guide sheath K203, Olympus, Tokyo, Japan) to perform rebiopsy at the same site 6 months before. This time, we combined with Guiding device (Guiding device, Olympus, Tokyo, Japan) as assisted tool.

Results: Within type peribronchial lesion, less than 1 cm, was noted at RB10. It was difficult to get sample while performing biopsy directly. After using Guiding device to dig at the lesion site, we got 6 pieces sample successfully. The final report of pathology was adenocarcinoma, with EGFR mutation (c.2573T>G; c.2369C>T). There was no ALK expression and negative PD-L1 expression.

Conclusion: Getting adequate rebiopsy sample is an important but difficult issue. Guiding device has 2 movable joints and is composed by steel. It is suitable to dig the post-treatment hard lesion to get tissue sample. As our experience, Guiding device is a good tool to assist EBUS-TBB rebiopsy.



RADIAL PROBE ENDOBRONCHIAL ULTRASOUND ASSISTED CONVENTIONAL TRANSBRONCHIAL NEEDLE ASPIRATION IN THE DIAGNOSIS OF SOLITARY PERIBRONCHIAL PULMONARY LESION LOCATED IN THE SEGMENTAL BRONCHI

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Background and Aims: The diagnosis of peribronchial pulmonary lesions located in the tertiary bronchi, also known as segmental bronchi, as well as, the 4th order and 5th order segmental bronchi is very difficult. Histopathological specimens cannot be easily obtained by endobronchial biopsies (EBBX) due to the patent but small segmental bronchial lumen. The aim of our study was to evaluate the diagnostic accuracy and safety of the novel technique with radial probe endobronchial ultrasound (R-EBUS) assisted conventional transbronchial needle aspiration (C-TBNA) in the diagnosis of solitary peribronchial pulmonary lesions located in segmental bronchi from 3th to 5th order.

Methods: From December 2014 to December 2015, 16 patients with computed tomography-confirmed solitary peribronchial pulmonary lesions located in segmental bronchi from 3th to 5th order were enrolled. The lesions were first located using radial probe endobronchial ultrasound to determine sites of conventional transbronchial needle aspiration, then, histopathological specimens were obtained using the technique of C-TBNA, and a final pathological diagnosis was made based on the findings from surgical specimens. Statistical analyses were performed for specimen results and complications.

Results: On pathological evaluation, 14 of the 16 specimens were malignant, including 8 adenocarcinomas, 4 squamous cell carcinomas, and 2 small cell carcinomas, while 2 were non-malignant diseases. The diagnostic accuracy rate, sensitivity and missed diagnosis rates were 87.5%, 87.5% and 12.5%, respectively. Combining the results of cytology and histologic samples obtained from C-TBNA the total diagnostic accuracy rate, sensitivity and missed diagnosis rate were 93.75%, 93.75% and 6.25%, respectively. There were 2 cases of bleeding complications >5 mL after C-TBNA, and both resolved with endobronchial management.

Conclusion: The combination of R-EBUS with C-TBNA was advantageous and safe for the diagnosis of solitary peribronchial pulmonary lesions located in the segmental bronchi. However, possible bleeding complications should be anticipated with needle aspiration. Further verification of this combined application should be investigated in larger clinical trials.

AP029

A NOVEL METHOD FOR TREATING THE REFRACTORY AND SEVERE BENIGN CENTRAL AIRWAY STENOSIS WITH OSCILLATING POSITIVE EXPIRATORY PRESSURE: TWO CASES REPORT

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Background and Aims: To appraise the safety and effectiveness of one novel method with oscillating positive expiratory pressure (OPEP) for treating the refractory and severe central airway stenosis.

Methods: Two cases were collected. One 84-year-old lady diagnosed as intrathoracic goiter suppressing the trachea with aggregated dyspnea (MRC score 4). One 22-year-old lady with complex left main bronchus (LMB) stenosis due to historic tuberculosis (MRC score 3). Obstructive ventilatory dysfunction were observed. Due to the high risk for invasive treatments, a complex conservative method was adopted including anti-infection, bronchial hygiene and OPEP. They were followed up more than 10 months.

Results: For the 84-year lady, dyspnea was improved (MRC score 1), lumens of trachea enlarged (Fig. 1), pulmonary function didn't changed.

For the 22-year-old lady patient, dyspnea relieved (MRC score 0), the LMB, left upper/lower lobe bronchus were enlarged (Fig. 2), pulmonary function also improved.

Conclusion: OPEP treatment may be a novel and non-invasive method for refractory benign central airway stenosis.

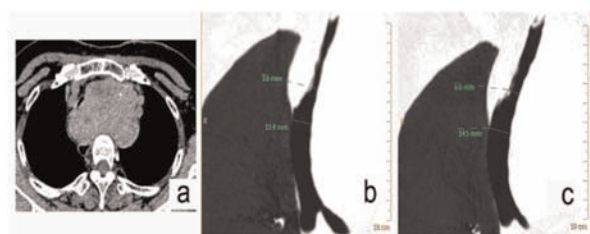


Figure1 Chest CT before and after Acapella treatment for severe tracheal stenosis due to the intrathoracic goiter

(a) Chest CT in cross section showed the severe tracheal stenosis in the proximal and middle trachea due to the intrathoracic goiter. (b) CT reconstruction showed the narrowest lumen was only 3.6mm in diameter, the distal end of the trachea was 12.4mm in diameter before treatment (c) The follow-up CT reconstruction showed that the narrowest lumen was enlarged to 6mm in diameter, the distal end of the trachea was enlarged to 14.5 after 10 months therapy of Acapella.

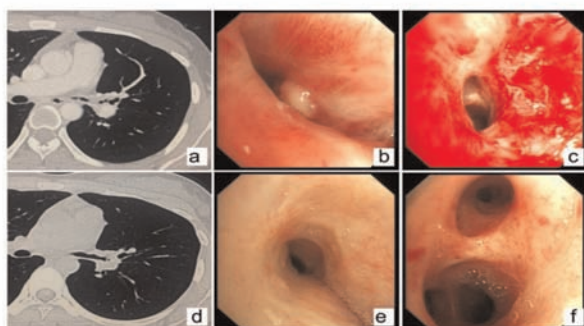


Figure 2 Chest CT and bronchoscopic findings of severe benign stenosis in left main bronchus before and after OPEP treatment

(a) The chest CT showed severe stenosis in the left main bronchus(LMB). (b)The bronchoscopic imaging showed the LMB was severe stenosis with chondromalacia and granulation tissue growing. (c) The distal of LMB and the ostial of left upper lobe and left lower lobe were severe stenosis, the diameter of the distal of LMB was only 3-4mm after therapeutic bronchoscopic procedures (d) Chest CT showed that the lumen of LMB was enlarged to 5-6mm after one-year's application of OPEP treatment. (e) The bronchoscopic imaging showed the LMB stenosis and chondromalacia was significantly improved after one-year treatment of OPEP. (f) The diameter of the distal LMB, left upper and lower lobe bronchus were all significantly increased after one-year treatment of OPEP.

AP030

A CASE OF BRONCHIAL FOREIGN BODY ASPIRATION CAUSED BY JAPANESE SPINY LOBSTER'S ANTENNA

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Background and Aims: Tracheobronchial foreign body aspiration (FBA) is an uncommon but potentially life-threatening event in adults. FBA requires immediate intervention but sometimes delayed the diagnosis because there are few symptoms.

Symptoms typically consist of a choking event followed by a cough and dyspnea, however, these findings are inconsistent and symptoms may mimic more chronic lung diseases such as asthma or chronic obstructive pulmonary disease.

This report describes a case of undetected a Japanese spiny lobster aspiration for the primary care doctors.

Methods: A 58-year-old man complained of a discomfort of a throat and persistent cough. He had visited a near internal medicine and prescribed ICS/LABA as cough variant asthma. After the treatment, his symptom did not get better so he was visited our hospital. A battery of tests was given to confirm the diagnosis.

Results: A computed tomography showed a calcification lesion in a right B8 bronchus. We reconstructed a coronal multiplanar reconstruction view and virtual bronchoscopy to evaluate the lesion and sharp and size. A cylindrical object was detected in the right B8 bronchus, which seemed a bronchial foreign body. A flexible bronchoscopy was performed to remove that.

A part of the Japanese spiny lobster had invaginated in the right B8 bronchus. That was removed by straight grasping forceps. The length was about 4 cm. After the bronchoscopy, his symptom was disappeared.

Conclusion: Recently, the image technologies are developed with the progress of the era, such techniques should be applied to maximize the use of new methods.

VB can also help to determine the shape and exact localization of the foreign body and this information may help to shorten the operative time, reduce the burden on the patient and lead to safer and more effective treatment.

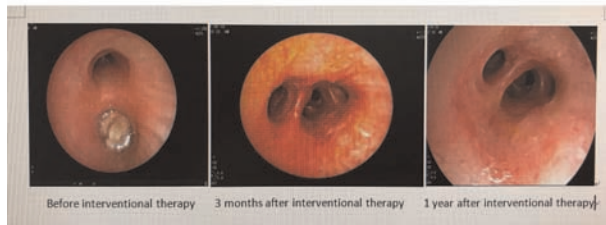
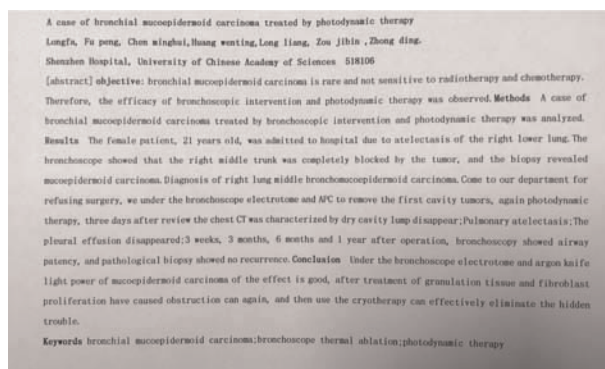
AP031

A CASE OF BRONCHIAL MUCOEPIDERMOID CARCINOMA TREATED BY PHOTODYNAMIC THERAPY

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Background and Aims: bronchial mucoepidermoid carcinoma is rare and not sensitive to radiotherapy and chemotherapy. Therefore, the efficacy of bronchoscopic intervention and photodynamic therapy was observed.



Methods: A case of bronchial mucoepidermoid carcinoma treated by bronchoscopic intervention and photodynamic therapy was analyzed.

Results: The female patient, 21 years old, was admitted to hospital due to atelectasis of the right lower lung. The bronchoscope showed that the right middle trunk was completely blocked by the tumour, and the biopsy revealed mucoepidermoid carcinoma. Diagnosis of right lung middle bronchomucoepidermoid carcinoma. Come to our department for refusing surgery, we under the bronchoscope electrotome and APC to remove the first cavity tumours, again photodynamic therapy, three days after review the chest CT was characterized by dry cavity lump disappear; Pulmonary atelectasis; The pleural effusion disappeared; 3 weeks, 3 months, 6 months and 1 year after operation, bronchoscopy showed airway patency, and pathological biopsy showed no recurrence.

Conclusion: Under the bronchoscope electrotome and argon knife light power of mucoepidermoid carcinoma of the effect is good, after treatment of granulation tissue and fibroblast proliferation have caused obstruction can again, and then use the cryotherapy can effectively eliminate the hidden trouble.

AP032

DOES BRONCHOSCOPY HAVE A RISK OF POSTOPERATIVE RECURRENCE?

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Background and Aims: Although CT guided biopsy has a slight risk of disseminating tumours, it is not well clarified whether there is a risk of spreading the tumour in bronchoscopy. Therefore, we analyzed surgical cases of lung cancer to assess if preoperative bronchoscopy increases postoperative recurrence in our hospital.

Methods: From January 1, 2008, to December 31, 2012, we evaluated patients who had radical surgery for lung cancer. We retrieved clinical information from those patients and analyzed it, assessing factors affecting postoperative recurrence and the difference in recurrence rate due to the performance of bronchoscopy in early stages of lung cancer. If the diagnosis is not made by bronchoscopy, it is classified as not bronchoscopy performed.

Results: Radical surgery for lung cancer was performed in 516 cases. Among them, 410 cases were analyzed excluding cases of preoperative chemotherapy or multiple previous surgeries. 259 cases (63.1%) were diagnosed with stage IA, 305 cases (74.4%) were diagnosed with solid type. The median follow-up period was 1966 days. Preoperative pathologic assessment by bronchoscopy was performed in 130 cases (31.7%), and recurrence was seen in 85 cases (20.7%). IA stage and solid type lung cancer prevalence were lower when bronchoscopy was not performed. Furthermore, as reported previously, we confirmed that the stage of progression, solid type (rather than ground glass nodule), pathological invasion of the veins and the lymph vessels are factors that raise the risk of postoperative recurrence.

Conclusion: If the patient is on IA stage, and the cancer was imaging diagnosed, direct surgery without bronchoscopic examination might reduce the risk of postoperative recurrence.

AP033

FACTORS INFLUENCE THE DIAGNOSTIC YIELD OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL BIOPSY IN PERIPHERAL PULMONARY LESIONS

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Background and Aims: Endobronchial ultrasound-guided transbronchial biopsy (EBUS-TBB) has been widely used in the diagnosis of peripheral pulmonary lesions (PPL) that cannot be visualized using a flexible bronchoscope. Different diagnostic accuracy of EBUS-TBB for PPLs has been reported. The purpose of this study was to evaluate the possible factors that influence the diagnostic yield of EBUS-TBB.

Methods: A retrospective chart review of patients who underwent EBUS-TBB for PPLs and finally diagnosis with malignancy from January 2014 to June 2017 was performed. We used the following factors for evaluation: (1) tumour size (≥ 3 cm vs < 3 cm), (2) location of tumour (upper lobe vs non-upper lobe), (3) position of probe (within vs adjacent to), (4) echogenicity (heterogeneous vs homogeneous), (5) biopsy times (≥ 5 vs < 5), (6) rapid on-site cytology exam (ROSE) (done vs non-done), and (7) computed tomography bronchogram (positive vs negative). Univariate and multivariate logistic regression models were used for the possible impact factors influencing the diagnostic yield of EBUS-TBB. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy rate were calculated via standard definitions.

Results: A total of 336 procedures were retrospectively evaluated in 293 patients. Echogenicity (heterogeneous vs homogeneous; 81.3 % vs 61.0 %, $P < 0.001$), biopsy times (≥ 5 vs < 5 ; 57.6% vs 81.7%, $P < 0.001$) and ROSE (done vs non-done; 88.4% vs 68 %, $P = 0.004$) were associated with higher TBB diagnostic yields. (Table) The total 336 procedures were also divided into ROSE and non-ROSE groups. In the ROSE group, the diagnostic yield (88.4% vs 68%, $P = 0.004$) and biopsy times (≥ 5 ; 84.9% vs 58.0%, $P < 0.001$) were significant higher compare to non-ROSE group.

Conclusion: The lung lesions with heterogenous echogenicity, more biopsy times and performed ROSE increase the diagnostic yield during EBUS-TBB.

Table 1. Univariate and multivariate analysis of possible factors influencing the accuracy of EBUS-TBB

Impact factor (No)	EBUS-TBB diagnostic yield (%)	Univariate p value	Multivariate p value	Odds Ratio (95% CI)
Tumor size				
< 3cm (129)	65.1 %	0.008	0.244	1.93 (1.18-3.15)
≥ 3cm (207)	78.3 %			
Location of tumor				
Upper lobe (174)	73.0 %	0.923	0.343	0.98 (0.60-1.58)
Non-upper lobe (162)	73.5 %			
Position of probe				
Within (292)	75.3 %	0.023	0.412	2.12 (1.10-4.08)
Adjacent to (44)	59.1 %			
Echogenicity				
Heterogeneous (203)	81.3 %	< 0.001	< 0.001	2.79 (1.70-4.58)
Homogeneous (133)	61.0 %			
Biopsy times				
< 5 (118)	57.6 %	< 0.001	< 0.001	3.27 (1.98-5.40)
≥ 5 (218)	81.7 %			
Perform ROSE				
Done (86)	88.4 %	< 0.001	0.004	3.58 (1.76-7.28)
Non-done (250)	68 %			
CT bronchogram				
Positive (280)	75.4 %	0.048	0.651	1.84 (1.00-3.36)
Negative (56)	62.5 %			

EBUS-TBB, endobronchial ultrasound-guided transbronchial biopsy; ROSE, rapid on-site cytology exam; CT, computed tomography

AP034

SAFETY EVALUATION OF RIGID BRONCHOSCOPIES AND THE RAPEUTIC PROCEDURES

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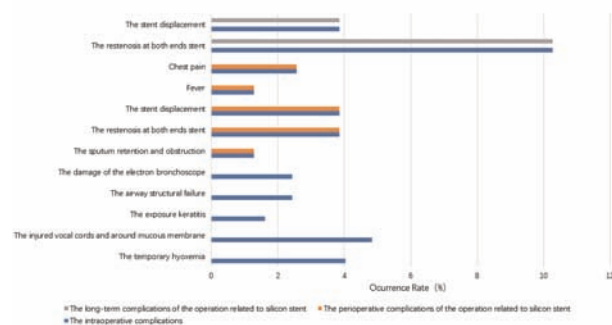
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Background and Aims: To evaluate the safety of rigid Bronchoscopy and the therapeutic procedures.

Methods: We retrospectively analyzed the clinical data of a cohort of 100 patients with benign lesions and malignant lesions who experienced the rigid bronchoscopy operation during April in 2014 to November in 2016 in Interventional Pulmonology Center of SMMU Respiratory and Critical Care Medicine Changhai Hospital. Totally received 124 procedures for the rigid bronchoscopy. To statistic the intraoperative complications of the rigid bronchoscopy, the perioperative and long-term complications of the procedures for airway silicone stents.

Results: The intraoperative complications of the rigid bronchoscopy contain the temporary hypoxemia (4.03%, 5/124), the injured vocal cords and around mucous membrane (4.83%, 6/124), the exposure keratitis (1.61%, 2/124), the airway structural failure (2.42%, 3/124), the damage of the electron bronchoscope (2.42%, 3/124), the placed failure of the rigid bronchoscopy (0.01%, 1/124); We have placed the 78 silicon stent totally (78/124), the perioperative complications of the operation related to silicon stent contain the sputum retention and obstruction (1.28%, 1/7), the restenosis at both ends stent (3.85%, 3/78), the stent displacement (3.85%, 3/78), fever (1.28%, 1/78), chest pain (2.56%, 2/78). The long-term complications of the operation related to silicon stent contain the restenosis at both ends stent (10.25%, 8/78), the stent displacement (3.84%, 3/78).

Complication	Period		
	The intraoperative complications	Perioperative	Long-term
The temporary hypoxemia	5	4.03	4.03
The injured vocal cords and around mucous membrane	6	4.83	4.83
The exposure keratitis	2	1.61	1.61
The airway structural failure	3	2.42	2.42
The damage of the electron bronchoscope	3	2.42	2.42
The placed failure of the rigid bronchoscopy	1	0.01	0.01
The perioperative complications of the operation related to silicon stent			
n=78			
The sputum retention and obstruction	1	1.28	1.28
The restenosis at both ends stent	3	3.85	3.85
The stent displacement	3	3.85	3.85
Fever	1	1.28	1.28
Chest pain	2	2.56	2.56
The long-term complications of the operation related to silicon stent			
n=78			
The restenosis at both ends stent	8	10.25	10.25
The stent displacement	3	3.84	3.84



Conclusion: The rigid bronchoscopy is a technique with high safety and less complication which is worth to be popularized and applied by clinic. The silicon stent placement under the rigid bronchoscopy can relieve the patients' clinical symptoms rapidly and improve the quality of life, but we need to emphasize health education and ensure strict follow-up after operation. Otherwise, we should focus on carrying out the standard training of the rigid bronchoscopy and related techniques which can improve the safety and reduce the complications.

AP035

USE OF CRYOBIOPSY DURING SEMI-RIGID PLEUROSCOPY

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Background and Aims: Semi-rigid pleuroscopy with forceps biopsy (FB) is the conventional way of diagnosing exudative pleural effusions with good sensitivity and specificity. Cryobiopsy (CB) has been used successfully in pleuroscopy in recent years.

This study aims to determine the diagnostic value, size and quality of CB compared with FB during semi-rigid pleuroscopy. The secondary aim was to evaluate the safety and ease of using cryoprobe.

Methods: 50 patients (27 males, 23 females) with exudative pleural effusions underwent semi-rigid pleuroscopy between 19 September 2013 and 20 April 2016 by a single interventional pulmonologist. 4 CB and 6 to 8 FB were obtained in each patient and patients acted as their own controls. These pleural biopsies were read by a single pathologist.

Paired t test was used to compare means and statistical significance was defined as $P < 0.05$.

Results: Diagnostic yield was similar and both techniques were highly successful in obtaining pleural tissue. The average length ($P = 0.003$) and depth ($P < 0.001$) of the biopsies were significantly larger for CB than FB. The average surface area of each biopsy for both CB and FB were comparable ($P = 0.747$).

For two patients (sarcomatoid mesothelioma and tuberculous pleurisy), FB obtained only blood clots and exudate. The diagnoses were clinched only on CB, which obtained specimens with a larger depth than the FB specimens.

There were no significant complications with both methods.

Conclusion: The diagnostic yield, safety and tolerability for both methods of biopsy are similar. The average biopsy length and depth of CB are significantly larger, which proves valuable in pleural pathologies where superficial pleural biopsies might yield false-negative results. Compared to FB, CB is a faster method, taking approximately 8 minutes to complete 4 biopsies. This translated to shorter procedural time and use of less sedation and analgesia. Limitations of CB include cost and availability.

AP036

ENDOBRONCHIAL BALLOON TAMPONADE ACHIEVING SUCCESSFUL CONTROL OF MASSIVE HAEMOPTYSIS SECONDARY TO METASTATIC LUNG DISEASE: A CASE REPORT

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Background and Aims: Massive haemoptysis is life-threatening and requires immediate intervention. We describe a massive haemoptysis case successfully controlled with endobronchial balloon tamponade and eventually, bronchial artery angiography and embolization. We present the case and discuss the bronchoscopic technique and different treatment options for massive haemoptysis.

Methods: Case Report

Results: A 71-year-old woman with papillary thyroid cancer with pulmonary metastasis, who previously had total thyroidectomy and tracheostomy tube insertion, presented with massive haemoptysis amounting to 500 mL of fresh blood in 24 h.

Urgent fiberoptic bronchoscopy revealed blood clots in the right upper lobe which were removed using biopsy forceps. Despite endobronchial cold saline and epinephrine administration, continuous bleeding was observed at the posterior segment of the right upper lobe.

An endobronchial balloon tamponade using modified Rusch EZ-blocker was inserted on the level of RB3. Inspection of the right upper lobe post inflation of the endobronchial tamponade showed no active bleeding. The balloon was deflated and removed after 72 h.

After improvement of kidney function, bronchial angiography and selective embolization was performed. An enlarged, tortuous bronchial branch of the intercostobronchial artery showed abnormal contrast staining and pseudoaneurysm formation indicating active bleeding. The intercostobronchial trunk was embolized using 250–500 micron PVA particles allowing complete devascularization. Angiogram post embolization showed non-visualization of the source of bleeding.

Conclusion: Urgent endobronchial balloon tamponade in our patient has proved life-saving, en route to definitive treatment with embolization. Presence of acute kidney injury prevented us from doing immediate angiography at the outset due to the need for contrast agent. She was eventually discharged well and ambulatory. Our case emphasizes crucial decision-making in the application of different strategies in the control of massive haemoptysis as proper decisions lessen cost and patient morbidity.

EVALUATION THE PHYSIOLOGICAL CHANGES OF CENTRAL AIRWAY ON MULTI-DETECTOR COMPUTED TOMOGRAPHY

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Background and Aims: To explore the physiological changes of central airway on multi-Detector computed tomography at deep inspiration breath holding (DIBH) and deep expiration breath holding (DEBH).

Methods: The data of 62 patients (38 males, 23 females) who performed enhancement computed tomography in our hospital during November 2014 and May 2015 were collected. Patients were grouped according to gender and age (18–45 years-old, 46–60 years-old, >61 years-old). Tracheal diameter at three level (Cricoid, intrathoracic inlet, 2 cm above carina), tracheal length, bronchial length and subcarina angle were measured.

Results: Average length of trachea from cricoid cartilage to carina is 103.91 ± 10.37 mm at DEBH, and 108.63 ± 11.31 mm at DIBH. There was a significant difference in the length of trachea between expiration and inspiration. The anteroposterior and transverse diameter of trachea at all the three level with significant difference between male and female. The change of tracheal diameter between DIBH and DEBH with significant difference, except the change of transverse diameter (TD) at the level of intrathoracic inlet. Average length of right and left main bronchus were measured as $13.2 \pm .60$ mm and $44.1 \pm .50$ mm in deep expiration, while $13.2 \pm .49$ mm and $44.2 \pm .11$ mm in deep inspiration. There was no statistically significant difference in age and gender group, even between expiration and inspiration, except the length of left main bronchus in male at DEBH. Average SCA is $81.7 \pm 4.56^\circ$ at DIBH, while $80.5 \pm 4.38^\circ$ at DEBH. The change of SCA between DIBH and DEBH with significant difference.

Conclusion: These findings about trachea and bronchus in our study may contribute to bronchoscopy examination, tube application, stent design and stenting. Also, MDCT is a useful tools in the evaluation of trachea and bronchus.

AP038

INITIAL EXPERIENCE ON PERCUTANEOUS CATHETER DRAINAGE FOR RESPIRATORY DISEASES IN SRI LANKA: AN AUDIT

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Background and Aims: Majority of intrapulmonary and pleural supportive collections are successfully treated with modern antibiotics. Percutaneous catheter drainage (PCD) is an alternative to surgery when medical therapy fails. However this treatment modality is yet underutilized in Sri Lanka.

Objective: To assess the success and complications of PCD for lung abscesses and empyema.

Methods: Patients with diagnosed lung abscess and loculated empyema from 01.01.2017 to 01.05.2018 were enrolled. PCD was performed according to standard protocol by an interventional radiologist. Standard antibiotics were administered to all patients. Data on demography, biochemical, microbiological and radiological investigations, complications, duration of PCD and hospital stay were collected.

Results: 12 patients underwent PCD, 11 (91.6%) were males. Age ranged from 38 to 81 years. There were 7 (58.3%) cases of empyemas and 5 (41.6%) lung abscesses, 01 was secondary to lung malignancy.

Duration of drainage was ranged from 4 to 18 days (mean 9.6). Duration of hospital stay ranged from 12 to 65 days (mean 27.9). None had major complications including haemorrhage, haemoptysis, pneumothorax or haemothorax. But, in one tube was dislodged and complicated with subcutaneous emphysema necessitating re-insertion of catheter. PCD was successful in 11 (91.6%) cases, in which 10 (90.9%) had complete clearance of abscess or empyema and 01(9.0%) had partial drainage of abscess. However, 01(8.3%) developed a trapped lung. 01 (8.3%) died due to septicaemia, in which surgery was deferred due to general debility.

Conclusion: PCD was an effective mode of treatment for lung abscesses and encysted empyema with 91.6% success. There were no major complications. This will be an effective alternative for major surgery with minimal discomfort to the patients and complications.

AP039

A CASE OF RIGHT LUNG REEXPANSION DUE TO TRACHEAL PERFORATION

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Background and Aims: The patient was a 42-year-old Chinese woman who presented with a diagnosis of right lung atelectasis due to endotracheal tuberculosis for nearly 6 months. Under the bronchoscope we attempted to get through the suspected opening of the right main bronchus, causing tracheal perforation during the coagulation process (Figure 1).

Methods: Later, patient's cough and chest pain worsen, followed by appearance of mediastinal, neck, and chest wall emphysema. After 4 days, the symptoms of cough, chest pain, and subcutaneous emphysema relieved, and part of the upper right lung reexpansion. After 3 months, all the right upper lobe reexpanded, part of the right middle lobe and the lower lobe reexpanded. At this time, the true right main bronchus opening under the bronchoscope appeared and the previous tracheal perforation hole healed (Figure 2).

Results: Under the bronchoscope, the electrocoagulation and balloon dilatation surgery was performed on right main bronchus opening obstruction position, and the right main and right upper lobe bronchial lumens were successfully opened (Figure 3).

Conclusion: Endotracheal tuberculosis is likely to cause tracheal stenosis, and even atresia, resulting in lung atelectasis. At this time, the strategy for lung reexpansion is mainly bronchoscopic intervention or lung-preserving surgery. In general, bronchoscopic interventional treatment is mainly through the electrocoagulation method to directly open the narrow part of the airway, and then the balloon expands the airway so that air can enter the distal airway and the distal blocked secretions are drained. In this case, the patient bypassed the narrow part of the airway and reached the distal airway through the "proximal airway- Mediastinum-distal airway" pathway that was inadvertently opened.

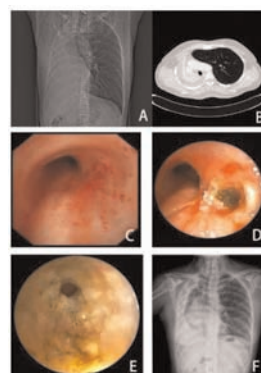


Figure 1 Image and bronchoscopy at the first treatment. At the time of the initial visit, the patient's CT examination revealed right lung atelectasis (A and B). The bronchoscope examination showed suspected opening of the right main bronchus (C), where electrocoagulation (D) was performed, resulting in perforation of the tracheal mediastinum (E). X-ray examination revealed cervical subcutaneous and mediastinal emphysema (F).

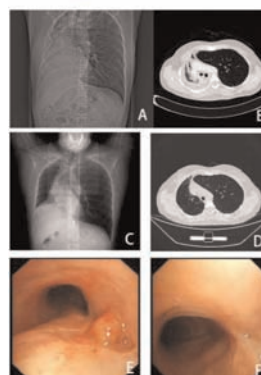


Figure 2 CT and bronchoscopic findings during 3 months follow-up. After 4 days, the upper right lung is partially reexpanded (A, B). After 3 months, the upper lobe of the right lung and the middle lobe were reexpanded (C, D). The perforation hole healed (F), and the true right main bronchus opening (G) appeared.

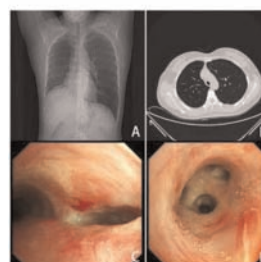


Figure 3 After the second treatment, followed up for 2 months, CT and bronchoscopy performance. The right upper lobe, part of the middle and lower lobes (A, B), and the right main bronchus and right upper lobe bronchial lumen (C, D) were seen under bronchoscopy.

AP040

THE IMPACT OF THE HIGH-FLOW NASAL OXYGEN TO THE SAFETY AND SEDATIVE QUALITY OF PATIENTS UNDERGOING BRONCHOSCOPY- PRELIMINARY DATA

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Background and Aims: The hypoxemia during propofol sedation of bronchoscope is a major safety issue in different studies. The impact of the high-flow nasal oxygen (HFNO) to patients undergoing bronchoscopic sedation is unknown. We hypothesises that patients underlying flexible bronchoscopy could benefit from high-flow nasal oxygen to prevent hypoxemia and hypoventilation comparing to current standard care.

Methods: Target controlled infusion of propofol targeted at 2 µg/mL and ± 0.2 µg/mL to maintain stable vital signs and sedative levels during bronchoscopy. Patients were randomized to Group 1, HFNO 60 L/min FiO₂:29% (study group, n = 6), or Group 2, HFNO 30 L/min FiO₂:29% (study group, n = 6), or Group 3, nasal cannula(NC) 2 L/min(control group, n = 7). The hypoxemia and hypotension during induction and propofol sedation were recorded.

Results: The patient characteristics and procedures performed are similar. There is no difference in proportion of patient with hypoxemia in three groups during induction (16.7 vs 0 vs 0%, respectively) and during procedure (33.3 vs 66.7 vs 42.9%, respectively). There is no difference in proportion of patient with hypotension in three groups during induction (0 vs 0 vs 14.3%, respectively) and during procedure (33.3 vs 0 vs 0%, respectively).

Conclusion: There is no difference in hypoxemia and hypotension in three groups undergo bronchoscopic sedation. Further patient enrolment and subgroup analysis will be done.

Table 2. Events of hypoxemia and hypotension during bronchoscopic sedation

	HFNO60L ^a (n=6)	HFNO30L ^a (n =6)	NC2L ^a (n =7)	P value ^c
Hypoxemia^a, n (%)^b				
during induction [#]	1(16.7)	0(0)	0(0)	0.632
during procedure [§]	2(33.3)	4(66.7)	3(42.9)	0.621
during recovery [§]	0(0)	0 (0)	1(12.5)	1.0
Hypotension[†], n (%)^b				
during induction [#]	0(0)	0(0)	1(14.3)	1.0
during procedure [§]	2(33.3)	0 (0)	0 (0)	0.175
during recovery [§]	4(66.7)	2 (33.3)	1(14.3)	0.171

Data are presented as number and percentage. ^aHypoxemia: oxyhemoglobin saturation < 90%. [†]Hypotension: (mean arterial pressure < 65 mmHg or systolic blood pressure < 90 mmHg). [#]From administration of propofol to the time point of Ce of induction. [§]From insertion of bronchoscope to removal. ^cDuration between complete bronchoscopy and regain orientation.

AP041

A SIMPLIFIED METHOD OF TRANSESOPHAGEAL NEEDLE ASPIRATION WITH AN ULTRASOUND-GUIDED BRONCHOSCOPE (EBUS-TENA)

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Background and Aims: Biopsy via the oesophagus plays an important role in the diagnosis of mediastinal lymphadenopathy and lesions, and the use of an ultrasound guided bronchoscope in the oesophagus (endobronchial ultrasound transesophageal needle aspiration, EBUS-TENA) has been proved reliable by accumulating evidence. However, EBUS relies on a high level of proficiency in sonography, and accurate identification of the anatomical structures is vital for successful harvest of samples. To circumvent the anatomical and sonographic difficulties, we have developed a simplified method of TENA.

Methods: Localization of the lesions is achieved mainly through chest CT scans instead of real-time ultrasound imaging. The distance of the lesion from the glottis or the cardia (D) was calculated by multiplying the number of planes between the glottis/cardia and the lesion (N) and the thickness of each plane (T), i.e. D = N*T. The position of the lesion relative to the oesophagus on the transverse plane is recorded by the clock position. It is of note that the clock position of the lesion when the patient lies before the pulmonologist in the procedure is different from that on the CT scan display. With these information, the lesion can be easily localized by the bronchoscope in the oesophagus, and the ultrasound probe serves to confirm the location of the lesion and distinguishes the surrounding tissues, which guarantees a safe and accurate puncture.

Results: In the 6 patients who received both procedures, the pathological diagnosis of samples harvested by the two techniques were identical (2 cases of non-small cell lung cancer, 2 adenocarcinoma, 1 lymphoma, 1 small cell lung cancer). Meanwhile, the simplified TBNA requires no sedation, lower oxygen flow, shorter procedural time and provokes less coughing compared with traditional EBUS-TBNA.

Conclusion: The adjustments of the simplified TENA technique are safe, simple, effective and patient-friendly compared with traditional EBUS-TENA and TBNA.

AP042

MOLECULAR ANALYSIS OF SMALL TISSUE SAMPLES OBTAINED VIA TRANSBRONCHIAL LUNG BIOPSY USING RADIAL PROBE ENDOBRONCHIAL ULTRASOUND

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Background and Aims: Radial probe endobronchial ultrasound using a guide sheath (EBUS-GS) is used to diagnose peripheral lung cancer. However, the accuracy of molecular analysis performed on EBUS-GS specimens remains unknown in patients with non-small cell lung cancer (NSCLC).

Methods: From December 2015 to September 2017, we retrospectively studied 91 patients with peripheral NSCLC who underwent surgery after EBUS-GS. Epidermal growth factor receptor (EGFR) mutational and anaplastic lymphoma kinase (ALK) translocation status obtained from surgical specimens served as the references.

Results: Compared to the reference data, EGFR mutational testing of EBUS-GS specimens was in 97% agreement, and the κ coefficient was 0.931 ($P < 0.001$) (Table). False-negative EGFR mutational data were obtained from three EBUS-GS specimens (3%) and the tumour cell numbers (estimated by pathologists) in these specimens were lower than those of other specimens. In addition, on ALK translocation testing, the results of all 91 patients were in agreement with the reference data (concordance rate of 100%, κ coefficient 1.000; $P < 0.001$).

Conclusion: We found that EBUS-GS could be used for molecular diagnosis, such as EGFR mutational and ALK translocation status, in patients with peripheral NSCLC.

Table. Comparisons of the EGFR mutational and ALK translocation results between the EBUS-GS and surgical specimens.

	Specimens		Correlation analysis	
	EBUS-GS (%)	Surgery (%)	Agreement rate	κ coefficient
EGFR mutation detected	35/91 (38)	38/91 (42)	97%	0.931
ALK-positive	5/91 (5)	5/91 (5)	100%	1.000

AP043

IS UNIORTAL VIDEO-ASSISTED THORACOSCOPIC SURGERY ACCEPTABLE AS A STANDARD SURGICAL TECHNIQUE FOR THE PRIMARY SPONTANEOUS PNEUMOTHORAX?

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Background and Aims: A multiportal video-assisted thoracoscopic surgery (m-VATS) has been recognized as a standard surgical technique for the primary spontaneous pneumothorax (PSP). However, recent advancement of surgical devices allows surgeons to perform more minimally invasive VATS such as single-incision VATS (uniportal VATS; u-VATS). In this study we evaluated the feasibility and efficacy of our u-VATS comparing with conventional m-VATS.

Methods: From January 2015 to May 2018, there were 158 patients with pneumothorax who underwent VATS at our hospital. Among this population, 95 patients were diagnosed as PSP and u-VATS was performed 26 patients, on the other hand, 69 patients underwent m-VATS. We compared u-VATS with m-VATS using propensity score matching and the following clinical factors were evaluated: postoperative pain scale, surgical procedure (resection or ligation), operative time, blood loss, number of autosuture, the use of fibrin glue, number of pleural covering mesh, period of postoperative drainage, postoperative hospital stay, and recurrence rate.

Results: 22 patients from each group were extracted. There were no significant differences in postoperative pain scale, surgical procedure, blood loss, number of autosuture, the use of fibrin glue, number of pleural covering mesh, and recurrence rate. However, operative time (41 ± 1.0 min vs $77. \pm 7.2$ min, $P < 0.01$), period of postoperative drainage (1 ± 6 days vs 2 ± 7 days, $P < 0.01$), and postoperative hospital stay ($2. \pm .6$ days vs 3 ± 7 days, $P < 0.01$) were shortened with statistically significant differences.

Conclusion: Our results indicate that u-VATS is acceptable as a one of standard surgical procedure for PSP.

AP044

CASE STUDY DOUBLE STENTING OF OESOPHAGUS AND AIRWAY IN PALLIATIVE TREATMENT OF PATIENT WITH OESOPHAGEAL CANCER

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Background and Aims: Advances oesophageal cancer often force bronchotracheal resulted narrow airway when the tumour increases its size, with invasive the back wall of trachea. Patients feel difficulty breathing, reduce quality of life. Double stenting of oesophagus and airway in palliative treatment is a good choice.

Methods: A 54-year-old male patient, with oesophageal cancer (T4N3M1) type squamous cell about 9 months, treated by radiation chemotherapy. He admitted to Bach Mai hospital because shortness of breath, dry cough, dysphagia and without lose weight.

Results: Physical examination revealed wheezing in both side of lung, BMI: 17.5, and no lymph node. A computed tomography of thorax showed a tumour of oesophagus located after tracheal, caused severe narrow tracheal, with the narrowest size was 3 mm (Fig. A). Flexible bronchoscopy showed a tumour from outside protrudes caused narrow about 80% area of tracheal. The patient would be performed a rigid bronchoscopy to placed a dynamic Y stent after that. But, we failed when tried intubation with hard tube. He was performed tracheostomy, and then placed a dynamic Y stent through tracheostomy. Oesophageal stenting was performed after 6 days, using a flexible endoscope. The stent's position was checked endoscopically. With double stent in airway and oesophageal, the symptoms of patient were reduced and increase quality of life.

Conclusion: Stenting in airway and oesophageal in patient with oesophageal cancer is palliative treatments which efficient. But this treatment should be reserved to very selected patients in end-stage disease. In the case patient could not be intubation with hard tube, push stent after tracheostomy is another alternative which may be consider.

AP045

FLEXIBLE BRONCHOSCOPE INTERVENTIONAL THERAPY UNDER MECHANICAL VENTILATION FOR SEVERE AIRWAY STENOSIS: CASE REPORTS

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Background and Aims: Severe airway stenosis can cause chest distress or gasp and even severe respiratory failure in a short time sometimes. Flexible bronchoscope interventional therapy is a major treatment for airway stenosis. Though there are usually complications occurred in this process, mechanical ventilation to some extent can help prevent these problems.

Methods: To analyse the treatment process of the two case report about flexible bronchoscope interventional therapy under mechanical ventilation for severe airway stenosis.

Results: Case 1: An old patient was diagnosed with lung cancer, COPD and respiratory failure. He received pericardiocentesis, drainage and medium flow oxygen due to massive pericardial and pleural effusion in the subordinate hospital. However, his oxygen saturation was 87% and the dyspnea didn't improve. His bronchoscopy showed the neoplasm completely obstructed the right bronchus. Considering his low oxygen saturation, he received naso tracheal intubation under sedation guidance. We used cauterization and electric knife to rid of the neoplasm and restore the patency of the trachea.

Case 2: A patient who was diagnosed with lung cancer suffered dyspnea. Bronchoscopy showed that the carina was widened, the bilateral main bronchi was seriously narrowed, and the right middle segment bronchus was basically obliterate. Considering the critical condition of his illness, we chose to implant a nitinol stent in his left main bronchus with mechanical ventilation. During the process, the vital signs were steady. After the operation, the dyspnea relieved.

Conclusion: Flexible bronchoscope interventional therapy is a major treatment for severe airway stenosis. Mechanical ventilation can help increase the safety in the process.

AP046

RECURRENT PNEUMOTHORAX IN SJOGREN SYNDROME

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Background and Aims: A patient who had a primary spontaneous pneumothorax is at risk of having a recurrence pneumothorax episode.¹ In Sjogren syndrome (SS), pneumothorax can be the first manifestation and recurrency can be happen. In 9–20% of cases, SS is associated with various respiratory symptoms and a female predominance.^{2,3}

Methods: A 35-year-old woman presented with acute dyspnea. She was previously diagnosed with SS in October 2017. On February 2018, she experienced pneumothorax two times and did not relieve after chest tube insertion so she referred to Respiratory Center Persahabatan Hospital. Her chest CT shows a left pneumothorax with multiple bullae and interseptal thickening lead to a suspicion of lymphocytic interstitial pneumonia. The bronchoscopy showed no abnormality. Video assisted thoracoscopic surgery (VATS) and bullectomy were performed due to

persistent air leaks. Histologically, there were alveoli-empysematous, focal lymphoid aggregates, infiltration of the peribronchiolar wall by lymphocytes with plasma cells and no cathamerial finding. *Interferon gamma release assay* (IGRA) test and Ca-125 marker were negative. Autoimmunity markers, including antinuclear antibodies (ANA) and anti *Sjogren syndrome antigen A* (SS-A) antibody were positive. *Rheumatoid factor* (RF), *anti-double stranded deoxyribonucleic acid* (ds-DNA) and *anti-neutrophil cytoplasmic antibodies* (ANCA) were negative. The levels of C3 and C4 were within normal limits. There were no evidence of *human immunodeficiency virus* (HIV) and *human T-cell leukaemia lymphoma virus* (HTLV) infection. *Acid fast bacilli* (AFB) examination and Gen Xpert from bronchial washing were negative

Results: Recurrent pneumothorax as the first clinical symptom of SS has not been previously reported in Indonesia. In female, usually we assumed the cause of pneumothorax is cathamerial. We suspected the presence of an underlying immune disorder due to the findings on chest CT and histologically finding.³

Conclusion: Although rare, SS should be considered in Indonesian female patient presenting with recurrent pneumothorax.

AP047

SUGAR FROSTING-LIKE LESION IS A HINT OF MESOTHELIAL HYPERPLASIA UNDER PLEUROSCOPY: A CASE REPORT

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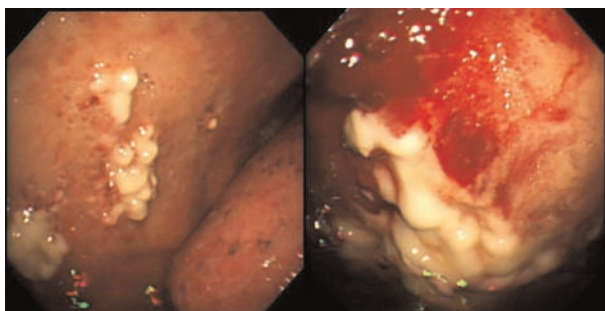
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Background and Aims: Malignant pleural mesothelioma is a neoplastic threat for everyone with asbestos exposure. We could see mesothelial hyperplasia, a kind of progressive change of pleura in reaction of various stimulation. No known relation between malignant pleural mesothelioma and mesothelial hyperplasia was confirmed. Here, we propose an unknown pleural effusion case with mesothelial hyperplasia. To show the characteristic of mesothelial hyperplasia under pleuroscopy.

Methods: We retrospectively recruited a patient who was diagnosed as mesothelial hyperplasia. The images of pleuroscopy was reviewed by two senior pulmonologists. The biopsied specimens were processed and diagnosed by an experience pathologist with respiratory system.

Results: Several white lesions were located over parietal pleura. The appearance of the lesions could be described as sugar frosting, which is usually decorated in the cake. The pleural effusion of the patient diminished gradually after antibiotic use.

Conclusion: Sugar frosting was a specific description of the case with mesothelial hyperplasia. More clinical data was needed to support the view of point.



BRONCHIAL OCCLUSION WITH ENDOBRONCHIAL WATANABE SPIGOT FOR HAEMOPTYSIS IN A MECHANICALLY VENTILATED PATIENT WITH EXTRACORPOREAL CIRCULATION

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Background and Aims: Bronchial occlusion with an endobronchial Watanabe spigot (EWS) can be an essential therapeutic measure in massive haemoptysis for intensive care patients when no other conventional options are available. Here, we report a critically ill patient with life-threatening haemoptysis salvaged by bronchial occlusion with an EWS.

Methods: A 68-year-old-man on mechanical ventilation and extracorporeal circulation after cardiovascular surgery had massive haemoptysis. He was deemed unfit for bronchial artery embolization (BAE) and surgery while in the intensive care setting; therefore, bronchial occlusion was tried using an EWS. Using a flexible bronchoscope, the site of bleeding origin was identified at the peripheral airway on the right B3, B4 and B5. Subsequently, two 7-mm EWS were inserted firmly, one each into the right B3 and B5 segment, and one 6-mm EWS was inserted into the right B4 segment.

Results: After bronchial occlusion, the haemoptysis ceased, and he was successfully weaned from mechanical ventilation and extracorporeal circulation.

Conclusion: Bronchial occlusion by EWS for haemostasis may be considered an optimal, and at times, definitive treatment in these situations.

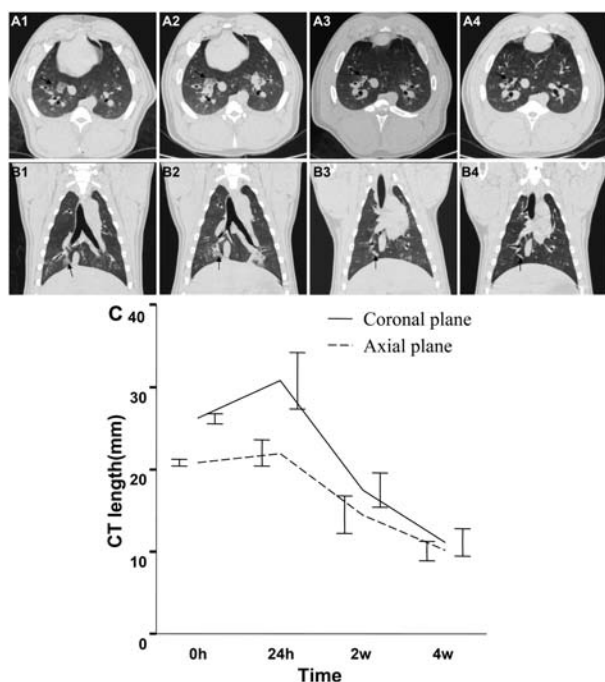
AP049

FEASIBILITY AND SAFETY OF FLEXIBLE BRONCHOSCOPY-GUIDED MICROWAVE ABLATION IN PORCINE LUNG: A NEW IMAGE-GUIDED MICRO-INVASIVE ABLATION METHOD FOR LUNG LESIONS

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Background and Aims: Transbronchial lung biopsy is an important diagnosis of peripheral lung cancer, while an effective treatment is absent. A flexible bronchoscopy-guided microwave ablation (MWA) antenna was devised and to be evaluated the feasibility and safety both in ex vivo and in vivo porcine models.



Methods: By antenna penetrated through surface of ex vivo porcine tissues, ablations ($n = 21$) were performed at 40–100 W in liver and ablations ($n = 9$) at 70–90 W in lung for 10 min. Temperatures of catheter and 10 mm, 15 mm, 20 mm away from the antenna tip were measured respectively. Under bronchoscopy in porcine lung, ablations ($n = 18$, 6 in ex vivo and 12 in vivo) were performed at 80 W for 5 min. Computed tomography (CT) was acquired perioperative, 24 h, 2 weeks, 4 weeks. Ablation zones were excised at 24 h and 4 weeks respectively. Long-axis diameter (DI) and short-axis diameter (Ds) were measured and tissues were sectioned for pathological examination. The data were analyzed with one-way ANOVA and T TEST, followed by the LSD post hoc test.

Results: In ex vivo liver, temperature and diameter had different changes between powers. In ex vivo lung, the temperature of 20 mm was over 60°C at 80 W for 28 ± 6 s. The ablations under bronchoscopy were successful in ex vivo and vivo lung. Lesions had different show on CT at different time. No complications occurred during operation. Coagulation necrosis was visible at 24 h, and repaired fibrous tissue was seen at 4 weeks.

Conclusion: The flexible bronchoscopy-guided MWA is feasible and safe that could become a potential interventional therapeutic tool in Peripheral Lung Cancers.

AP050

IMPROVED HOSPITALISATION STAY WITH INDWELLING PLEURAL CATHETER

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Background and Aims: The mainstay of treatment for symptomatic recurrent pleural effusion was previously limited to intermittent thoracentesis or pleurodesis. Indwelling pleural catheter (IPC) have been used by our centre since 2015 for treatment of symptomatic recurrent pleural effusion. IPC is a tunnelled pleural tube that allows patient to do self-drainage at the comfort of their home. Our study aim at looking whether IPC insertion reduces hospitalisations.

Methods: This is a retrospective study of patient who had IPC inserted from 2015 at a single tertiary referral hospital in Malaysia. Patient's demographic data, diagnosis, duration of stay in hospitalisation pre and post IPC and number of pleural procedures prior to IPC were recorded. Data were analysed using SPSS Version 20.

Results: 13 IPC have been inserted in a single centre by our team with mean patient's age 56.5 ± 13.4 year old (range 37–76 years old). Indications were malignant pleural effusion (76.9%) and hepatohydrothorax (23.1%). Patient's diagnosis included adenocarcinoma (53.8%), lung cancer (unspecified) (15.4%), liver cirrhosis (23.1%) and small cell lung cancer (7.7%). There were only 2 cases of infection (15.4%) (at 5 months and 11 months after insertion respectively). Mean duration of stay was 15.0 ± 8.7 days with a mean no of thoracentesis of 2.1 ± 0.9 times before the IPC insertion. Mean duration of stay after IPC was 2.7 ± 3.3 days. There was a significant reduction in duration of hospitalisation with mean difference of 11.6 ± 10.2 days (95% CI 3.11–20.14, $P = 0.014$).

Conclusion: This highlights that IPC intervention reduces hospitalisation and is associated with low complication rate. Its use is not just limited to malignant pleural effusion but could include non-malignant condition such as hepatohydrothorax.

AP051

MANAGEMENT OF EARLY AIRWAY RESTENOSIS AFTER THE PLACEMENT OF METAL COVERED STENT: A CASE REPORT

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Background and Aims: The formation of granulomas and scarring are common complications after endotracheal intubation, which causes airway stenosis and dyspnea. Airway stenting, including metal stents and silicone stents, has been well recognized to be effective on relieving airway stenosis, especially for those who do not respond well to cryotherapy and electrocuting. Long-term placement of metal stents is usually complicated with airway stenosis, whereas early complications have been rarely reported.

Methods: The patient with severe dyspnea for 10 days was admitted to our department on Jan.1, 2017. He received endotracheal intubation 2 weeks ago. Bronchoscopic examination showed trachea stenosis caused by the proliferation of granulation tissue and scars formation. Cryosurgery and balloon dilatation were subsequently performed but did not work well. Therefore, a metal covered stent (18 mm*50 mm) was placed on Jan. 6, after which his symptom of dyspnea was relieved. Bronchoscopy on Jan. 9 showed slight proliferation of granulation tissue, so cryotherapy was then given. But subsequent bronchoscopy revealed that granulation tissue and scars were increasing. Based on these observations, metal stent was removed. Cryotherapy, high frequency electrocuting and balloon dilatation were performed for multiple times under bronchoscope. On Mar.5, a silicon stent was placed under rigid bronchoscopy. His symptom of dyspnea got greatly relieved, and subsequent regular bronchoscopic examinations only showed slight proliferation of granulation tissue.

Results: After 9 months, the silicon stent was removed, and airway stenosis was not seen. The patient has been followed up so far, and no dyspnea is reported.

Conclusion: Tracheal restenosis within 2 weeks after the placement of metal stents is rarely seen. Investigations focusing on its prevalence are needed to determine whether metal stents should be routinely used in post-intubation airway stenosis. Comprehensive managements are required once restenosis occurs, including the removal of metal stent, endoscopic therapies (cryosurgery and balloon dilatation) and the placement of silicon stent.

Cell and Molecular Biology 1

AP052

THE ASSOCIATION OF VANADIUM PENTOXIDE AND INFLAMMATORY RESPONSE IN PATIENTS WITH COPD AND IN HUMAN BRONCHIAL EPITHELIAL CELL

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is characterized by lung inflammation. Air pollution is strongly related to chronic obstructive pulmonary disease (COPD). Vanadium (V) is major transition metal often adhered to particulate matter and emitted into the atmosphere as vanadium pentoxide (V₂O₅) by the combustion of fossil fuels and metallurgic industry activities. Particulate matter (PM) air pollution contributes to inflammation-related processes including COPD. Our aim is to evaluate the effect of vanadium on the inflammatory response *in vitro* and in patients with COPD.

Methods: The expression of proinflammatory cytokine and chemokine mRNA analyzed by real-time PCR. Reactive oxygen species (ROS) level determined by flow cytometry using DCF-DA staining. Cytometric bead-based assays were used to quantify inflammatory cytokines in the culture media and the plasma of healthy and COPD subjects. p-ERK and p-JNK expression were performed by western blot. Statistical analyses were performed using unpaired t-test at $P < 0.05$ with GraphPad Prism version.

Results: Our finding identified a positive relationship between the concentration of vanadium in urine and the expression of inflammatory factor (IL-8, MCP-1) in plasma of patients with COPD. Moreover, V₂O₅ induces IL-8, MCP-1, IP-10 and CXCL-11 mRNA expression and increase ROS production in BEAS-2B human bronchial epithelial cell. Treatment with N-acetylcysteine protects against V₂O₅-stimulated ROS production and down-regulation of IL-8, MCP-1, IP-10 and CXCL-11 mRNA expression in BEAS-2B cells. MAPK pathways are typically involved in inflammation. V₂O₅ treatment increase p-ERK and p-JNK expression in BEAS-2B stimulated with V₂O₅.

Conclusion: Our finding demonstrate that inflammatory response in patient with COPD is associated with vanadium, a usually component of particulate matter. And V₂O₅ induce excessive inflammation through activating MAPK mediated oxidative stress signalling in BEAS-2B human bronchial epithelial cell. These evidence show that vanadium and its oxidant may contribute to chronic inflammation in patient with COPD.

AP053

GENETIC ASSOCIATION OF RS2227589 POLYMORPHISM WITH PULMONARY EMBOLISM RISK IN CHINESE POPULATION

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Background and Aims: Genetic variants for gene SERPINC1 has been shown to be associated antithrombin III deficiency, which subsequently contributed to the susceptibility to venous thrombosis. However, several studies showed the conflicting results regarding the association of

SERPINC1 gene polymorphisms (rs2227589) with risk of thrombosis. The present study conducted a case-control study to further evaluate the association of the variant rs2227589 with antithrombin III deficiency and pulmonary embolism (PTE) risk in a Chinese population that has not been studied yet.

Methods: A case control study was performed on 101 patients and 199 healthy control. The allele frequency of SERPINC1 variant rs2227589 was analyzed by Sequenom assay. Active antithrombin III level was detected by an automatic coagulation analyser. A meta-analysis including 9 cohorts with 5419 venous thromboembolism (VTE) affected individuals and 8836 control subjects was performed.

Results: Total 27(26.7%) subjects were diagnosed with antithrombin III deficiency. Our results showed that antithrombin III plasma activities are slightly lower in the T allele carriers than that in C allele carriers, though it is not statistically significant. There was no significant correlation between rs2227589 genotype and antithrombin III plasma level. The recessive model showed that rs2227589 was significantly associated ($P = 0.026$) with an increased risk [OR:2.31, 95%CI (1.09–4.89)] of PTE. The meta-analysis showed that rs2227589 polymorphism was associated with an increased risk of VTE in the additive model [OR:1.10, 95% CI (1.02–1.20), $P = 0.01$] but not in the recessive model.

Conclusion: Our study demonstrated that variant rs2227589 is associated with increased risk of PTE in Chinese population but didn't showed any correlation with antithrombin III plasma level. Meta-analysis showed significant association between rs2227589 and VTE risk in the additive genetic model.

AP054

MITOCHONDRIAL MEMBRANE POTENTIAL IN CHILDREN WITH INTERSTITIAL LUNG DISEASES (ILD)

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Background and Aims: Pathogenetic basis of majority of interstitial lung diseases (ILD) in children is long-term inflammatory process characterized by cell respiration dysfunction. Cell level disorders of respiration are conducted with mitochondrial membrane potential ($\Delta\psi_m$) deviations. This study is aimed to determination of $\Delta\psi_m$ disturbance in children with ILD.

Methods: Seventy-seven children were evaluated (median age 9 ± 2 years). Sixty-six children had lung malformations (83%), eleven of them (17%) had ILD as an outcome of chronic/acute lung diseases.

$\Delta\psi_m$ was assessed by using flow cytometry analysis of cells stained with 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazole-carbocyanide iodine (JC-1, MitoScreen kit; BD Biosciences).

Results: Analyzing the $\Delta\psi_m$ parameters it was revealed that children with ILD had 1.7 times more lymphocytes with decreased $\Delta\psi_m$ than in control group ($52.5 \pm 15\%$ vs $31.1 \pm 8\%$ respectively, $P < 0.001$). It reveals of mitochondrial apoptosis pathway in children with chronic pathology. Cluster analysis was made. It divided children in three groups depends on $\Delta\psi_m$ level. First cluster includes children with approximately normal $\Delta\psi_m$ ($33.9 \pm 41\%$ lymphocytes with decreased $\Delta\psi_m$). Children in second cluster comparing to first one had 1.5 times more lymphocytes with decreased $\Delta\psi_m$. ($51.0 \pm 69\%$, $P < 0.05$). Rest 53.2% of children combined in third cluster that was characterized by low $\Delta\psi_m$ values. ($73.7 \pm 45\%$, $P < 0.05$). This level of $\Delta\psi_m$ can be used as a criterion of cell energetic deficit state in children with ILD because this group had the biggest number of children (68% of them) with 3–5 recurrences per year.

Conclusion: Mitochondrial membrane potential of lymphocytes decreasing indicates mitochondrial oxidation disorders. It reveals lack of

cell energetics sufficiency of lymphocytes in 53.2% of children with ILD even in remission. This data can be used as a criterion of cell energetic deficit state

AP055

INHIBITION OF NEUTROPHIL ELASTASE CONTRIBUTES TO ATTENUATION OF LIPOPOLYSACCHARIDE INDUCED ACUTE LUNG INJURY DURING NEUTROPENIA RECOVERY IN MICE

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Background and Aims: Patients in whom neutropenia recovery is complicated by pneumonia have an increased risk of acute lung injury (ALI) and detrimental outcomes. The aim of the present study was to investigate whether inhibition of neutrophil elastase (NE) is effective in lipopolysaccharide (LPS)-induced ALI during neutropenia recovery in a murine model, and whether it upregulates the activation of the MerTK signalling pathway.

Methods: Cyclophosphamide was given to mice to induce neutropenia. Seven days later, they were administered LPS by intratracheal instillation. Sivelestat, a neutrophil elastase inhibitor, was given by intraperitoneal injection once daily starting on day 0 and continuing until mice were sacrificed on day 5 (preventive group). Alternatively, sivelestat was given after, instead of before, LPS administration on day 2 (therapeutic group).

Results: Sivelestat attenuated the lung oedema and histopathological changes associated with LPS-induced lung injury. The accumulation of neutrophils and the concentrations of TNF- α , IL-6, and MPO in bronchoalveolar lavage (BAL) fluids were inhibited effectively by sivelestat. The expression of ICAM-1 and NF- κ B p65 was also reduced after sivelestat administration. The protein and gene expression of MerTK tended to increase with sivelestat treatment.

Conclusion: Sivelestat significantly attenuated LPS induced ALI during recovery from neutropenia, and this effect was associated with MerTK induction. These findings suggest that NE inhibition could be a promising means of alleviating lung inflammation without increasing susceptibility to infection in ALI/ARDS during neutropenia recovery.

Table 1 Results of BAL fluid analysis (10³/ml) in the five experimental groups

	Control	C + LPS	C + LPS + Pre-S (100 mg/kg)	C + LPS + Pre-S (200 mg/kg)	C + LPS + Post-S (100 mg/kg)
Total cells	4.82 $\pm$ 4.40	52.40 $\pm$ 32.82	15.98 $\pm$ 9.72*	14.62 $\pm$ 9.83*	15.98 $\pm$ 31.58*
Macrophages	3.83 $\pm$ 2.18	10.11 $\pm$ 5.43	7.14 $\pm$ 3.36	8.40 $\pm$ 5.55	5.56 $\pm$ 1.12
Lymphocytes	0.46 $\pm$ 0.54	1.26 $\pm$ 1.10	1.09 $\pm$ 0.53	1.03 $\pm$ 0.75	0.57 $\pm$ 0.68
Neutrophils	0.00 $\pm$ 0.00	36.63 $\pm$ 11.46	11.80 $\pm$ 5.97*	5.23 $\pm$ 5.19*	13.80 $\pm$ 16.37

Results are presented as the mean $\pm$ SD

C cyclophosphamide, LPS lipopolysaccharide, S sivelestat, Pre-S pretreatment with sivelestat, Post-S post-treatment with sivelestat

* $p < 0.05$ for C + LPS versus C + LPS + pre-S or post-S

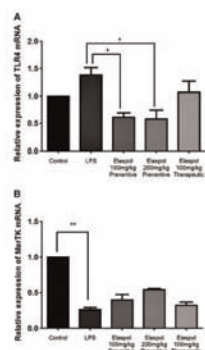


Fig. 2 Effects of sivelestat on mRNA expression of TLR4 and MerTK measured in lung tissues. a mRNA expression of TLR4 was increased by LPS and significantly reduced by sivelestat treatment. b mRNA expression of MerTK was significantly decreased by LPS and tended to increase with sivelestat treatment. LPS lipopolysaccharide, Pre-sivelestat pretreatment, Therapeutic sivelestat post-treatment. n = 5 in each group. (* $p < 0.05$, ** $p < 0.01$)

AP056

DUAL BRONCHODILATOR SUPPRESSES CIGARETTE SMOKE EXTRACT-INDUCED AUTOPHAGIC CELL DEATH IN HUMAN BRONCHIAL EPITHELIAL CELLS

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Background and Aims: Autophagy is a highly conserved self-degradative process which balance sources of energy in many physiological conditions. Chronic obstructive pulmonary disease (COPD) is a progressive life-threatening disease caused mainly by cigarette smoking. LABA/LAMA combination significantly ameliorate the decline in lung function in patient with COPD. Recently, several evidences suggest that increased autophagy contributes to COPD pathogenesis. Moreover, the effect of muscarinic receptor antagonists and β 2-agonists on regulating autophagy have been documented. We hypothesised that autophagy may be a potential novel target for dual bronchodilator treatment in an *in vitro* model that mimics COPD.

Methods: BEAS-2B human bronchial epithelial cells were pre-treated with olodaterol/tiotropium or indacaterol/glycopyrrolate followed by exposure to cigarette smoke extract for 6 h. Autophagy was determined by flow cytometry, acridine orange staining and western blot. MTT assay, Annexin V assay and propidium iodide staining were used to evaluate cell death, apoptosis and cell cycle arrest. Oxidative stress were performed by flow cytometry, DCFDA staining. Statistical analyses were performed using GraphPad Prism. P -values ≤ 0.05 were considered significant.

Results: Olodaterol/tiotropium or indacaterol/glycopyrrolate treatment decreased formation of AVO (lysosomes and autophagolysosomes), the ratio of LC3-II/LC3-I and Beclin1 expression without affecting apoptosis and cell cycle progression in BEAS-2B cells stimulated with CSE. Moreover, olodaterol/tiotropium and indacaterol/glycopyrrolate treatment reversed CSE-induced cell death, respectively. Oxidative stress is a major inducer of autophagy. In our finding, olodaterol/tiotropium and indacaterol/glycopyrrolate both decrease intracellular ROS level in BEAS-2B cells stimulated with CSE. In comparison, indacaterol/glycopyrrolate combination has a stronger inhibitory effect on autophagy and oxidative stress than olodaterol/tiotropium.

Conclusion: These data provide a novel evidence that dual bronchodilator retards bronchial epithelial cells death through regulating autophagy via inhibiting oxidative stress in BEAS-2B cells stimulated with CSE, which suggest that autophagy may be a potential novel mechanism of the action of dual bronchodilator treatment in COPD.

AP057

SPECIFIC SPHINGOSINE KINASE 1 INHIBITOR, SK-1-I ATTENUATES NEUTROPHIL ELASTASE INDUCED AIRWAY INFLAMMATION AND GOBLET CELL HYPERPLASIA IN MICE

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Background and Aims: Neutrophil elastase (NE) is known to cause airway inflammation and plays a pivotal role in pathogenesis of COPD. It has been reported that sphingolipid including sphingosine 1-phosphate (S1P) mediates both inflammation and apoptosis in various organs. As S1P is produced via activation of sphingosine kinase 1 (SphK1) and has

been reported to increase in sputum from COPD patients, we hypothesized that inhibiting SphK1 will decrease S1P synthesis and attenuates NE-induced airway inflammation.

Methods: Human NE (50 µg/mouse) or vehicle was administered intranasally into C57BL/6 mice on days 1, 4, and 7. To evaluate the effect of S1P on elastase-induced airway inflammation, sphingosine kinase 1 inhibitor (SK1-I) (5 mg/kg in PBS) was administered intranasally into C57BL/6 mice 1 h before NE administration. Bronchoalveolar lavage fluid (BALF) and lung sections were analyzed on day 11. We measured total cell counts and S1P secretion in BALF. We also evaluated the effect of SK1-I on airway inflammation and goblet cells by determining the Alcian blue/PAS-positive area in lung sections (evaluated by a semiautomatic imaging system, WinROOF® (Mitani corporation, Japan)).

Results: NE increased total cell number ($9.3 \pm .75 \times 10^{-4}$ vs $51.5 \pm 1.1 \times 10^{-4}$ per mL, $P < 0.01$) and neutrophil count ($0.0 \pm .04 \times 10^{-4}$ vs $34. \pm 2.7 \times 10^{-4}$ per mL, $P < 0.001$) in BALF, and induced airway goblet cell hyperplasia. NE also increased S1P secretion ($P < 0.05$) in BALF. Treatment with SK1-I inhibited NE-induced increase of total cell numbers ($13. \pm .73 \times 10^{-4}$ per mL, $P < 0.05$), neutrophil count ($2.6 \pm .28 \times 10^{-4}$ per mL, $P < 0.01$), and KC ($P < 0.01$) in BALF. SK1-I attenuated NE-induced goblet cell hyperplasia.

Conclusion: Inhibiting SphK1 caused significant reduction in NE-induced neutrophilic airway inflammation and goblet cell hyperplasia in mice. Our results suggest that the inhibition of S1P signalling could be a new therapeutic strategy for COPD.

AP058

TILIROSIDE CAN MODULATE UPPER AIRWAY SECRETION BY THE INHIBITION OF CALCIUM ACTIVATED CL^- CHANNEL, ANO1

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Background and Aims: Mucous cell hyperplasia and airway smooth muscle (ASM) hyperresponsiveness are hallmark features of inflammatory airway diseases, including asthma. Increasing evidence suggests that calcium-activated chloride channels (CaCCs) ANO1 play an important role in transepithelial transport and mucus overproduction in the airway epithelium. Recent data shows that ANO1 is increased in the airways of asthmatics, particularly in secretory cells and the treatment of inhibitor of ANO1 downregulates mucin secretion and methacholine-induced ASM contraction, two debilitating features of chronic asthma.

Flos Magnoliae (FM, Chinese name: Xin-yi) is an oriental medicinal herb commonly used for symptomatic relief of upper airway disease. In this study, we examined the effects of FM extract and its chemical constituents on the modulation of ANO1 channels to evaluate for use in therapeutic agents for treatment of asthma.

Methods: A 30% ethanolic extract of FM was prepared. Human ANO1 over-expressed HEK293T cells were treated with FM extract or its five chemical constituents. Modulation of ANO1 activity was measured by using a conventional whole-cell patch-clamp technique.

Results: We revealed that FM_{EtOH} (30, 100, and 300 µg/mL) and its chemical constituent tiliroside inhibited ANO1 activity in ANO1-overexpressing HEK293T cells. In addition, we showed that the treatment of airway epithelial cell line Calu-3 with interleukin-4 significantly increased ANO1 current (I_{ANO1}), but not cystic fibrosis transmembrane conductance regulator (CFTR)-mediated chloride current (I_{CFTR}). FMEtOH and tiliroside specifically modulated I_{ANO1} .

Conclusion: Our results suggest that FM extract and its chemical constituent, tiliroside, may have a therapeutic potential for respiratory inflammatory disease through modulating the activities of ANO1.

AP059

REGULATORY MECHANISMS OF SYSTEMIC INFLAMMATION IN RESPIRATORY PATHOLOGY

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Background and Aims: Chronic systemic inflammation is a pathogenetic mechanism underlying airway obstruction and most systemic manifestations in COPD and asthma. Chronic airway inflammation is regulated by a complex network of systemic mediators.

Aim: To establish the role of mediators of the immune, endocannabinoid, lipoxygenase and nitroxidergic systems in the regulation of inflammation in moderate and severe COPD and controlled asthma.

Methods: Flow cytometry, gas-liquid chromatography, enzyme immunoassay.

Results: A commonality of immune disorders in COPD and asthma has found. It has revealed that T helper (Th) immune response depending on the disease severity or the disease control is multi-type. The mixed phenotypes appear and it is followed by development Th17 type of immune response associated with the disease progression. The common mechanisms of maintenance of systemic inflammation also include a decrease in the expression of cannabinoid receptors type 2 (CB2), an increase in the synthesis of nitric oxide, a hyperproduction of cytotoxic eicosanoids that is a result of metabolic changes in fatty acids (FA), an imbalance between their pro- and antiinflammatory oxy derivatives. The substantial reorganization of FA composition of mitochondrial membrane is a sign of mitochondrial dysfunction determining the formation of the hypoxia. The endocannabinoid system and its receptors play a special role in the inflammation control. The increased CB2 expression contributes keeping the balance between pro- and antiinflammatory mediators under normal conditions. Inhibition of CB2 expression induces limiting the function of endocannabinoid system, which leads to the immune system activation. The correlation between the level of nitric oxide and the pathological process severity indicate that the dysfunction of nitroxidergic system make a contribution to the development of the respiratory diseases.

Conclusion: The obtained knowledge broadens our understanding of the etiopathogenesis of respiratory diseases and also can explain the key mechanisms of the development of extrapulmonary pathology induced by the chronic inflammatory process.

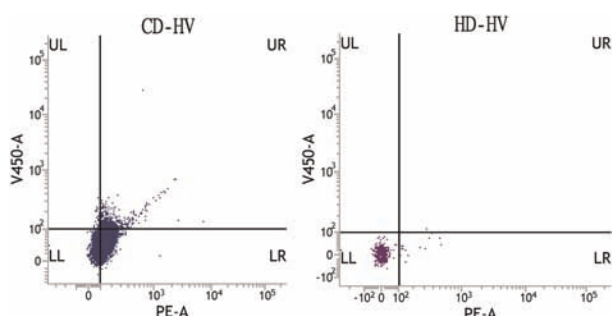
AP060

POLARIZATION OF ALVEOLAR MACROPHAGE IN MODEL OF DIET INDUCED OBESE MICE WITH VENTILATOR INDUCED LUNG INJURY

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Background and Aims: Ventilator induced lung injury (VILI) confers significant sequelae of mechanical ventilation in critical care, and lung protection strategy had been developed. However, the impact of obesity on ventilator induced lung injury is not fully understood. One recent search found fat-fed mice significantly attenuated ventilator-induced lung injury. Alveolar macrophages (AMs) is known to be pivotal in initiating acute lung injury. In the present study, we supposed that the obesity may affect the polarization of AMs and subsequent development of acute lung injury.



Methods: C57BL/6 mice were divided into two groups: control group with normal diet, and obese group fed with 60% high fat diet. All mice were intubated and mechanically ventilated for 6 h. Tidal volume was set at low tidal volume (~0.012 mL/gm) and high tidal volume (~0.024 mL/gm), respectively. Following it, bronchoalveolar lavage fluid (BALF) were collected and sent for analysis.

Results: Ventilator induced lung injury is attenuated in diet induced obese mice. Control group with VILI expressed more M1-polarization (F4/80+ CD11c+ CD206 – CD38+) and it's less expressed in diet-induced obesity (DIO) mice group.

Conclusion: Ventilator induced lung injury is attenuated in DIO mice, probably resulted from less M1-polarization of alveolar macrophages.

AP061

DEVELOPMENT OF A METHOD TO PREDICT THE PERSISTENT PULMONARY INFLAMMATION BY NANOPARTICLES AT AN EARLY STAGE WITH GENE EXPRESSION LEVEL

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Background and Aims: Previously, we reported that nanosized nickel oxide (NiO) and cerium oxide (CeO₂) induced persistent pulmonary inflammation of rat by intratracheal administration with histopathological analysis and BALF analysis including neutrophilic number and cytokine expressions but nanosized titanium dioxide (TiO₂) and zinc Oxide (ZnO) did not. This time, we performed microarray analysis with mRNA using rat lung tissue. The objective of this study is to identify new genes which is useful for evaluating persistent pulmonary inflammation induced by nanoparticles.

Methods: The nanosized NiO of 1.0 mg dispersed in distilled water (0.4 mL) were intratracheally administered to each 5 rats. Total RNA was purified from rat lung at 3 days, 1 week, 1 month after administration. The microarray analysis with mRNA was performed using mixed total RNA in the 5 rats administrated with 1.0 mg NiO after 1 month. Five mRNAs with increased expression were selected and expression levels of these genes in lung tissues on 3 days, 1 week, 1 month after administration of four kinds of nanoparticles (TiO₂, ZnO, CeO₂ and NiO) were quantified by real-time PCR. The average ratio between the administration group and the control group was determined for five genes, and the number of genes whose mRNA expression level increased 5-fold or more or 10-fold or more was determined.

Results: Among the five genes, the number of genes increased by 10 times or more after administration of 1 mg of TiO₂, ZnO, CeO₂ and NiO was 0, 0, 3 and 5 genes after 3 days, 0, 0, 4 and 5 genes after one week, 0, 0, 5 and 4 genes after 1 month, respectively.

Conclusion: It was suggested that persistent pulmonary inflammation by nanoparticles could be predicted within 1 month after intratracheal administration by analyzing the expression levels of five genes in the lung tissue.

DICHLOROACETATE, AN INHIBITOR OF AEROBIC GLYCOLYSIS, AMELIORATES NEUTROPHILIC AIRWAY INFLAMMATION THROUGH SUPPRESSING TH17 POPULATION AND INDUCING REGULATORY T CELL POPULATION

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Background and Aims: Neutrophilic airway inflammation is insensitive to steroids and is thereby considered as a substantial clinical problem. Recent advances in the field of immunometabolism support the concept that Th1, Th2, and Th17 cells utilize large amounts of glucose and exhibits increased aerobic glycolysis to meet their energetic and anabolic demands, whereas Treg cells primarily use fatty acid oxidation. Pyruvate dehydrogenase kinases (PDKs) are gate-keeping enzymes for regulating aerobic glycolysis and inhibition of PDKs can suppress the metabolic process. This study aimed to investigate the effect of dichloroacetate (DCA), a known PDK inhibitor, on neutrophilic airway inflammation.

Methods: Mouse model of neutrophil-dominated airway inflammation was used in this study to test the effect of DCA *in vivo*. Inflammatory cell infiltration in the lungs and goblet cell hyperplasia were determined using histological staining. Total and differential cell counts were evaluated in the bronchoalveolar lavage (BAL) and mRNA expression of cytokines in the lungs was analyzed by real-time PCR analysis. In addition, responses of T cell subsets in lymph nodes were detected by FACS analysis.

Results: Histological staining showed that treatment with DCA ameliorates inflammatory cell infiltration into lung tissue and goblet cell hyperplasia. BAL cells from DCA-treated mice showed less infiltration of total inflammatory cells and lower neutrophil and eosinophil counts compared with those in control mice. In addition, DCA significantly decreased mRNA expression of IL-4 and IL-17A in lung tissues of mice with neutrophilic asthma, whereas IFN-gamma expression was not changed. IL-10 expression was slightly increased by DCA treatment, although there was no statistical significance. Moreover, FACS analysis on lung-draining lymph nodes showed that DCA significantly decreased Th2 and Th17 populations and increased Treg population, whereas Th1 population was not affected.

Conclusion: In conclusion, these findings suggest that DCA ameliorates neutrophilic airway inflammation through suppressing Th17 population and inducing Treg population.

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AP062

PREVALENCE AND CLINICAL CHARACTERISTICS OF AIRWAY DISEASES IN PATIENTS WITH ULCERATIVE COLITIS

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Background and Aims: Ulcerative colitis (UC) is a systemic disease that may involve the lungs. Among pulmonary manifestations, airway diseases, such as bronchiolitis and bronchiectasis, have been reported to be the most frequent manifestations; however, little is known

about their prevalence and clinical characteristics. To clarify the prevalence and clinical characteristics of airway diseases associated with UC, we retrospectively assessed patients with UC and airway diseases at our hospital.

Methods: We reviewed chest images (chest X-ray and CT) of patients with UC admitted to our hospital between January 2011 and July 2016 and examined the presence of airway lesions (bronchiectasis or bronchiolitis). If bronchiectasis or bronchiolitis were detected in chest images, we reviewed the patients' medical records from admission to July 2017 in detail to examine patient's characteristics, clinical manifestations, treatments, and clinical course and exclude other diseases causing airway lesions.

Results: The study group comprised 277 women and 383 men with a mean age of 42.2 years; 14 patients had bronchiolitis and bronchiectasis with no known cause other than UC. Among the 14 patients, only eight exhibited respiratory tract symptoms. All eight patients complained of productive cough, seven of whom underwent total or sub-colectomy, and airway diseases developed within 1 year after colectomy in most patients. All eight patients were alive, and their pulmonary function was preserved. Three patients were treated with corticosteroid inhalation and macrolide, three with inhalation and oral corticosteroid, and two were refractory to oral corticosteroid and thus were treated with corticosteroid, oral corticosteroid, and tacrolimus.

Conclusion: The frequency of clinically significant airway diseases in UC was approximately 1%.

Almost all patients underwent colectomy, and airway diseases developed within 1 year after colectomy. In refractory cases, tacrolimus seems to be effective.

AP063

ANALYSIS OF ADVERSE REACTIONS AND RISK FACTORS TO SCIT IN CHILDREN WITH ALLERGIC

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Background and Aims: It's common that children with allergy received local adverse reactions after SCIT and their symptoms were light and easy to be relieved. To observe children with allergy who received adverse reactions after house dust mites specific subcutaneous immunotherapy (SCIT), and excavate the risk factors of adverse reactions, in order to provide more information for clinical practice of SCIT.

Methods: The clinical data was collected and retrospectively analyzed in child patients with allergy who received SCIT from December 2007 to July 2013 in Department of Pediatrics, First Affiliated Hospital of Guangzhou Medical University. We calculated the incidence of local and systemic adverse reactions, and made the analysis by using GAMMs to find the risk factors that may produce adverse reactions.

Results: Among 163 patients who received SCIT have 7870 injections. An average of 48.28 injections were received, with a minimum of 14 injections and a maximum of 67 injections. The incidence of local and systemic adverse reactions were 21.21% and 2.21% respectively. The clinical symptoms and signs of local adverse reactions mainly were local wheal, vaccinal areola, pruritus and induration which could alleviate by oneself; the clinical symptoms and signs of systemic adverse reactions was acute attack of asthma which could alleviate after spray treatment timely. The results of analysis showed that gender, month, weekly-

injection and dose were statistically significant ($P > 0.05$). These may be the risk factors of adverse reactions.

Conclusion: In our research, the incidence of systemic adverse reactions was low and the degree of systemic adverse reactions was mild and moderate. It may be severe so that we need to control closely. The risk factors of adverse reactions included female, September, 50 weekly-injection and the dose is over 75,000SQ.

AP064

ASIA PACIFIC SURVEY OF PHYSICIANS ON ASTHMA AND ALLERGIC RHINITIS (ASPAIR): DATA FOR THREE HYPOTHETICAL CASE STUDIES

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Background and Aims: The Asia-Pacific Survey of Physicians on Asthma and Allergic Rhinitis (ASPAIR) was undertaken to provide a better understanding on physicians' management and treatment of patients with coexistent asthma and allergic rhinitis (AR).

Methods: In this cross-sectional survey across six countries, 1204 physicians (general physicians and paediatricians) were interviewed using a structured questionnaire that included 3 hypothetical case studies to understand physicians' assessment practices, diagnosis and treatment of coexistent disease using practical examples. Results for the case studies are presented.

Results: In a case study of a 12-year-old boy with asthma, presenting with nasal and ocular symptoms of AR (Figure 1), the most common follow-up was assessment of both nasal and asthma symptoms. 75% of physicians diagnosed coexistent asthma and AR, and the most commonly prescribed treatment was inhaled corticosteroids (Figure 1). There was variation across countries in the diagnosis of this case with interviewed physicians in China, Malaysia and Thailand being more likely to diagnose coexistent disease (93%, 92% and 94% respectively), while physicians in the Philippines being less likely (35%), showing a higher tendency to diagnose one disease. Similar results were observed for the other case studies, which included a 32-year-old female with AR presenting with symptoms of wheeze and breathlessness on exertion, and a 25-year-old male with a history of atopy, presenting with breathlessness, wheezing, sneezing, nasal congestion, and watering of eyes.

Conclusion: These data suggest an under-diagnosis of coexistent asthma and AR in the Asia-Pacific region, but this varies across countries, with physicians interviewed in China, Malaysia and Thailand most likely to diagnose co-existent disease, and the Philippines least likely. Overall, inhaled corticosteroids are commonly utilized in patients with co-existent disease, while intranasal corticosteroids appear to be underutilized in this population.

Funding: GSK (206753)

Figure 1: Case study: Male, 12 years with asthma, on inhaled corticosteroids. Has symptoms of sneezing, nasal itchiness, watery eyes, affects his breathlessness

Q1: What follow-up would you do?	Q2: What is your diagnosis?	Q3: What is your preferred treatment?																																
<table><tr><th></th><th>Top Physician responses (mean (range))</th></tr><tr><td>History/frequency nasal symptoms:</td><td>69% (17%-91%)</td></tr><tr><td>History/frequency asthma symptoms:</td><td>68% (29%-89%)</td></tr><tr><td>History/frequency Eye symptoms:</td><td>43% (2%-84%)</td></tr><tr><td>Number/frequency exacerbations:</td><td>41% (1%-82%)</td></tr><tr><td>Family history allergic</td><td>41% (13%-78%)</td></tr></table>		Top Physician responses (mean (range))	History/frequency nasal symptoms:	69% (17%-91%)	History/frequency asthma symptoms:	68% (29%-89%)	History/frequency Eye symptoms:	43% (2%-84%)	Number/frequency exacerbations:	41% (1%-82%)	Family history allergic	41% (13%-78%)	<table><tr><th></th><th>Physician responses (mean (range))</th></tr><tr><td>Coexistent asthma and allergic rhinitis</td><td>75% (35%-94%)</td></tr><tr><td>Asthma</td><td>10% (2%-19%)</td></tr><tr><td>Allergic rhinitis</td><td>13% (1%-47%)</td></tr></table>		Physician responses (mean (range))	Coexistent asthma and allergic rhinitis	75% (35%-94%)	Asthma	10% (2%-19%)	Allergic rhinitis	13% (1%-47%)	<table><tr><th></th><th>Top Physician responses (mean (range))</th></tr><tr><td>Inhaled corticosteroids:</td><td>68% (44%-88%)</td></tr><tr><td>Oral antihistamines</td><td>45% (26%-69%)</td></tr><tr><td>Intranasal corticosteroids:</td><td>41% (0-76%)</td></tr><tr><td>LTBA</td><td>35% (6%-58%)</td></tr><tr><td>SABA</td><td>20% (5%-32%)</td></tr></table>		Top Physician responses (mean (range))	Inhaled corticosteroids:	68% (44%-88%)	Oral antihistamines	45% (26%-69%)	Intranasal corticosteroids:	41% (0-76%)	LTBA	35% (6%-58%)	SABA	20% (5%-32%)
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AP065

UNCONTROLLED BRONCHIAL ASTHMA: A RARE CASE OF CHURG-STRAUSS SYNDROME ARCHIE APOSTOL¹

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Background and Aims: A 69-year-old female, hypertensive and diabetic with maintenance medications was admitted to our hospital due to progressive infected skin lesions on both lower extremities. She had a history of recurrent hospital admissions due to episodes of cough and difficulty of breathing, managed as a case of bronchial asthma in acute exacerbation with salmeterol + fluticasone 250 mcg, 2 puffs BID as maintenance medication. Despite good compliance with inhaled medication, she still had bouts of difficulty of breathing and emergency room visits. The reason for recent admission was infected skin lesions on both lower extremities which started as pruritic, purplish, papular rashes distributed over the dorsa of both feet. On admission, skin punch biopsy with direct immunofluorescence study and Haematoxylin and Eosin staining (H & E) were done. Immunofluorescence study revealed negative for IgG, IgM, IgA and C3 but H and E staining result was consistent with vasculitis. Moreover, she was positive for p-ANCA which supported the working diagnosis of Eosinophilic Granulomatous Polyangiitis (EGPA), also known as Churg-Strauss Syndrome. Intravenous steroid was initiated which resulted to improvement of symptoms as well as resolution of the skin lesions. She was discharged improved and advised to take Azthioprine 50 mg/tab, 1 tablet bid and prednisone 10 mg/tab, 1 tab once a day.

AP066

ANALYSIS OF DISTRIBUTION CHARACTERISTICS OF TIGE AND SIGE IN PATIENTS WITH RESPIRATORY ALLERGIC DISEASES

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Background and Aims: To explore the distribution characteristics of serum total immunoglobulin E (tIgE) and specific immunoglobulin E (sIgE) in patients with respiratory allergic disease.

Methods: A total of 1129 patients with respiratory allergic disease were detected serum tIgE and sIgE by fluorescence enzyme-linked immunosorbent assay. The average age was 12 (7, 42.5) years old. SPSS 22.0 software was used for statistical analysis.

Results: The positive rate of tIgE of the patients enrolled in the study was 81.85%. As the age group grow up, the peak of tIgE positive rate appeared in 7-16 years old group, the positive rate was 94.33%. Then the positive rate decreased to 61.47% in ≥60 years old group. The average level of tIgE of male was higher than female [293.0(110.0,730.3) kU/L vs 184.0(69.0,468.0) kU/L]. The difference was statistically significant ($Z = -5.288$, $P < 0.001$). The major inhaled allergens of patients with respiratory allergic disease were Dermatophagoides farinae 84.43% (347/411), house dust mites 66.96% (756/1129) and tropical mites 63.10% (106/168) and the major food allergens were shrimp 27.12% (147/542), milk 26.23% (107/408) and egg white 22.11%(88/398). The sensitization peak of house dust mites, Dermatophagoides farinae, tropical mites, cat dander and dog dander appeared in 7-16 years old group, Aspergillus fumigatus appeared in ≥60 years old group. The correlation

between house dust mites and Dermatophagoides farinae was the highest in inhaled allergens ($r_s = 0.937$, $P < 0.001$), shrimp and crab was the highest in food allergens($r_s = 0.928$, $P < 0.001$), *Blatella germanica* and shrimp was the highest in inhaled and food allergens ($r_s = 0.881$, $P < 0.001$).

Conclusion: Adolescent stage is the sensitization peak of inhaled allergens in patients with respiratory allergic disease. In addition to the common inhaled allergens, the detection of mould fungi sIgE cannot be ignored for the elderly patients.

AP067

MAPPING MIMOTOPES FOR HOUSE DUST MITE ALLERGEN DER F 7 USING A SPECIFIC MONOCLONAL ANTIBODY

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Background and Aims: Mimotope mapping can be useful for identifying conformational epitopes of allergens, enabling future work for the development of diagnostic and therapeutic tools for allergies.

Methods: We previously cloned and expressed the recombinant group 7 allergen from the house dust mite Dermatophagoides farinae (Der f 7), a species that is a common cause of indoor allergy worldwide. Here, we performed mimotope mapping by probing a phage display library with specific monoclonal antibodies against recombinant Der f 7 to identify potential conformational epitopes of this allergen. Thirteen mimotopes were detected using 3 monoclonal antibodies generated from hybridoma cells.

Results: These mimotopes shared the common sequence —XX [LST]P[-E][L]MLPLR[-S]-. Further, potential conformational epitopes were identified at residues 1–7, 10, 27, 76–81, 92, and 130–133 of Der f 7, and key amino acids for these epitopes were deduced to be 2P, 3I, 10E, 27E, 78E, 79E, 81I, 130S, and 132E.

Conclusion: These sequences offer potential targeting sites for blocking antibodies that could provide immunotherapy for individuals with hypersensitivity to Der f 7.

Table 1- The amino acid sequences for positive clones

Monoclonal antibody	Random peptide sequences	Frequency	OD values in ELISA	Formula	Theoretical pI	GRAVY
5G11	FSYSPTAPLNM	1	1.061	C ₆₂ H ₈₄ N ₁₆ O ₁₅ S ₁	8.75	-0.375
	HIYYISELLPM	2	2.157-2.649	C ₆₄ H ₁₀₂ N ₁₆ O ₁₅ S ₁	5.24	0.500
	KYLPEILRPSS	1	0.403	C ₆₂ H ₁₀₂ N ₁₆ O ₁₅	8.59	-0.625
	KHLPEFMLPQLP	1	1.238	C ₆₃ H ₁₀₂ N ₁₆ O ₁₅ S ₁	6.75	-0.233
	SEWDQYLRLYLW	1	1.504	C ₆₁ H ₁₀₂ N ₁₆ O ₁₅	4.37	-0.733
5D10	SAKALPEILWPM	6	0.263-0.499	C ₆₄ H ₁₀₂ N ₁₆ O ₁₅ S ₁	5.72	0.442
	VSEKPMALDFKF	13	2.166-2.681	C ₇₀ H ₁₀₂ N ₁₆ O ₁₅ S ₁	8.56	0.533
	NQSFLPLDFPFR	2	1.109-1.151	C ₇₁ H ₁₀₂ N ₁₇ O ₁₅	5.84	-0.250
5G7	GHPDNLTLRSP	9	0.874-1.173	C ₇₂ H ₈₄ N ₁₆ O ₁₅	6.74	-0.642
	HMSHPMLALRST	3	1.106-1.202	C ₆₈ H ₈₂ N ₁₆ O ₁₅ S ₂	9.76	-0.133
	HKSPLMQPVRFP	1	1.274	C ₆₄ H ₁₀₂ N ₁₆ O ₁₅ S ₁	11.00	-0.667
	WTTPHAMALRS	1	1.198	C ₆₂ H ₈₂ N ₁₆ O ₁₅ S ₁	9.76	0.058
	DGTPHPMLALRS	1	1.128	C ₇₂ H ₈₂ N ₁₇ O ₁₅ S ₁	6.74	-0.417

Theoretical isoelectric point (pI), Grand average of hydropathicity (GRAVY), ProtParam

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AP068

THYMOMA (WORLD HEALTH ORGANIZATION TYPE B3) WITH NEUROENDOCRINE DIFFERENTIATION: A RARE TYPE OF THYMOMA

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Background and Aims: Thymomas are a common primary tumour of the anterior mediastinum, although they are rare (1.5 cases/million). Thymomas has long been confused with thymic carcinoid but has been regarded as a histologically distinct entity since 1972. Although thymic carcinomas often contain tumor cells having a neuroendocrine feature, thymomas with neuroendocrine features are extremely rare.

Methods: We present a case of a 66 year old female, Filipino who came in due to incidental finding of anterior mediastinal mass on chest-X-ray during annual check-up. Patient was asymptomatic and physical examination was unremarkable. CT of the Chest with contrast showed a lobulated soft tissue density enhancing mass in the superior anterior mediastinum, to consider thymoma. There was no enlarged mediastinal, hilar nor axillary lymph nodes noted.

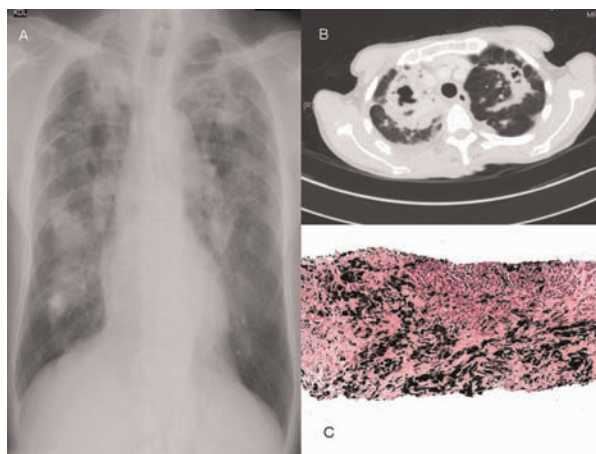
Results: Patient underwent resection of anterior mediastinal mass through VATS. Patient tolerated the procedure well and post-operative course was uneventful. Histopathology revealed undifferentiated neoplasm, consideration was thymoma vs squamous cell carcinoma of the thymus. CK19 which has 100% sensitivity for B3 thymoma was positive. Synaptophysin and chromogranin were likewise positive which demonstrates neuroendocrine differentiation. CK7, CK20 and S100 were negative. Histologically, there was no presence of neuroendocrine cells despite the positivity of chromogranin and synaptophysin. The pathologists final interpretation was Thymoma (WHO Type B3, Masaoka Stage I) with neuroendocrine differentiation.

There have been case reports of Thymoma with neuroendocrine differentiation combined with Multiple Endocrine Neoplasia Type 1 and hyperparathyroidism. Presently, this patient is asymptomatic and has not shown any signs and symptoms related to MEN1 nor any autoimmune disorder.

Conclusion: To date it is still unclear whether neuroendocrine differentiation is associated with increased malignancy in thymic epithelial tumours. Hence, long-term follow up in these patients is recommended (Chest CT scan every 6 months for 2 years then annually for 10 years).

Results: An elderly man, chronic smoker of 25-pack-year cigarette smoking history presented with cough productive of blackish sputum and weight loss for 1 month. Significant past medical history included partial gastrectomy for gastric carcinoma. Prior to his retirement, he had worked in a wood charcoal processing plant (in transport and packaging) and had daily exposure to charcoal dust for 14 years. On examination, he was cachexic but examination was otherwise unremarkable. Chest X-ray showed bilateral opacities; the computed tomography (CT) scan of the thorax revealed bilateral large geographic masses (the largest 2 showed cavitation), multiple solid nodules and emphysema (see Figure – Image A and B). Spirometry showed a moderate obstructive abnormality; forced expiratory volume in 1 second (FEV₁) was 0.97 L (50% predicted) and FEV₁/FVC ratio was 58%. CT-guided biopsy of the largest upper lobe cavitary lesion was performed to exclude malignancy. Histology revealed abundant anthracotic pigments and necrotizing granulomatous inflammation with no evidence of malignancy (see Figure – Image C). A diagnosis of pneumoconiosis with progressive massive fibrosis complicated by pulmonary tuberculosis was made. Further occupational history did not reveal exposure to any inorganic dust. His symptoms resolved and weight returned to baseline following anti-tuberculous therapy and smoking cessation. Radiology remained stable for two years on follow-up.

Conclusion: Chronic exposure to carbonaceous material other than mineral coal may result in similar radio-pathological appearance to coal-worker pneumoconiosis. In similar cases, detailed history taking to include occupational exposure to organic charcoal dust is recommended.



AP069

PNEUMOCONIOSIS FOLLOWING CHRONIC CHARCOAL DUST EXPOSURE: DESCRIPTION OF A RARE ASSOCIATION AND A CASE PRESENTATION

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Background and Aims: Pneumoconiosis can occur following long-term exposure to coal dust. Pneumoconiosis due to organic charcoal dust is rarely reported and has not been described in Singapore where primary industry is uncommon.

Methods: We describe a case of pneumoconiosis associated with chronic wood charcoal dust exposure.

AP070

QUANTIFYING MYELOID-DERIVED SUPPRESSOR CELLS IN PLEURAL EFFUSION CAN DISTINGUISH TUBERCULOSIS FROM PNEUMONIA

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Background and Aims: Tuberculous pleural effusion (TPE) is the second most common form of extrapulmonary tuberculosis (TB) and a common cause of pleural effusion in endemic tuberculous areas. However, it is still a difficult problem to make a precise and quick diagnosis of TPE from parapneumonic pleural effusion (PPE). In this study, we evaluated myeloid-derived suppressor cells (MDSC) in pleural fluid to distinguish TPE from PPE.

Methods: Patients diagnosed pleural effusion were enrolled from January 2016 to February 2018. We analyzed various immune cells including T, B, NK, and MDSC in pleural fluid and peripheral blood.

Results: The frequency of lymphocytes (T, B, NK cells) in pleural fluid were significantly higher in TPE than PPE. In contrast, the frequency of polymorphonuclear (PMN)-MDSC in pleural fluid were significantly lower in TPE compared to PPE. There was no significant difference of immune cells frequency in blood between TPE and PPE. An area under the ROC curve of 0.92 was obtained using PMN-MDSC frequency as the indicator for TPE identification. PMN-MDSC in PPE produced high level of reactive oxygen species and suppressed the production of interferon gamma from T cells after non-specific stimulation.

Conclusion: The levels of MDSCs in TPE were significantly lower than that in PPE. Therefore, the frequency of MDSCs in pleural fluid can be utilized to distinguish TPE from PPE.

AP071

SAFETY OF PRE-OPERATIVE PULMONARY FUNCTION TESTING IN LEFT MAIN CORONARY ARTERY DISEASE

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Background and Aims: Chronic obstructive pulmonary disease frequently coexists with ischemic heart disease, and is associated with poor post-operative outcomes after coronary artery bypass grafting (CABG). Therefore, pre-operative pulmonary function tests (PFTs) are recommended. ATS/ERS PFT guidelines list myocardial infarction (MI) within one month as a contraindication, but no safety data exist regarding PFTs in other potentially unstable cardiac conditions, such as left main coronary artery disease (LMCAD). We therefore studied the safety outcomes of pre-operative PFTs in patients with LMCAD.

Methods: A retrospective review of patients who had CABG for LMCAD ($\geq 50\%$ angiographic narrowing) or LMCA-Equivalent Disease (LMEQD, $\geq 70\%$ proximal left circumflex and proximal left coronary artery narrowing) was performed at our institution between July and December 2017. Patients who had PFTs (PFT group) were compared to those that did not (non-PFT group). Primary outcome was rate of MI or serious cardiac arrhythmia in the PFT group prior to surgery. Post-operative outcomes compared between the two groups were: days in the Intensive Care Unit (ICU), days on ventilator, pneumonia rates and total hospital length of stay. Data were analysed using paired *t*-test and Fisher's exact test.

Results: Forty-five patients underwent CABG for LMCAD/LMEQD; 18/45 (40%) were included in the PFT group. No patient had a MI or cardiac arrhythmia post PFTs. There was no significant difference between the PFT group and the non-PFT group for days in ICU (4.38 vs 4.0 days, $P = 0.22$), average time on ventilator (1.5 vs <1 days, $P = 1$), or pneumonia rates (16% vs 22%, $P = 0.72$). There was a trend towards shorter total length of stay in the PFT group (17.9 vs 24.4 days, $P = 0.07$).

Conclusion: In this small sample size of patients with LMCAD/LMEQD, PFTs do not appear to pose a risk of precipitating MI or arrhythmia, and are safe to perform prior to major cardiac surgery for this population.

AP072

APPLICATION OF NOCTURNAL OXYGEN THERAPY/BILEVEL POSITIVE AIRWAY PRESSURE (BIPAP) TO TREAT PATIENTS WITH CHRONIC LUNG DISEASE AND NOCTURNAL OXYGEN DESATURATION WHO REQUIRED HOSPITALIZATION

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Background and Aims: Long-term oxygen therapy (LTOT) is the only component of the management of chronic obstructive pulmonary disease (COPD) that improves survival in patients with severe daytime hypoxemia. Several studies have demonstrated deterioration in oxygen saturation during sleep in patients with COPD. The suggestion has been made that the natural progression of COPD to chronic pulmonary hypertension, severe hypoxemia, right heart failure, and death is dependent upon the severity of nocturnal desaturation. However to detect hypoxia in patients with respiratory diseases during hospitalization by using overnight pulse oximetry and apply correct home oxygen devices is still uncommon in Taiwan. We aimed to study the clinical efficacies of nocturnal oxygen or bilevel positive airway pressure (BiPAP) in patients with intermittent nocturnal hypoxia

Methods: Between June 2016- April 2018, 47 patients were screened during admission in Taiwan. Inclusion criteria were patients with COPD or other chronic lung diseases proved by series of chest images and pulmonary function tests. All of them had normal result of daytime oxygen saturation. A total 30 patient (63.8%) with intermittent nocturnal hypoxia noted at overnight pulse oximeters was included. Three patients with concomitant hypercapnia were assigned to receive nocturnal BiPAP, other 27 patients were assigned to receive nocturnal oxygen. Paired overnight pulse oximeter was performed before and after oxygen/BiPAP support.

Results: After oxygen/BiPAP supplement, basal SpO₂ increased from 90.3 to 96.5%, $P < 0.001$; total hypoxia (SpO₂<88%) duration decreased from 62.2 to 6.3 min, $P < 0.001$; hypoxia event decreased from 75.8 to 9.5, $P < 0.001$. None of these 30 patients readmitted within 14 days, 9 patients readmitted within 90 days.

Conclusion: It is feasible to apply overnight pulse oximetry to detect nocturnal oxygen desaturation in patient with chronic lung diseases and normal daytime oxygen saturation. Nocturnal oxygen/BiPAP may improve SpO₂, decrease hypoxic events and duration in patients with intermittent nocturnal hypoxia.

AP073

A CASE OF EMPYEMA CAUSED BY ESOPHAGOPLEURAL FISTULA SUCCESSFULLY TREATED WITH SELF-EXPANDABLE METALLIC STENT

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Background and Aims: Esophagopleural fistula (EPF) is a rare condition that is caused by several benign, malignant and idiopathic diseases.

Methods: We report an elderly patient with EPF secondary to oesophageal ulcer successfully treated with self-expandable oesophageal metallic stent.

Results: An 83-years-old woman was seen in our hospital because of high fever, dyspnea and decreased appetite. A chest X-ray and

computed tomography revealed the massive right pleural effusion and air bubbles in it. After she was hospitalized on the same day, we immediately started antimicrobial therapy and inserted chest drainage tube with a primary diagnosis of empyema. While in a chest drainage procedure, apparent food residue was found through the chest drainage tube. For this reason, we suspected EPF, and then we urgently performed upper esophagogastrroduodenoscopy. From endoscopic findings, surface at the lower oesophageal mucosa was ulcerous and irregular, suggesting highly suspicious of malignancy. In addition, large fistulous tract was also confirmed at the anal side. However, microscopic findings of mucosa did not reveal malignancy. Because of the inoperable case (patient with marginal cardiorespiratory function), we selected the endoscopic stent replacement by using the self-expandable metallic oesophageal stent to seal the fistula. 3 days after oesophageal stent was replaced, she recovered in a condition that was able to take food by mouth.

Conclusion: Here we report a case of empyema caused by EPF secondary to oesophageal ulcer. Oesophageal stenting is one of the considerable therapies for geriatric patients with cardiorespiratory complications.

AP074

INFECTED BULLOUS LUNG DISEASE

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Background:

Bullous lung disease is formation of contained pockets of air and fluid in one or more portions of the lungs. Most cases is caused by prolonged exposure to biomass fuel smoke and cigarette smoke. The natural history of bullous lung disease generally gradual progression of dyspnea and air-flow obstruction.

Aims: To share experience in managing patient who was diagnosed of infected bullous lung disease in Hospital Raja Perempuan Zainab 2.

Methods: Medical record review. All results were analyzed including the laboratory and radiographic findings.

Results: A 53-year-old man who was an active smoker, work as a bus driver presented with sudden onset shortness of breath associated with productive cough for one month, fever, lethargic and weight loss 10 kg. His physical examination revealed significant fever, tachypnea, tachycardia, and decreased breath sounds over the both lung field. Investigation revealed leukocytosis (16.8×10^9 cell/L) with predominant granulocytes and thrombocytosis (651×10^9 cell/L). No lymphadenopathy. CXR showed air fluid level with bilateral lung bullae. CT thorax done suggestive of infected, fluid filled bullae with largest bullae occupied the right lower lobe (size $9.9 \times 10.6 \times 15.4$ cm³). Chest drainage was inserted under CT guidance and pus drained 1000 mL. Sputum and pus culture were no significant growth and all tuberculosis work up also negative. He was given antibiotic for six weeks. Clinically he responded to the medical treatment.

Conclusion: Exposure to organic or inorganic dusts, industrial chemicals, and outdoor air pollution have all been postulated have greater risk for developing bullous lung disease but the most stronger association were cigarette and biomass fuel smoke exposure.

AP075

SKIN DEEP: A CASE OF DERMATOMYOSITIS INITIALLY PRESENTING WITH PLEURAL EFFUSION

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Background and Aims: Dermatomyositis is a rare autoimmune inflammatory process presenting with symmetric proximal muscle

weakness preceding or followed by skin lesions. We report a case of dermatomyositis initially presenting with pleural effusion before developing rashes and proximal muscle weakness.

Methods: A 46-year old female with no comorbidities presented with four weeks of anorexia described as having a metallic taste. No associated symptoms. Chest X-ray showed bilateral pleural effusion, exudative on thoracentesis. Pleural fluid analysis was negative for bacteria or malignant cells. Drainage of 1 L was done, followed by more than one week course of intravenous antibiotics. However, pleural effusion did not resolve.

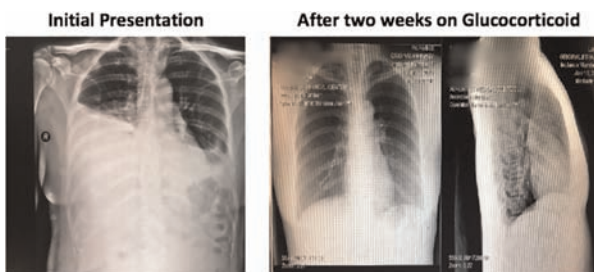
Upon shifting to oral antibiotics, patient developed pruritic maculopapular rashes over the face, neck and arms which progressed despite holding antibiotics and giving antihistamines. Glucocorticoid was started. After two weeks, proximal muscle weakness of all extremities developed with the presence of 'V-sign' and 'shawl sign'. A repeat X-ray showed clearing of the effusion with no interstitial findings. ANA was positive and CKMM level was markedly high. Other rheumatologic tests were unremarkable. Methotrexate and Glucocorticoid were then started, providing improvement of symptoms.

Results: Dermatomyositis commonly presents with rashes (100%) and proximal myopathy (95.2%). Interstitial Lung disease (ILD) may occur (28.6%) but pleural involvement is rare with only three reported cases and all were associated with ILD.

Dermatomyositis is confirmed using the Bohan and Peter Criteria and our patient qualified for a definite diagnosis.

Glucocorticoids and immunosuppressants are mainstay treatment. Pleural effusion involvement was observed to have good response to treatment, in contrast to ILD which was associated with higher mortality thus should be ruled out in patients with pleural effusion.

Conclusion: Autoimmune diseases are known for classical manifestations, but rarely mimic common diseases thus high index of suspicion is warranted to avoid delays in the management.



AP076

LONG UVULA: AN UNUSUAL CAUSE OF CHRONIC COUGH IN AN ADULT

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Background and Aims: Chronic cough, is a distressing symptom with significant impairment in quality of life. In evaluating chronic cough the need for a guideline based approach with a meticulous clinical assessment cannot be over emphasized.

We report a case of a long uvula as an unusual cause of chronic cough which may have been detected earlier had a thorough physical examination was performed, avoiding many expensive and potentially life threatening investigations.

Methods: A 27-year-old male presented with a history of chronic dry cough lasting for six months. There was no aetiological clues in the history such as chest pain, breathlessness, fever, weight loss or

haemoptysis. There were no triggers identified. No history of rhino sinusitis, post nasal drip or GERD. A nonsmoker and did not have any other environmental or occupational exposures. The initial clinical examination was unremarkable. However this had failed to examine the throat. He then underwent a series of investigations

Results: Blood count, inflammatory markers and sputum for AFB were negative. HRCT and Bronchoscopy were unremarkable.

While undergoing investigations, patient received therapeutic trials of steroids, bronchodilators, antihistamines, PPI, with no effect. A reevaluation examination revealed a long uvula touching the back of the throat and ENT team when consulted performed an uvulectomy which completely resolved the cough.

Conclusion: A long uvula as a cause of chronic cough is rarely encountered in literature and likely to be missed.

It can touch various structures in the upper airway, irritation leading to chronic cough.

Most of the reports regarding an elongated uvula causing chronic cough are from paediatric age group.

Management of the condition is surgical excision and is curative.

This case illustrates the importance of thorough clinical examination in diagnosing chronic unresolving symptoms. Unusual aetiologies need to be kept in mind and hunted for when usual common causes do not explain a condition.



AP077

PLEURA-CONTACT SIGN FOR PREDICTING INDETERMINATE LUNG NODULES IN PATIENTS WITHOUT CANCER HISTORY YU-PING CHANG^{1*}, YU-MU CHEN¹, CHIEN-HAO LAI¹, CHIUNG-YU LIN¹, MENG-CHIH LIN¹

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Background and Aims: Due to advances in chest computed tomography (CT) screening, more small lung nodules were detected. Nodule size, shape, ground-glass opacity (GGO) component was found associated with malignant potential. But whether nodule location affect malignant risk is unknown. Thus, our study aims to see if lung nodule location could be used to predict malignant potential.

Methods: Lung nodules less than 2 cm in size identified by chest CT from 2003/01/01 to 2016/12/31 were collected. In patients without cancer history, 144 nodules were collected and analyzed. All 144 nodules were

tissue-proved using wedge resection or lobectomy. Pleura-contact sign (PCS) was defined as peripheral lung nodule with contact to pleura.

Table 1. Pathology of lung nodules

Nodules < 1 cm in size			
Pathology	PCS positive	PCS negative	P=0.436
Benign lesion	13 (93%)	39 (85%)	
Malignant lesion	1 (7%)	7 (15%)	
Nodules 1-2cm in size			
Pathology	PCS positive	PCS negative	P=0.010
Benign lesion	25 (78%)	26 (50%)	
Malignant lesion	7 (22%)	26 (50%)	

Results: Of 144 nodules, 103 nodules were benign and 41 nodules were lung cancer. As in table 1, for 60 nodules less than 1 cm in size, 14 nodules were positive for PCS (13 benign lesion, 1 malignant lesion); 46 nodules were not pleura-contacted (39 benign lesion, 7 malignant lesion), and *P*-value was 0.436. For 84 nodules measured 1–2 cm in size, 32 nodules were pleura-contacted (25 benign lesion, 7 malignant lesion); 52 nodules were not (26 benign lesion, 26 malignant lesion), and *P*-value was 0.010.

Conclusion: Pleura-contact sign may predict benign origin for small nodules measured 1–2 cm in size found in patients without cancer history.

AP078

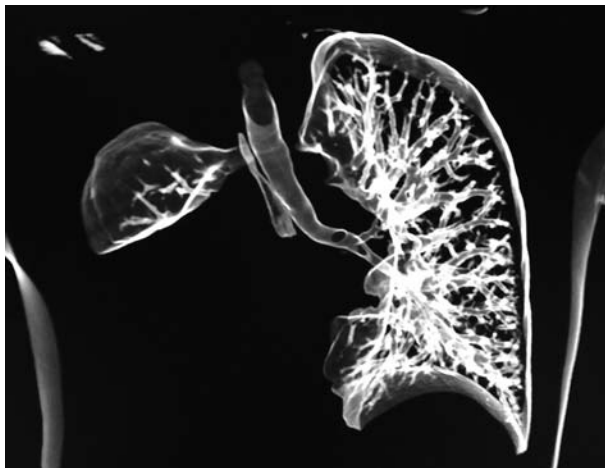
A RARE CASE OF ADOLESCENT IDIOPATHIC SCOLIOSIS WITH RIGHT LUNG AGENESIS IN A 16 YEAR OLD FEMALE JACOB VINIEGAS^{1*}

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Background and Aims: Lung agenesis is a rare congenital anomaly that develops during embryogenesis when there is a disruption of evolution of the primitive lung bud leading to complete absence of the lung, bronchi, and the main pulmonary artery. It may be associated with other anomalies, involving cardiovascular, skeletal, gastrointestinal and genitourinary system. Bilateral lung agenesis is incompatible with life while unilateral lung agenesis may be present to varying degrees of severity. The left lung is affected more frequently than the right, males predominate over females and the majority of cases exhibit other congenital abnormalities. Several older reports prove that other anomalies are more associated with right sided agenesis and persons with right sided agenesis mostly die within first year of their life, due to greater association of cardiac malformations and the risk of mediastinal shift.

Methods: A case report.

Results: A 16-year-old female was diagnosed with adolescent idiopathic scoliosis. On Chest X-ray showed lateral curvature to the right and atelectasis on the right lower lobe. The patient was admitted for surgical correction of the scoliosis. On CT scan of the spine, there was an incidental finding of an absence of the right main bronchus down to the right lung. The surgical procedure was rescheduled. Chest CT scan with contrast confirmed the absence of the right lung. The patient was admitted for the surgical procedure without complications.



Conclusion: The clinical presentation of patients with unilateral lung agenesis may vary. It is usually diagnosed in childhood, but patients with no associated anomalies and/or mild symptoms may survive into adulthood and live a normal life. Associated congenital anomalies, involving cardiovascular, skeletal, gastrointestinal and genitourinary system, should be suspected while working up these patients. Patients presenting for surgery require special anaesthetic considerations due to restrictive lung disease and potential pulmonary hypertension.

AP079

A CASE OF PULMONARY LANGERHANS CELL HISTIOCYTOSIS DEVELOPED AFTER COMPLETED ANTI-TUBERCULOSIS TREATMENT

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Background and Aims: Pulmonary Langerhans cell histiocytosis (PLCH) is an uncommon diffuse cystic lung disease related to clonal proliferation of dendritic cells and macrophages, and may affect other organs. However, the incipient radiological finding might be nodular lesion. The onset of PLCH is usually insidious, and the manifestations are nonspecific. PLCH mainly occurs to adults aged between 20 and 40 years, especially in cigarette smokers.

Methods: (Case Presentation) This 56-year-old male with 90 pack-years of smoking history presented with dyspnea for a week. The associated symptoms included productive cough, sneeze, and rhinorrhoea. There was no specific finding on physical examination and infection parameters. Pulmonary function test revealed obstructive pattern with negative bronchodilator test. Chest radiograph disclosed suspicious tumor in the left lung. Computed tomography (CT) showed an irregular non-enhanced lesion in the superior segment of left lower lobe, partial atelectasis of the right middle lobe, and bullae with paraseptal emphysema and varicose bronchiectasis in the left upper lung. The patient received video-assisted thoracoscopic surgery (VATS) wedge resection for tissue biopsy, and the pathology result of the tumor was granulomatous inflammation with caseous necrosis. The smear and nucleic acid amplification test for *Mycobacterium tuberculosis* complex of the tissue were also positive. He received a 6-month anti-tuberculous treatment. However, after the completed anti-tuberculous treatment, a newly developed nodular lesion in the right lower lung was noted on the follow-up CT. VATS segmentectomy revealed Langerhans cell histiocytosis.

Results: Smoking cessation was instructed. He received regular follow-up with inhaled dual bronchodilators and remained in stable condition for >6 months.

Conclusion: We present a case of PLCH developed in a patient with completely-treated tuberculosis to highlight the importance of regular image follow-up in patient who has received anti-tuberculous treatment.

AP080

COMPARISON OF TWO NONINVASIVE DEVICES FOR MEASURING RESPIRATORY RATES WITHOUT A FACEMASK DURING WALKING

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Background and Aims: Exercise increases the respiratory rate (RR) to meet the increased ventilator demand. RR is measured using a flowmeter attached to a facemask, which is accurate but potentially alters respiratory frequency. Recently, a new noninvasive and portable system for measuring RR using chest wall movement was developed. We investigated the validity of the system and compared its ability with that of the traditional impedance pneumography (IP) during walking.

Methods: RR data during the walking test were collected from 13 young healthy volunteers (five males). The test protocol included an initial phase of quiet standing (3 min) and a walking phase (6 min) at a belt speed of 2–7 km/h. The speed changed every 2 min by 2 km/h. The top speed was decided on the basis of the participant's demographic characteristics. The participants wore stretchable strain sensors (STRs) surrounding the upper ribcage (C-STRETCH-R, Bando Chemical Industries Ltd.) and thoracic impedance was measured using an IP (BSM-3562, Nihon Kohden). The root-mean-square difference (RMSD) from the standard flowmeter (FM) fixed on the participant's face mask (AE-310S, Minato Medical Science Co. Ltd.) was obtained as an accuracy measurement. A paired *t* test was used to compare the RMSD values of STR and IP.

Results: During quiet standing, the mean (SD) RMSD value was 1.1 (0.4) bpm with STR and 1.4 (0.6) bpm with IP. During walking, the mean (SD) RMSD value was 2.5 (1.2) bpm with STR and 4.4 (2.5) bpm with IP. No statistically significant difference in RMSD values was found between STR and IP during quiet standing ($P = 0.28$, Cohen's $d = 0.61$) and walking ($P = 0.13$, Cohen's $d = 1.02$).

Conclusion: The experiment demonstrated that STR and IP measurements had similar agreement with those obtained using FM during walking. Further studies should investigate their clinical validity in patients with respiratory diseases.

AP081

NUTRITIONAL STATUS ASSESSMENT OF PULMONARY OUTPATIENTS OF UNIVERSITY OF SANTO TOMAS HOSPITAL

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Background and Aims: Patients with pulmonary diseases such as pneumonia, tuberculosis, COPD, and asthma are vulnerable to nutritional deficiencies such as malnutrition and under nutrition. Malnutrition Universal Screening Tool is a tool that has shown its strength for application with adult patients across all health care settings. It is a five-step screening tool to identify patients who are malnourished and at risk of malnutrition.

Methods: A cross-sectional study design with the aid of the standardized questionnaire (MUST) in gathering important data on the nutritional status of pulmonary outpatients at University of Santo Tomas Hospital.

Results: Patients who belong to high risk comprised about 31.9%, medium risk 26.9% and low risk at 41.2%. There were about 32.6% of the patients with low risk had an infectious outcome. Among the medium risk, more patients (70.7%) had an infectious outcome. Further, medium risk patients were 7.4 times more likely to have an infectious outcome as compared to low risk (OR = 7.4). The relationship was significant (P -value = 0.000). There were about 32.6% of the low-risk patients with infectious outcomes while about 78.3% of the patients with high risk have infectious outcomes. Those with high risk are 5.0 times more likely to have an infectious outcome as compared to low risk (OR = 5.0). The relationship was significant (P -value = 0.000).

Conclusion: The relationship between risk stratification (Medium risk vs Low risk) and type of pulmonary out-patient (infectious vs non-infectious) is significant. The relationship between risk stratification (High risk vs Low risk) and type of pulmonary out-patient (infectious vs non-infectious) is significant.

AP082

EFFICACY AND SAFETY OF GLUCOCORTICOIDS IN THE TREATMENT OF SEVERE COMMUNITY-ACQUIRED PNEUMONIA: A META - ANALYSIS

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Background and Aims: The aim of the study is to evaluate the efficacy and safety of glucocorticoid in the treatment of severe community acquired pneumonia via meta-analysis.

Methods: Several databases including Chinese and English database such as PubMed, EMBASE, Cochrane Library, EBASO, Medline, Google Scholar, Science Dicit, CBM, CNKI and so on were searched for related studies published in English or Chinese up to January, 2018. Randomized controlled trials (RCTs) of corticosteroids in hospitalized adults with severe CAP were included. The inclusion and exclusion criteria were used to screen the literature which fulfil the requirement. In addition, we brought the Jadad scale into play to evaluate the quality of the inclusion literature, and extract data by means of the Cochrane system evaluation manual. Meta-analysis was performed by a random-effect model with RevMan 5.3 software.

Results: We included 10 RCTs enrolling 665 severe CAP patients. Compared with conventional treatment, adjunctive corticosteroids significantly reduced all-cause mortality (OR = 0.38, 95%CI:0.22–0.65, Z = 3.46, P = 0.005(<0.05)). In subgroup analysis by duration of corticosteroids, we found that prolonged and medium corticosteroids therapy significantly reduced all-cause mortality (OR = 0.44, 95%CI:0.24–0.82, Z = 2.58, P = 0.01), (RR = 0.35, 95% CI:0.36–0.76, Z = 2.66, P = 0.008). C-reactive protein after three days' therapy significantly reduced (MD = -59.58 mg/L, 95%CI:-88.1–-33.04, P < 0.0001) the risk of septic shock (OR = 0.19, 95% CI:0.10–0.36, P < 0.0001) and need for mechanical ventilation (OR = 0.33, 95%CI:0.21–0.52, P < 0.00001). Adjunctive corticosteroids exactly had no influence in gastrointestinal haemorrhage (OR = 0.80, 95%CI:0.23–2.83, P = 0.73) and super infection (OR = 2.62, 95%CI:0.92–7.48, P = 0.07).

Conclusion: 1. Compared with conventional treatment, our results suggested that adjunctive corticosteroids therapy decreased all-cause mortality in patients with severe CAP, and prolonged (5–9 days), medium corticosteroids treatment was more beneficial for severe CAP.

2. The study indicated that corticosteroids treatment was safe. The use of whole-body corticosteroids is not associated with the risk of super infection and upper gastrointestinal bleeding in the patients with severe community acquired pneumonia and reduced the risk of septic shock and the need for mechanical ventilation.

AP083

PULMONARY ANGIOSARCOMA MIMICKING PULMONARY EMBOLISM - A CASE REPORT

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Background and Aims: Angiosarcoma of the pulmonary artery is a rare type of malignant vascular tumor characterized by anaplastic cells arising from blood vessels that are rapidly proliferating and extensively infiltrating, hence tends to be aggressive.

Methods: A 36-year-old female presented as shortness of breath for 6 weeks associated with orthopnea and bipedal edema.

Results: CT Pulmonary Angiogram revealed pulmonary embolism, hence patient was given heparin drip and eventually shifted to factor XA inhibitor and discharged. Persistence of shortness of breath prompted readmission. A review of previous CT Pulmonary Angiogram showed a pulmonary artery mass. Patient underwent pulmonary endarterectomy and excision of the pulmonary artery mass, whose histopathologic findings, revealed pulmonary angiosarcoma.

Conclusion: The pulmonary artery angiosarcoma often mimicks the presentation of pulmonary embolism and a high index of suspicion is important in order to diagnose and manage this rare and highly aggressive disease. Thoracoscopy or open lung biopsy are the diagnostic methods but definitive diagnosis will involve histopathological and immunohistochemical findings. Management options include surgical resection, radiation, and chemotherapy, however, these tumours have a very poor prognosis.

AP084

USE OF ACE INHIBITOR AND RISK OF POST-STROKE PNEUMONIA: EVIDENCE-BASED STUDY

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Background and Aims: Post-stroke pneumonia is a complication of stroke with the highest mortality. The proposed pathophysiology of post-stroke pneumonia is aspiration due to dysphagia in stroke patients. One way to reduce the risk of post-stroke pneumonia is the use of ACE inhibitor, which stimulate cough reflex to prevent aspiration. In Indonesia, it is not yet known whether the use of ACE inhibitor in stroke patients reduce the risk of post-stroke pneumonia.

Methods: Articles were searched in four electronic databases: Pubmed, Proquest, EBSCOHost, and Scopus. Articles were selected based on the relevance to the clinical questions and met the inclusion and exclusion criteria. Two selected articles were appraised based on its validity, importance, and applicability, and according to Oxford Center of Evidence-Based Medicine 2011.

Results: Appraisals were made for two chosen articles; an RCT article and a meta-analysis article. RCT study conducted in 10 countries shows that ACE inhibitor given to stroke patients reduce the risk of post-stroke pneumonia. Meta-analysis study reviews four studies from Japan shows that ACE inhibitor given to the patients reduce the risk of post-stroke pneumonia.

In our patient's case, a 57 years old female has loss of consciousness, right-sided hemiparesis, and aphasia due to stroke. Patient has hypertension for 10 years and has been given captopril, one of ACE inhibitors drugs. After 10 days of treatment in the hospital, there were no sign of pneumonia, such as fever, cough, dyspnea, and rhonchi.

Conclusion: Although there are no research on the use of ACE inhibitors and the risk of post-stroke pneumonia in Indonesia, but due to the high prevalence of stroke, pneumonia, and post-stroke pneumonia in Indonesia, as well as the availability of ACE inhibitors in Indonesia, ACE inhibitors can be given to stroke patients to reduce the incidence of post-stroke pneumonia in Indonesia.

COPD 1

AP085

LIFE SPACE ACTIVITY IN THE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Physical inactivity is an important feature for COPD patients. To evaluate physical activity (PA), two major methods, that is, direct method and questionnaire are applicable. We evaluated physical activity in patients with COPD cross-sectionally and longitudinally using LSA (Life space assessment) score, which is one of questionnaires for PA. The aim of this study is to evaluate the factors which affect physical activity.

Methods: We enrolled 162 stable subjects from Kyoto University Hospital outpatient clinic. They took interview, pulmonary function test, and questionnaires such as mMRC, CAT, LSA, and PHQ9 (depression assessment). After one year, we performed same assessment again, to evaluate longitudinal changes of each index.

Results: Finally, 152 patients (male : female = 143 : 9, median age 71, median %FEV1 63.9) were analyzed cross-sectionally. LSA significantly correlated with age, %DLCO, mMRC, CAT, PHQ9 and weakly with %FRC ($P = 0.06$). And age, PHQ9 and CAT were significant determinants in multivariate analysis. In longitudinal analysis, LSA changes correlated with %FRC changes only.

Conclusion: Patients' physical activity is affected by symptoms and mental status, on the other hand, hyperinflation could be most important functional factor on changes of physical activity. In this point of view, deflation by pharmacological and/or non-pharmacological approach is important for maintain physical activity in COPD patients.

AP086

A HOME-BASED APPROACH TO BETTER BREATHING IN CANTERBURY - A PILOT STUDY

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Background and Aims: Despite the strong evidence behind pulmonary rehabilitation PR, the programme is still not well attended by people living with chronic respiratory illnesses. The need for a new PR approach was required. The home based programme was chosen as the alternative approach to be piloted and analysed for its effects.

Methods: Ten-week prospective interventional cohort study

The home based patients were given an information pack. The patients were instructed to do the exercises according to the "Move on up" DVD. Patients were asked to complete the walking diary, ideally on a daily basis for the duration of the programme. The patients were informed that there would be a weekly contact to maintain their motivation in the programme and answer any questions they came up during the programme.

Results: 21 participants were successfully recruited from the pool of previous participants who had withdrawn from the Canterbury PR service.

The control group was a random selection of 70 previous participants who had completed the centre based Canterbury PR.

The mean age for the home-based group was significantly younger than the control group by almost 6 years.

The home-based programme appeared more effective in reaching the New Zealand Māori community when compared to the control group.

The home-based programme performed equally well in achieving significant improvement in all of the outcome measures ($P < 0.05$).

Conclusion: This study has successfully demonstrated that home-based PR is an effective alternative to the gold standard centre-based PR when managing people living with COPD. Despite the fact that the home-based group participants were recruited from a harder to engage and more severe group, the home-based PR was an enabler to positive and significant improvements to the participants in all outcome measures.

The Demographic data and end of programme results

VARIABLE	HOME-BASED	CENTRE-BASED
Sample size	21	70
Gender		
Male	11 (52%)	24 (34%)
Female	10 (48%)	46 (66%)
Mean age in years	68.76	74.61
Ethnicity		
NZ European/Pākehā	15 (71%)	52 (74%)
NZ Māori	3 (14%)	3 (4%)
Other European	2 (10%)	2 (3%)
Pasifika	0	0
Asian	0	0
Other	1 (5%)	12 (17%)
Spirometry		
Mild (FEV1 > 80%)	0	2 (3%)
Moderate (50% < FEV1 < 80%)	5 (24%)	26 (37%)
Severe (30% < FEV1 < 50%)	11 (52%)	28 (40%)
Very Severe (FEV1 < 30%)	4 (19%)	14 (20%)
No FEV1 data	1 (5%)	0
CRQ (mean)		
Dyspnoea	14.2	15.8
Emotional Function	30.1	32.9
Mastery	18.7	19.1
Fatigue	13.7	15.8
HADS (mean)		
Anxiety	7.0	6.8
Depression	5.6	5.0
1MSTST (mean)	18.3	Did not perform
CAT score (mean)	19.7	Did not perform
EQ-5D (mean)		
Index	0.59	0.62
Visual analogue	5.85	6.67

AP087

POTENTIAL THERAPEUTIC STRATEGY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE USING PIOGLITAZONE AUGMENTED-WHARTON'S JELLY-DERIVED MESENCHYMAL STEM CELLS

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Background and Aims: A recent study reported that mesenchymal stem cells (MSC) indicate potential cellular therapeutic properties for chronic obstructive pulmonary disease (COPD), which is characterized by emphysema. We examined the potential therapeutic effect of Wharton's Jelly derived mesenchymal stem cells (WJMSCs) augmented with pre-treatment of pioglitazone on lung regeneration mouse emphysema models.

Methods: We used two mouse emphysema models, elastase-induced model and cigarette smoke-induced model. Into the mice, we intravenously injected WJMSCs (1×10^4 /mouse) pretreated with or without pioglitazone for 7 days. We measured the emphysema severity by mean linear intercepts (MLI) analysis using lung histology. We compared the mice treated with pioglitazone-augmented WJMSCs (pioWJMSCs) to the mice treated with none-augmented WJMSCs as well as to the control mice with no treatment of WJMSCs.

Results: Pioglitazone-augmented WJMSCs appeared more regeneration of lung emphysema than none-augmented WJMSCs in the two mouse emphysema models. In the elastase-induced emphysema model, the MLIs were $59.0 \pm .42 \mu\text{m}$ ($n = 6$), $72.8 \pm .87 \mu\text{m}$ ($n = 6$), for pioglitazone-augmented WJMSCs treated mice, and none-augmented WJMSCs treated mice, respectively ($P < 0.01$). Both pioglitazone-

augmented WJMSCs and none-augmented WJMSCs showed the regeneration effect in the cigarette smoke emphysema model. MLIs were $41.2 \pm .98$ ($n = 6$) for WJMSCs and $38.9 \pm .61$ μm ($n = 6$) for pioWJMSCs compared to the smoking control mice [$51.6 \pm .36$ μm ($n = 6$)]. The mean improvement of MLI appeared numerically better in pioglitazone-augmented WJMSCs than in none-augmented WJMSCs treated mice but did not reach statistical significance ($P = 0.0715$).

Conclusion: Pioglitazone-augmented WJMSCs may have an augmented effect of lung regeneration compared to the none-augmented WJMSCs in mouse emphysema model.

AP088

ASSOCIATION BETWEEN SELF-MANAGEMENT BEHAVIOURS OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND THE TYPES OF HEALTHCARE SERVICES: CROSS-SECTIONAL QUESTIONNAIRE STUDY
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Background and Aims: In Japan, self-management interventions for patients with chronic obstructive pulmonary disease (COPD) are provided in several healthcare settings such as outpatient clinics or home-care services. To consider appropriate interventions in each service, we examined associations between self-management behaviours of elderly patients with COPD and the types of healthcare services they received.

Methods: We conducted a cross-sectional questionnaire survey and medical record review of elderly patients with COPD who received care through an outpatient clinic (OC), outpatient rehabilitation (OR), or home-care rehabilitation/nursing (HC). We evaluated self-management behaviours using 34 originally developed items including strategies to minimize dyspnea, appropriate behaviours to maintain physical and mental health status, and communication with healthcare professionals or family members. Logistic regression analyses were performed to examine associations between self-management behaviours of the elderly patients and the three types of healthcare services.

Results: Data from 76 older adults (mean age: 78.0 years old) were analyzed: 12, 31, and 25 patients were in the OC, OR, and HC group, respectively. Participants in the HC group had the most severe COPD condition, followed by those in the OR and OC groups. 80–91% of the participants effectively practiced self-management behaviours for disease management (e.g., therapy adherence, smoking cessation), while 33–74% of the participants practiced regular exercise, prevention of infection, strategies to minimize dyspnea, and communication with healthcare professionals or family members. Participants in the OR and HC groups scored higher compared to those in the OC group, particularly for breathing to the rhythm of the movements, vaccination against influenza, stretching exercises, and muscle training, even after level of dyspnea and patient age were controlled.

Conclusion: This study suggests that interventions for breathing techniques and home exercise should be considered for those attending OC, and that interventions for patients with more severe conditions are needed for those receiving OR or HC.

DIAPHRAGMATIC CONTRACTION DURING HIGH-INTENSITY INSPIRATORY MUSCLE TRAINING IN COPD PATIENTS

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Background and Aims: High-intensity inspiratory muscle training (IMT) has been applied frequently to improve the inspiratory muscle strength of chronic obstructive pulmonary disease (COPD) patients. However, it remains unclear whether the diaphragm contracts during high-intensity IMT. The aim of this study was to compare the diaphragmatic contraction on ultrasound imaging among different loads of IMT in patients with stable COPD.

Methods: Ten outpatients with stable COPD (all men; mean age, 66 ± 6 years; BMI, 22.1 ± 2.8 kg/m²; FEV₁, $49.6 \pm 20.4\%$ predicted) were recruited. The participants underwent IMT at 0% (deep breathing), 20%, 40%, and 60% of maximal inspiratory mouth pressure (P_{Imax}) using the POWERbreathe KH2TM. Diaphragmatic contraction during IMT was assessed by B-mode ultrasound as the rate of change of diaphragm thickness (Tdi), which was measured in the zone of apposition that corresponded to the eighth of ninth right intercostal space at the anterior and middle axillary line. The rate of change of the Tdi ($\Delta\text{Tdi}\%$) between the thickness at the end of maximal inspiration and at rest was calculated. Repeated measures of analysis of variance and paired t-test adjusted by the Shaffer correction were performed to compare the $\Delta\text{Tdi}\%$ among the loads of IMT.

Results: The $\Delta\text{Tdi}\%$ during IMT was significantly lower at 60% P_{Imax} ($54.8 \pm 30.1\%$) than at 0% ($86.7 \pm 19.4\%$, $P < 0.001$); 20% ($92.3 \pm 23.2\%$, $P < 0.001$); and 40% of P_{Imax} ($87.5 \pm 30.5\%$, $P < 0.001$). There was no significant difference among the 0%, 20%, and 40% loads.

Conclusion: Our results suggested that efficacy of diaphragm contraction declined at high-intensity IMT in COPD patients. Moreover, ultrasound imaging was useful to assess the diaphragmatic contraction during IMT and to set the load of IMT.

AP090

CHRONIC KIDNEY DISEASE LEADS TO ADVERSE CARDIOVASCULAR EVENTS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS USING INHALED LONG-ACTING BRONCHODILATORS

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Background and Aims: Chronic kidney disease (CKD) has been identified as a common comorbidity of chronic obstructive pulmonary disease (COPD). The kidneys represent an elimination pathway for long-acting bronchodilators. However, the adverse effects with inhaled long-acting bronchodilators were not well documented among COPD patients with CKD.

Methods: The study enrolled spirometrically confirmed COPD patients received inhaled long-acting bronchodilators from 2015 to 2017. The estimated creatinine clearance rate (Ccr) was calculated using the Cockcroft-Gault formula, an estimated Ccr < 60 mL/min was defined as renal insufficiency. Medical records were reviewed and clinical data, including age, gender, smoking status, comorbidities, lung function stage, bronchodilator regimens, and treatment duration were analyzed. Major

adverse cardiovascular events occurring after long-acting bronchodilators inhalation were recorded.

Results: A total of 1487 COPD patients were included. 393 of them (26.4%) had CKD. The overall incidence of cardiovascular events was higher significantly in COPD patients with CKD compared to those without CKD when treated with inhaled long-acting bronchodilators (14.5% vs 4.7%, odds ratio [OR]: 3.47, $P < 0.001$). The corresponding rate of acute decompensated heart failure and acute myocardial infarction were significantly higher in COPD patients with CKD (7.6% vs 2.2%, OR: 3.53, $P < 0.001$; and 5.9% vs 2.0%, OR: 3.18, $P < 0.001$, respectively). Other clinical factors as age, gender, severity of lung function, treatment duration and types of medication were found to not be associated with cardiovascular events.

Conclusion: COPD patients with CKD could be associated with higher risk of adverse cardiovascular events while using inhaled long-acting bronchodilators. It is important to prescribe long-acting bronchodilators inhalation with greater awareness in COPD patients with preexisting renal disease.

AP091

A STUDY OF THE DETECTION OF ORAL BACTERIA IN COPD PATIENTS

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Background and Aims: Respiratory infection constitutes the most common cause of acute exacerbation among COPD patients and worsens prognosis of COPD, yet there are few studies that examined the effect of the increase of periodontal disease bacteria and the change of oral bacterial flora on respiratory infection. This research was conducted for the purpose of clarifying the oral conditions of COPD patients.

Methods: Subjects were 32 COPD patients who visited the Department of Respiratory Medicine in a university hospital in Fukuoka city from Feb 2017 to Jan 2018. Pulmonologists selected subjects in the research and explained its purpose to them verbally and in written form. We acquired basic information on subjects from their medical records, Detection of oral bacteria in COPD patients oral bacteria test, and self-administered questionnaires on oral health which were developed by authors. This research was conducted with approval of the Clinical Research Support Committee, Fukuoka University Hospital.

Results: Subjects were 27 males (84.4%) and 5 females (15.6%). The number of patients with stages I, II, III, and IV were 9 (28.1%), 18 (56.3%), 4 (12.5%), and 1 (3.1%). Twenty patients had used inhaled steroids (62.5%), whereas twelve patients (37.5%) had not. An oral bacteria test was performed among 27 patients, detecting nine samples of bacteria from eight patients. There were 5 *Candida albicans*, 1 *Candida glabrata*, 2 *K. pneumoniae*, and 1 *S. maltophilia*. Among them, six patients used inhaled steroids.

Conclusion: Gold recommended the use of bronchodilators and inhaled steroids for Stage II COPD treatment. Among 23 patients at Stages II, III, and IV, 17 patients (77.3%) used inhaled steroids. Among eight patients with bacteria, six patients used inhaled steroids, implying the necessity to check if they perform mouth care after inhalation. It is also necessary to examine if these bacteria become the cause of pneumonia.

THE TREND OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON INTENSIVE CARE UNIT ADMISSION FROM 2003 TO 2013 IN TAIWAN

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Background and Aims: To investigate the trend of chronic obstructive pulmonary disease (COPD) patients admitted in intensive care unit (ICU) in Taiwan from 2003 to 2013.

Methods: A retrospective study was conducted to analyze the registered database compiled by the National Health Insurance provided by the Department of Health, Taiwan.

We selected a national population admitted to ICU from 2003 to 2013. Patients older than 40 years with a COPD diagnosis were enrolled. The date of the ICU admission as the index date. The baseline of comorbidities was identified before the index date. Comorbidities included diabetes, hypertension, diabetes mellitus, coronary artery disease, stroke, dyslipidemia, cancer, and end-stage renal disease.

Results: We found that the number of COPD patients in ICU increased from 12,384 in 2003 to 13,308 in 2013 (P for trend $< .0001$). The mean age $\pm$ standard deviation from 2003 to 2013 was 76.66 ± 9.48 and 78.32 ± 10.59 years old, respectively. The percentage of COPD patients in ICU in age group ≥ 70 years old decreased markedly. The trend of COPD patients per 10,000 ICU patients was decreased in both male and female groups. The length of ICU stay and in-hospital mortality was increased from 2003 to 2013, with 21.58 to 23.14 days and 14.97% to 30.98%, respectively.

Conclusion: The number of COPD patients in ICU increased in Taiwan over past 11 years. The mean age, length of ICU stay, hospital mortality, and comorbidities were shown in a increased pattern. We use of a nationwide population-based database could provide sufficient sample size, generalizability, and statistical power to assess the COPD patients in ICU status in Taiwan.

AP093

CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH THORACIC CAGE REDUCTION UPON MOVEMENT LEADING TO LOW BACK PAIN AND LUMBER HYPEREXTENSION

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Background and Aims: This study aimed to clarify the relationship between thoracic cage disorder and spine curvature in individuals with chronic obstructive pulmonary disease (COPD), including the presence of low back pain.

Methods: The participants included 11 individuals with COPD (mean age, 72 years; mean body mass index, 22.5 kg/m²; FVC, 90.2%pred; and FEV₁, 56.1%pred). The difference in the circumference of inspiratory and expiratory rib cage was evaluated. Participants were divided into two groups: low- circumference change diameter rib cage group (stiff group) and normal rib cage group (control group); the cut-off value was 3.5 cm. The spine curvature was measured using the skin-surface device, spinal mouse[®], in standing, full flexion, and full extension positions.

Results: Lumbar extension angle significantly increased in the stiff group (median, 15.5° vs 7.0°; $P = 0.022$), and low back pain also frequently occurred.

Conclusion: Low back pain frequently occurred in COPD patients with stiff thoracic cage disorder, associated with hyperextension of the lumbar spine. In participants with decreased thoracic cage movement, lumbar extension has been thought to increase and is presumably involved in the occurrence of low back pain.

AP094

IDENTIFICATION OF KEY MODULES AND HUB GENES OF COPD PHENOTYPES WITH WEIGHTED GENE COEXPRESSION NETWORK ANALYSIS

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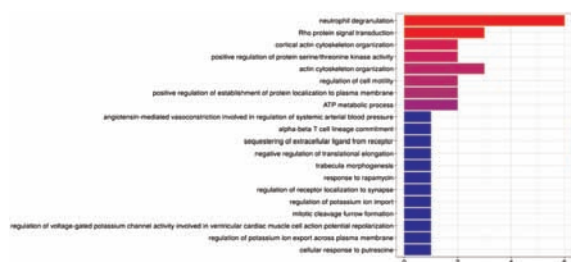
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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease with multiple molecular mechanisms. Gene expression studies in lung tissue of chronic obstructive pulmonary disease have provided biological insight and underscored possible mechanistic between bronchiolitis and emphysema in COPD.

Methods: This is a secondary study on microarray dataset (GSE69818) downloaded from Gene Expression Omnibus (GEO) at the National Center for Biotechnology Information (NCBI), which included 70 lung tissue samples of COPD. First, we contributed co-expression modules via weighted gene co-expression network analysis (WGCNA) and investigated the functional enrichment analysis of co-expression genes in terms of GO and KEGG. Subsequently, the correlation between the module eigengene and the external index was calculated. Lastly, Differential coexpression (DiffCoEx) was used to analyze the differential co-expression of genes between emphysema and bronchiolitis.

Results: Twelve co-expression modules were identified, containing 8150 differentially expressed genes identified from the 70 lung tissue samples. Functional enrichment analysis of the co-expression modules showed that the pink module, which has positive correlation with emphysema, GOLD4 and DLCO_S(DLCO<60%), enriched in progresses of neutrophil degranulation and Rho protein signal transduction. Five differential co-expression modules were determined using DiffCoEx, the genes in the turquoise module, which enriched in cilium assembly, cilium movement, proteolysis and apoptotic mitochondrial changes, were co-expressed in emphysema group, and the genes in blue and brown modules were co-expressed in bronchiolitis group. Green and yellow modules can be regarded as the same module in bronchiolitis group, but they are divided into two modules in emphysema group.

Conclusion: The study suggests that cilium assembly, cilium movement, proteolysis and apoptotic mitochondrial changes, neutrophil degranulation and RhoA/ROCK pathway may be involved in progression of emphysema.



BACTERIAL COLONIZATION DID NOT AFFECT THE DECLINE OF PULMONARY FUNCTION AMONG BRONCHIECTASIS PATIENTS

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Background and Aims: Bronchiectasis is a disorder characterized mainly by destruction of bronchial wall. Sometimes bronchiectasis patients demonstrate obstructive pulmonary function impairment. Although mechanism remains unclear, chronic inflammation induced by bacterial colonization may influence to impairment. To clarify whether or not bacterial colonization affected to decline pulmonary function, we investigated the relationship between bacterial colonization and pulmonary function test among bronchiectasis patients.

Methods: This is a single institute, retrospective study. Chest CT proven bronchiectasis patients whom done for repeated pulmonary function test were included. Clinical data such as 1) bacteria colonization, 2) pulmonary function test, especially forced expiratory volume in 1 second (FEV1), and 3) severity of bronchiectasis were analyzed.

Results: 28 patients, 7 male and 21 female, were included in this study. Female patients tended to show the severe decline of FEV1 rate (-119.5 mL/year in female vs -67.5 patients in male). In 29 patients *Pseudomonas aeruginosa* were detected in 13 patients, *Haemophilus influenzae*; 10, *Klebsiella pneumoniae*; 5, nontuberculous mycobacteria; 8, *Acinetobacter* spp.; 3. None of bacteria affects the decline rate of FEV1. Conversely, non-*P. aeruginosa* colonization groups demonstrated more severe pulmonary function impairment significantly compared to *P. aeruginosa* colonization groups. Macrolides were administered in 12 patients. Also macrolide use did not slow the decline rate of FEV1. Severity of bronchiectasis based on Bronchiectasis Radiologically Indexed CT score, also did not affect.

Conclusion: Bronchiectasis contributed to the decline of pulmonary function test, especially in Δ FEV1/year. In this study, bacterial colonization, macrolide use, and severity of bronchiectasis might not affect the decline of FEV1. Other factors for the impairment of pulmonary function should be investigated in future study.

AP096

LOW SOCIOECONOMIC STATUS AND INCIDENCE OF AIRWAY OBSTRUCTION IN KOREA: A COMMUNITY-BASED COHORT STUDY

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Background and Aims: Socioeconomic status (SES) is one of the most powerful determinants of health. There remains a limited understanding of the association between SES and chronic obstructive pulmonary disease (COPD). We examined the association between SES and COPD Incidence using data from community based cohort.

Methods: Data for 4 years from the Ansong-Ansan cohort were analyzed, and a total of 6,758 adults ≥ 40 years of age who underwent spirometry were enrolled in this study. Airway obstruction was defined as forced expiratory volume in 1 s/forced vital capacity ratio < 70%, and patients were classified by SES. Univariate and multivariate logistic regression were used to estimate odds ratios in relation to SES, age, gender and body mass index as possible confounders.

Results: In this study COPD prevalence was 8.4%. A total of 283 patients were newly diagnosed with COPD during follow-up. COPD was more frequent in LSES subjects compared with other higher SES subjects in both education and low household (6.0% vs 4.1% and 7.3% vs 3.5%). In the multivariate logistic regression analysis when adjusted for gender, age, smoking history and BMI, the lower educational level remained an independent risk factor for COPD (OR 1.440, 95% CI 1.005–2.064, $P = 0.047$).

Conclusion: In this analysis of community based cohort, lower education, lower household income, were associated with COPD incidence. Especially strong correlation with educational degree even after adjusting for other confounding factors including age, sex, BMI and smoking in LSES subjects.

AP097

PATIENTS WITH PULMONARY INFECTIONS AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A RETROSPECTIVE CLINICAL STUDY OF 170 CASES

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Background and Aims: Long-term smoking causes chronic obstructive pulmonary disease (COPD), the prevalence of which increases with aging. Conversely, most deaths due to pneumonia are reported in individuals aged >75 years. Thus, infection management plays a vital role in the prognosis of COPD. This study aimed to assess the impact of COPD with pulmonary infections on the prescience of prognosis and recurrence.

Methods: We retrospectively examined 170 patients with pneumonia-associated COPD and acute exacerbation at Izumi City General Hospital in 2016. Dyspnea was diagnosed as assessed using the Modified British Medical Research Council (mMRC) questionnaire. They were investigated with ex-prescription for COPD, hospitalization frequency, and sputum culture findings.

Results: We examined 170 patients (136 males and 34 females; mean age: 76.5 ± 9.9 years) comprising 111 patients with pneumonia-associated COPD and 59 with COPD acute exacerbation. From patients' sputum culture in both the groups, the five predominant bacterial species isolated were *Haemophilus influenzae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae*. In both the groups, *S. pneumoniae* did not exhibit any change in the mMRC score and hospitalization frequency; however, *H. influenzae*, *P. aeruginosa*, and *K. pneumoniae* exhibited mMRC score ≥ 2 . Both *P. aeruginosa* and *K. pneumoniae* exhibited higher hospitalization frequency in the pneumonia group but did not affect the hospitalization frequency in the acute exacerbation group. Furthermore, *M. catarrhalis* was detected in several cases of increased hospitalization and high mMRC scores.

Conclusion: This study suggests that *P. aeruginosa* and *K. pneumoniae* cause pulmonary functional disorder, and *M. Catarrhalis* could be associated with exacerbation frequency and pulmonary dysfunction. Hence, controlling these pathogenic bacteria can contribute to the improvement of COPD prognosis.

ACUPUNCTURE THERAPY FOR ACUTE EXACERBATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE:

A LITERATURE ANALYSIS OF CLINICAL STUDY

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Background and Aims: Acute Exacerbation of Chronic obstructive pulmonary disease (AECOPD), contributing strongly to the overall severity and burden of disease, is a major negative impact on hospital admission and death. Acupuncture therapy (AT) might result in clinically important improvements in quality of life and symptoms of COPD patients, however, many factors influencing the genuinely efficacy of AT. Therefore, this study aims to analyze the factors and rules of AT for AECOPD based on clinical research literature.

Methods: We searched the MEDLINE, clinical trials registers, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chongqing VIP and Wanfang Data from January 1990 to May 2017. The Literatures of AECOPD treated by AT were collected and analyzed by the information on the first author, year of publication, types and characteristics of AT.

Results: Twenty-six articles were included. Acupuncture was usually combined with western medicine, Chinese medicine, moxibustion, acupuncture sticking and auricular acupuncture. Sixteen articles involved three therapeutic methods, and ten articles with two therapeutic methods. Manual acupuncture (24 articles) was the most popular stimulus modality. Fifty acupoints were reported, and the frequency of Zusanli (ST36) (15 articles), Danzhong (CV17) (12 articles), Fenglong (ST40) (11 articles), Taixi (KL3) (11 articles) and Feishu (BL13) (11 articles) was more than 40%. The commonest needle retention time was 30 minutes (12 articles), followed by 20 minutes (4 articles). The major treatment frequency was once daily (17 articles), followed by once every other day (5 articles). Reinforcing and reducing method was reported in 15 articles, needling manipulation 7 articles, and needling response (de qi) 6 articles.

Conclusion: The results indicate that manual acupuncture is the major stimulus modality of AT for AECOPD. The acupoints selection, needle retention time and treatment frequency are the main factors, which should be described in detail.

AP099

PRODUCTION OF REACTIVE PERSULFIDE SPECIES IN LUNGS OF PATIENTS WITH COPD AND THEIR EFFECTS ON LUNG-RESIDENT CELLS

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Background and Aims: The mechanisms of the impaired antioxidant capacity in COPD remain unclear. Reactive persulfide species, such as glutathione persulfide (GSSH), cysteine persulfide (CysSSH) and glutathione trisulfide (GSSSH), are recently recognized, highly reactive and extremely powerful non-enzymatic antioxidants. By means of a novel liquid chromatography-tandem mass spectrometry analysis (LC-MS/MS), we recently reported a decrease in GSSH, CysSSH and GSSSH, in the

lung-resident cells and epithelial lining fluid obtained from COPD patients. Although glutathione (GSH) is believed to be the primary non-enzymatic antioxidant, it has not been fully elucidated how oxidative stress affects the intracellular amounts of persulfides and thiols in lung cells. It is unknown whether a persulfide donor provides protective effects against the oxidative stress-induced cellular injury and inflammation.

The aims of this study were the following: 1) To examine whether oxidative stress affects the amounts of reactive persulfides as well as those of GSH and cysteine (CysSH) in the lung-resident cells; 2) to investigate the effects of a persulfide donor on the oxidative stress-induced cellular injury and production of proinflammatory mediators.

Methods: After treatment with hydrogen peroxide (H_2O_2), the amounts of reactive persulfides in lung-resident cells were measured by LC-MS/MS. Cellular injury, the production of reactive oxygen species (ROS) and the release of proinflammatory mediators, such as interleukin-8 and matrix metalloproteinases, from lung-resident cells were measured after treatment with H_2O_2 with or without a persulfide donor pretreatment.

Results: Treatment with H_2O_2 significantly reduced the amounts of intracellular reactive persulfides (i.e., GSSH and CysSSH), whereas the amounts of glutathione and cysteine did not change. The persulfide donor significantly reduced the H_2O_2 -induced cellular injury, the production of ROS and release of proinflammatory mediators.

Conclusion: Reactive persulfides may act as primary non-enzymatic antioxidants in lung-resident cells, and a persulfide donor may have potential as a novel antioxidant and anti-inflammatory strategy.

AP100

SERIAL CHANGES IN EXERCISE CAPACITY, QUALITY OF LIFE AND CARDIOPULMONARY RESPONSES AFTER PULMONARY REHABILITATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Patients with chronic obstructive pulmonary disease (COPD) often have poor health-related quality of life (HRQL), exercise capacity and cardiopulmonary function. Pulmonary rehabilitation is beneficial to improve exercise capacity and HRQL after exercise training. However, changes in HRQL, exercise capacity and cardiopulmonary function during exercise training remain unclear. Here, we investigated serial changes in HRQL, exercise capacity and cardiopulmonary function during pulmonary rehabilitation.

Methods: Forty-three subjects with COPD were studied. All subjects participated in a 3-months, hospital-based outpatient pulmonary rehabilitation program with 2 sessions per week. Subjects were comprehensively evaluated at baseline and at 8, 16, and 24 sessions after pulmonary rehabilitation with spirometry, HRQL, cardiopulmonary exercise test, respiratory muscle strength, and dyspnea.

Results: Mean forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) in these subjects was $76.5\% \pm 22.3\%$, and the mean FEV1 was 1.03 ± 0.49 L/min, ($49.5 \pm 19.9\%$ of predicted). There were no significant changes in FEV1, FVC, and tidal volume after 24 sessions of pulmonary rehabilitation (all $P > 0.05$). After 8 sessions of pulmonary rehabilitation, there were significant improvements in the SGRQ-symptom domain, exertional dyspnea, and oxygen pulse (all $P < 0.05$). Maximal VO_2 , SGRQ-activity and SGRQ-impact domains, maximal inspiratory pressure, maximal expiratory pressure and mean blood pressure were significantly improved after 16 and 24 sessions of pulmonary rehabilitation (all $P < 0.05$).

Conclusion: Pulmonary rehabilitation results in significant improvements in exercise capacity, HRQL, and cardiopulmonary function in patients with COPD. Eight sessions of exercise training lead to improvement of symptoms and exertional dyspnea. Additional sessions lead to further improvement of symptoms and exertional dyspnea. In addition, 16 to 24 sessions further result in improvement of exercise capacity, activity, respiratory muscle strength and blood pressure. On the basis of our study findings, we suggest patients receive 16 to 24 sessions of pulmonary rehabilitation.

AP101

PDPI VERSION OF COPD SCREENING QUESTIONNAIRE VALIDITY AS A SCREENING TOOLS

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Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) has become a global health problem. Early detection is essential, highlighting the need for efficient measurement tools. Diagnosis of COPD using spirometry is quite difficult due to lack of facility, especially in primary health cares. Although the Indonesian Society of Respirology (ISR/PDPI) version of COPD screening questionnaire was developed as a screening tool, its validity remains unclear in population-based studies. This study was performed to determine the validity of the COPD screening questionnaire.

Methods: A descriptive analytical study using cross sectional approach and diagnostic test was performed to compare COPD screening questionnaire with spirometry test (gold standard). Persistent airflow obstruction (AO) was defined by post-bronchodilator FEV1 / FVC < 0.7 . The sensitivity and specificity of the COPD screening questionnaire score for identifying AO was assessed with logistic regression analysis.

Results: The five items of COPD screening questionnaire had a significant correlation with spirometry test results ($P < 0.05$). The best cut of points on the ROC curve based on the results of the diagnostic test was 4.5 points. At this point, the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio value, negative likelihood value and accuracy were 95.8%, 63.0%, 69.7%, 94.4%, 2.59, 0.066 and 78.4% respectively.

Conclusion: The PDPI version of COPD screening questionnaire appeared to be an adequate measurement for screening of possible airflow obstruction prior to spirometry test.

Tabel 1. Evaluation of cut of points PDPI COPD screening questionnaire

Cut Off	Diagnostic test					
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR
3.5	100,0%	56,3%	57,6%	100,0%	2,29	-
4.5	95,8%	63,0%	69,7%	94,4%	2,59	0.066

*PPV=positive prediction value, NPV= negative prediction value, PLR= positive likelihood ratio, NLR= negative likelihood ratio

AP102

EFFICACY AND SAFETY OF HIGH-DOSE BUDESONIDE/FORMOTEROL (320/9 µG) IN PATIENTS WITH BRONCHIOLITIS OBLITERANS SYNDROME AFTER ALLOGENEIC HSCT

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Background and Aims: Bronchiolitis obliterans syndrome (BOS) is a rare, progressive and irreversible airway disease associated with significant mortality after allogeneic hematopoietic stem-cell transplantation (HSCT). Combination treatment with budesonide/formoterol 160/4.5 µg, montelukast and *n*-acetylcysteine showed benefit with BOS patients in our previous study. In this study, we investigated the therapeutic effect of high-dose budesonide/formoterol 320/9 µg among patients who were diagnosed with BOS after allogeneic HSCT and who were already having treatment with budesonide/formoterol 160/4.5 µg.

Methods: Sixty-nine patients diagnosed BOS after an allogeneic HSCT who already had been treated with budesonide/formoterol 160/4.5 µg and increased the drug dose to 320/9 µg were enrolled in this study. Pulmonary function test (PFT) and COPD assessment test (CAT) were performed before and after changing of the drug dose. Efficacy was assessed within 3 months after increasing the drug dose; the primary variable was changes in forced expiratory volume in 1 second (FEV1) and CAT score. Safety was assessed as the incidence of pneumonia within 3 months after increasing the drug dose.

Results: After 3 months of high-dose budesonide/formoterol treatment (budesonide/formoterol 320/9 µg), mean FEV1 increased 29 mL (budesonide/formoterol 160/4.5 µg, 1.68 L vs budesonide/formoterol 320/9 µg, 1.71 L), $P = 0.468$. Mean CAT score also decreased from 17.8 to 17.5, ($P = 0.711$). In safety assessment, 7 patients got pneumonia within 3 months before budesonide/formoterol 320/9 µg treatment and 7 patients got pneumonia within 3 months after budesonide/formoterol 320/9 µg treatment and there was no significant difference between two groups.

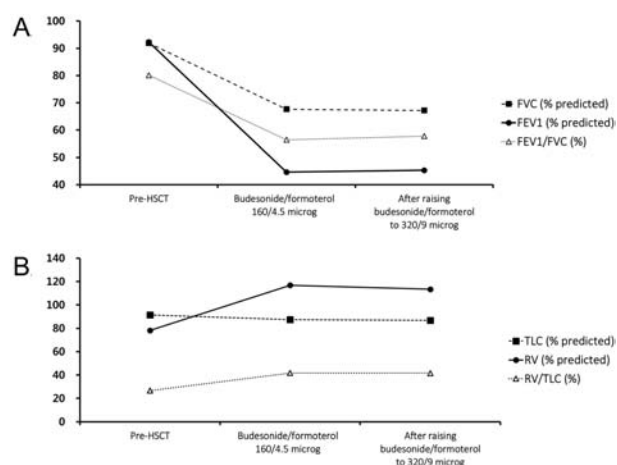


Fig. 1 Changes in pulmonary function 3 months after raising dose of combination therapy from 160/4.5 microg to 320/9 microg. **A.** After 3 months of combination treatment, FEV1 (% predicted) slightly increased, $p=0.468$. FEV1/FVC also increased after raising dose of combination therapy, but the results were not significant. **B.** RV (% predicted) slightly decreased after raising dose of combination therapy, whereas TLC (% predicted) did not change.

Conclusion: There were no significant differences between budesonide/formoterol 320/9 µg and budesonide/formoterol 160/4.5 µg treatment to pulmonary function and quality of life with diagnosed BOS patients after

allogeneic HSCT. And there was no significant difference in the incidence of pneumonia, indicating that there was no safety difference between two doses.

AP103

EFFECT OF DAI-KENCHU-TO ON COPD EXACERBATIONS IN ELDERLY PATIENTS: A RETROSPECTIVE STUDY USING A NATIONWIDE DATABASE IN JAPAN

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a common disease worldwide and is burdensome particularly in the elderly. The aim of this study was to evaluate the effect of dai-kenchu-to, a most prescribed traditional Japanese herbal Kampo medicine, on COPD exacerbations in elderly patients who were discharged after hospitalization for a COPD exacerbation. The primary outcome was COPD exacerbations requiring hospitalization or death. The secondary outcome was the frequency of COPD exacerbations, including exacerbations in the outpatient settings, per 30 days.

Methods: We used Japanese Diagnosis Procedure Combination Database (DPC) with outpatient's data. Using the covariates including age, sex, body mass index, Barthel index, comorbid diagnosis as well as treatments before and during initial hospitalization, propensity scores were calculated. Then 1-to-4 matching with propensity scores was conducted between patients whom dai-kenchu-to has been prescribed and whom dai-kenchu-to has not been prescribed. Log rank test was performed to compare the survival curves for hospitalization for COPD exacerbations or death. Poisson regression with generalized estimation equation was performed to compare the overall frequency of COPD exacerbations. A two tailed significance level of 0.05 was used in all statistical analysis.

Results: Before propensity score matching, number of patients in dai-kenchu-to group and in non-dai-kenchu-to group were 740 and 19,595, respectively. After 1-to-4 propensity score matching, number of patients in each group were 355 and 1,420. The log rank test comparing survival curves from the two groups did not show a statistically significant difference in propensity score matched patients. Incidence rate ratio of the frequency of COPD exacerbations per 30 days was 0.71 (95% confidence interval 0.54 – 0.94; $P = 0.018$) after propensity score matching.

Conclusion: Dai-kenchu-to may reduce overall frequency of COPD exacerbations but not severe exacerbations requiring hospitalization.

AP104

CORRELATION BETWEEN RESPIRATORY CAPACITY, BODY MASS INDEX, SIX-MINUTES WALKING TEST, RESTING HEART RATE AND SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity-mortality worldwide. COPD not

only in pulmonary damage but also to multi-systemic impairment with repercussions on skeletal muscles and the ability to undertake effort. Pulmonologist using the guidelines of diagnosis and classification criteria in GOLD 2014 which used six minutes walking test, body mass index, the degree of obstruction and the risk of exacerbation. However, the assessment of patients with COPD in early stage is very difficult because of physical limitations, the degree of obstruction and the functional capacity to its current status only slightly below normal. In addition, the advanced stages of COPD patients also have many other co-morbid. Most of them is cardiovascular disease which can affects the measurement of several parameters

Methods: Cross-sectional study

Results: Analysis of 30 patients tested with four parameters were cross sectional study (α : 0.05) with various analysis shows there is a correlation between inspiratory capacity ($P < 0.001$), six minutes walking test ($P < 0.002$), body mass index ($P < 0.012$) and the severity of COPD in a negative prognostic value. There was no correlation between resting heart rate and the severity of COPD

Conclusion: Six minutes walking test, inspiratory capacity and the body mass index were correlated with severity of COPD. Parameters that have the strongest correlation with the severity of COPD is inspiratory capacity.

AP105

SAM PROTECTS AGAINST AUTOIMMUNE EMPHYSEMA OF RATS

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Background and Aims: Our previous study showed that perforin regulatory elements were hypomethylated in T cells from rats with autoimmune emphysema. This study aimed at investigating the protective effects of S-adenosylmethionine (SAM), methyl donor in the development of autoimmune emphysema.

Methods: Thirty SD rats were randomly divided into three groups: normal control group ($n = 10$), autoimmune emphysema group (model group, $n = 10$) and SAM intervention group (intervention group, $n = 10$). The autoimmune emphysema group was treated with intraperitoneal injection of human umbilical vein endothelial cells plus complete Freund's adjuvant. SAM intervention group was treated with intraperitoneal injection of human umbilical vein endothelial cells, complete Freund's adjuvant and SAM, while the normal control group only with equal volume of liquid and complete Freund's adjuvant. Twenty-one days later, the lung tissue sections were stained with haematoxylin and eosin (HE) to observe the morphological changes. Mean liner interval (MLI) and mean alveolar number (MAN) were quantitatively measured. The left lung was subjected to alveolar lavage to prepare BALF. The levels of mean methylation of perforin regulatory elements in T cells, TNF- α , IL-8, MMP-9, anti-vascular endothelial cell antibody (AECA), Malondialdehyde Content (MDA), superoxide dismutase (SOD), activities of glutathione catalase (GSH-Px), and the glutathione (GSH) were investigated.

Results: The MLI in model group was higher than that in normal control group, while MAN was decreased (all $P < 0.05$). Compared with model group, MLI in intervention group was decreased, MAN increased (all $P < 0.05$). The levels of TNF- α , AECA and MAD in BALF in intervention group were lower than those in model group while GSH, SOD, GSH-Px were higher on the contrary (all $P < 0.05$).

Conclusion: SAM may protects against autoimmune emphysema of rats by increasing levels of perforin regulatory elements methylation in T cells and GSH, SOD, and GSH-Px and decreasing the levels of TNF- α , AECA and MAD.

RISK FACTORS FOR THE ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation. Acute exacerbation of COPD (AECOPD) is an important event that threatens patient quality of life and worsens prognosis. We aimed to investigate the characteristics of COPD patients and risk factors for AECOPD.

Methods: We retrospectively analyzed COPD patients who visited our hospital from 2014 to 2016. AECOPD was defined as an episode requiring treatment with oral corticosteroid and/or antibiotics, or a visit to the emergency room, or hospitalization.

Results: We enrolled 216 patients (186 men, median age: 74 years, 27 current smokers, 175 ex-smokers) in this study, of whom 45 were complicated by bronchial asthma. Severity of airflow limitation was staged according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria as follows: stage 1, 28 patients; stage 2, 111 patients; stage 3, 50 patients; and stage 4, 27 patients. During the study period, 91 patients suffered AECOPD. A multivariate Cox proportional hazard model showed that having an episode of AECOPD within the past year (hazard ratio [95% confidence interval] = 2.510 [1.630–3.865], $P < 0.001$), GOLD classification of 3/4 (2.367 [1.545–3.627], $P < 0.001$), using inhaled corticosteroids (1.627 [1.027–2.576], $P = 0.038$), using oral glucocorticoids (2.874 [1.013–8.151], $P = 0.047$), and the presence of bronchial asthma (1.677 [1.001–2.807], $P = 0.049$) were risk factors for AECOPD.

Conclusion: These results suggested that having an episode of AECOPD within the past year, severe airflow limitation, using inhaled corticosteroids or oral glucocorticoids and the presence of bronchial asthma may be risk factors for AECOPD. Prevention of exacerbations and appropriate treatment are highly desirable for patients with these risk factors.

AP107

PROGNOSTIC UTILITY OF THE DECAF SCORE TO PREDICT IN-HOSPITAL MORTALITY AMONG PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ADMITTED AT CHINESE GENERAL HOSPITAL

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality. The DECAF score, consisting of the dyspnea score, eosinopenia, consolidation, acidemia and atrial fibrillation, is a simple clinical prediction tool that can stratify patients hospitalized with acute exacerbation of COPD (AECOPD) into clinically relevant risk categories. This study aims to determine the prognostic value of the DECAF score in predicting mortality among patients with AECOPD at the Chinese General Hospital and Medical Center.

Methods: This is a prospective cohort study among COPD in exacerbation patients admitted at Chinese General Hospital. Laboratory and imaging test included complete blood count, chest X-ray, arterial blood gas, and ECG. Stable-state dyspnea was assessed using the extended Medical Research Council Dyspnoea (eMRCd) Score. The DECAF Score were recorded on admission and risk stratification was done following the scoring system. Performance of the tool was assessed by measuring the area under the ROC curve (AUROC). A 95% confidence level was considered significant.

Results: A total of 77 patients were included in this study, 68 (88.3%) male and 9 (11.7%) female. The mean age is 72.5 and mean smoking

history in pack years is 39.5. Fifty two (67.5%) patients were classified as low risk, 14 (18.2%) as intermediate risk, and 11 (14.3%) as high risk. The mean days of hospital stay is 10.4. 72 patients (93.5%) were discharged improved, and 5 (6.5%) patients died. Those who died had a DECAF score >2, showing a statistically significant relationship between DECAF score and mortality ($P = .00002$). A DECAF Score (>2) has 100% sensitivity, 91.67% specificity, AUC of 0.958, PPV is 45.46 and NPV of 100.00.

Conclusion: The DECAF Score which incorporates indices routinely available at the time of hospital admission, is an effective clinical tool that can risk stratify and predict mortality in patients hospitalized with an exacerbation of COPD.

AP108

QUALITY OF LIFE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE BASED ON CLINICAL PHENOTYPES

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Background and Aims: Spanish chronic obstructive pulmonary disease (COPD) guideline classifies COPD into 4 clinical phenotypes: non-exacerbator (A), asthma-COPD overlap (B), exacerbator with emphysema (C) and exacerbator with bronchitis (D).

Methods: A cross-sectional study of quality of life (QOL) based on COPD phenotypes utilizing St George's Respiratory Questionnaire (SGRQ-c) conducted in University Malaya Medical Center from 1 June 2017 – 31 May 2018.

Table 1. Demographic, clinical characteristic and SGRQ-c score according to clinical phenotypes.

Characteristics	COPD Phenotypes (n, %)				*p value
	A 54 (28.6)	B 25 (13.2)	C 35 (18.5)	D 75 (39.7)	
Age (years)	74.1±8.1	70.0±13.1	72.7±8.7	70.7±9.2	0.151
Gender (n, %)					0.986
Male	50 (92.6)	23 (92.0)	32 (91.4)	70 (93.3%)	
Female	4 (7.4)	2 (8.0)	3 (8.6)	5 (6.7%)	
Ethnic (n, %)					0.734
Malay	19 (35.2)	10 (40.0)	12 (34.3)	32 (42.7)	
Chinese	27 (50.0)	9 (36.0)	18 (51.4)	30 (40.0)	
Indian	8 (14.8)	6 (24.0)	5 (14.3)	13 (17.3)	
Smoking status (n, %)					0.333
Current	16 (29.6)	11 (44.0)	16 (45.7)	21 (28.0)	
Previous	38 (70.4)	14 (56.0)	19 (54.3)	54 (72.0)	
MMRC (n, %)					0.003
0-1	23 (42.6)	8 (32.0)	16 (45.7)	12 (16.0)	
2-4	31 (57.4)	17 (68.0)	19 (54.3)	63 (84.0)	
GOLD class (n, %)					0.001
1-2	33 (61.1)	15 (60.0)	16 (45.7)	29 (38.7)	
3-4	21 (38.9)	10 (40.0)	19 (54.3)	46 (61.3)	
SGRQ-c score					
Symptoms	36.8±19.9	59.2±25.1	43.3±23.6	61.7±20.4	<0.001
Activities	48.9±32.5	58.0±34.6	56.8±27.8	70.5±25.1	0.001
Impact	40.9±20.1	44.8±32.1	36.9±24.8	56.0±27.2	0.001
Total	42.6±20.1	51.5±25.9	44.0±21.4	61.5±20.9	<0.001

*Chi-square for categorical variables; ANOVA test for means of continuous variables.

Results: Of 220 patients, 189 patients with post bronchodilator force expiratory volume in 1 second (FEV1)/force vital capacity (FVC) of <0.70 were recruited. Their demographic, clinical characteristics and SGRQ-c score are as shown in Table 1. Patients with phenotype C and D had poorer modified medical research center (MMRC) performance status and global initiative for COPD (GOLD) class based on FEV1. Nevertheless, only patients with phenotype D had significant higher total SGRQ-c score than others. They also scored significant higher in sub-components of COPD symptoms, activities and impacts. Patients with phenotypes B had numerically higher SGRQ-c total and symptoms score than those with phenotype A and C. The total and sub-components SGRQ-c score of patients with phenotype A and C were almost similar.

Conclusion: Patients with phenotype D had poorest QOL, followed by phenotype B. These groups of patients need additional medical attention, in terms of pharmacology treatment, physiotherapy and rehabilitation.

AP109

BUFEI YISHEN GRANULES SUPPRESS ALVEOLAR EPITHELIAL APOPTOSIS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE RATS: VIA PERK/EIF2 α SIGNALING

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Background and Aims: The present study was initiated to explore the effect of Bufei Yishen granules (BY) against alveolar epithelial apoptosis via regulating by PERK/eIF2 α signalling in chronic obstructive pulmonary disease (COPD) rat model.

Methods: Rats were randomized into Control, Model, BY, and aminophylline (APL) groups. COPD rats were induced by cigarette-smoke and bacterial exposures (weeks 1–8), and were administrated with normal saline, BY granules or aminophylline from week 9 to 16. Pulmonary function (VT, PEF) was measured every 4 weeks. Lung tissue histology and ultrastructure, alveolar epithelial apoptosis index, PERK, eIF2 α , bcl-2 and Bad mRNA as well as protein expressions of PERK, eIF2 α , p-PERK, p-eIF2 α in lung tissues were measured.

Results: VT, PEF decreased from week 8 in COPD rats ($P < 0.05$). Compared with Model group, VT, PEF were higher in BY groups at week 16, while only VT was higher in APL group ($P < 0.05$). Markedly histological and ultrastructural changes, including thickened respiratory membrane, vacuolar lamellar corpuscle and reduced mitochondria, were found in COPD rats and were alleviated in the treated groups, especially in BY group. The epithelial apoptosis index significantly increased in COPD rats ($P < 0.01$), and it decreased in BY and APL groups, while that in BY group was lower than in APL group ($P < 0.01$). PERK, eIF2 α , Bad mRNA increased and Bcl-2 mRNA decreased in COPD rats. PERK, eIF2 α and Bad mRNA decreased in BY group ($P < 0.05$). PERK and Bad mRNA in BY group was lower than that in APL group ($P < 0.05$). The protein expression of PERK, eIF2 α , p-PERK, p-eIF2 α increased in Model group ($P < 0.01$). PERK, p-PERK, p-eIF2 α expression in BY group and p-eIF2 α APL group decreased compared with Model group ($P < 0.05$).

Conclusion: Bufei Yishen granules has the beneficial effects in COPD and can inhibit alveolar epithelial apoptosis, the activation of PERK/eIF2 α signalling might be involved in the underlying mechanisms.

A NEW PARALLEL TWO-STEP ALGORITHM FOR THE TREATMENT OF COPD

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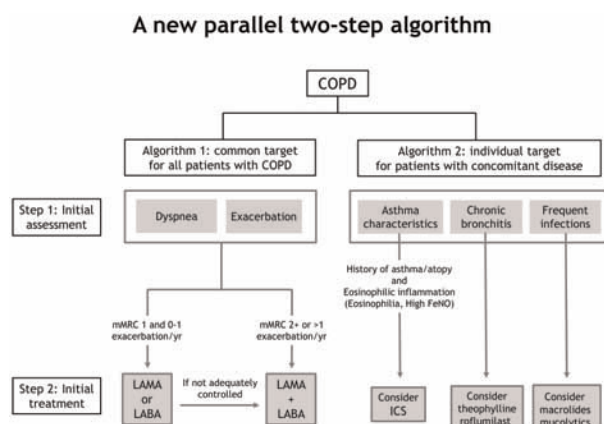
Background and Aims: In 2017, Miravittles and Anzueto demonstrated 'a new two-step algorithm for the treatment of COPD'. This is a simple treatment algorithm based on the severity of symptoms and phenotypes or treatable traits. In this, patient specialized assessment targeting eosinophilic inflammation, chronic bronchitis, and frequent infections, is recommended after exacerbation or deterioration in symptoms occurs despite bronchodilation therapy. However, recent studies have revealed the clinical characteristics of patients who should be added second controllers such as ICS. We consider treatable traits should be assessed and intervened as early as possible. Moreover, the algorithm is necessary to be adapted to the situation of clinical practice, taking into account the patients' characteristics.

Methods: We propose 'a parallel two-step algorithm' based on the evidence of recent studies.

Results: Once the diagnosis of COPD, The first decision is to divide into two targets parallelly based on the common target for all patients with COPD (Algorithm 1) and the individual target for patients with concomitant disease (Algorithm 2). In Algorithm 1, the initial assessment should be based on the level of dyspnea and the frequency of exacerbations. After the initial assessment, patients with a mMRC score 0–1 or one exacerbation during the previous year may start treatment with a mono-bronchodilator, whereas patients with either a mMRC score ≥ 2 or with more than one exacerbation in the previous year should start with a dual-bronchodilator.

In Algorithm 2, the initial assessment should be based on the asthma characteristics, chronic bronchitis, and frequent infections. After the initial assessment, patients with asthmatic characteristics may consider treatment with ICS, while patients with chronic bronchitis may consider treatment with theophylline and/or roflumilast, while patients with frequent infections may consider treatment with macrolides and/or mucolytics.

Conclusion: This proposal might be considered as an approach based on personalized therapy and useful to the development of COPD management.



EFFECTIVENESS OF PHARMACEUTICAL CARE ON THE PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ATTENDING A COMMUNITY HOSPITAL IN THAILAND

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Background and Aims: Drug related problems (DRPs) in chronic obstructive pulmonary disease (COPD) could cause the negative outcome. The effectiveness of pharmaceutical care which could decrease DRPs remained unassessed.

This study aimed to evaluate the effectiveness of pharmaceutical care on DRPs and clinical outcomes.

Methods: The quasi study was carried out in outpatients of Paknam-Chumphon Hospital from April, 2017 to April, 2018. Adult diagnosed COPD patients which attending the COPD clinic more than six months were included in the study. All patients were assessed for medication and clinical outcomes before and after 6 months of pharmaceutical care interventions. Relevant data were gathered and analyzed using a paired t-test, χ^2 test and logistic regression analysis ($\alpha = 0.05$).

Results: Total 120 patients were assessed. The majority of patients were male (66.7%) with the mean age of 67.7 years (SD = 12.3). After interventions, the number of DRPs was decreased from 134 to 36 (73.13%). Most DRPs before the interventions were inappropriate inhaler technique (29.2%) and inappropriate drug selection (19.2%) which were decreased to 14.2% and 3.3% respectively. The factors associated with DRPs including COPD type, exacerbation, COPD Assessment Test (CAT) score and dyspnea score were assessed. The predicted factor for DRPs was CAT score ≥ 10 with OR 11.1 [95% CI 1.02–12.5]. The significant of clinical outcomes improvement were found in force expiratory in one second (FEV₁) (67.47% vs 70.31%, $P = 0.001$), peak expiratory flow rate (PEFR) (62.83% vs 66.54%, $P = 0.001$), targeted dyspnea score 0–1 (70.2% vs 84.3%, $P = 0.012$), CAT score < 10 (66.1% vs 86.0%, $P = 0.001$), COPD type A and B (47.5% vs 72.5%, $P = 0.001$) and also significantly decreased the exacerbation and hospitalization rate.

Conclusion: DRPs in COPD patients associated with many factors and could predicted with CAT score ≥ 10 . Pharmaceutical care could resolve DRPs and revealed the effectiveness by enable COPD patients to achieve the desired therapeutic outcomes.

EFFECTIVENESS OF A PULMONARY REHABILITATION PROGRAM IN A REHABILITATION HOSPITAL DAY CENTRE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS FROM PRIMARY CARE CLINICS

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Background and Aims: Pulmonary Rehabilitation (PR) is evidence-based in managing chronic obstructive pulmonary disease (COPD) patients. However, PR is often underuse by both medical professionals and patients. This study aims were to identify potential COPD patients from primary care clinics and recruit them for PR; to classify COPD patients into different Groups according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and to evaluate the program's effectiveness.

Methods: Potential COPD patients were screened by primary care physicians in two clinics using lung function test and COPD assessment test (CAT) score. PR was carried out in a rehabilitation hospital day

centre with interdisciplines of a respiratory physician, nurse, physiotherapists and occupational therapist. Regular sessions on education, exercise tolerance training, energy conservation and stress management training were given. Pre and post PRP outcomes included: body weight; body mass index; CAT score; puff technique; lung function test; 6-minute walk distance (6MWD); Chronic Respiratory Disease Questionnaire (CRQ); Shortness of breath questionnaire and Hospital anxiety and depression score were collected.

Results: A total of 40 COPD patients with 6 Group A patients, 13 Group B patients, 12 Group C patients and 9 Group D patients underwent an average 18 sessions training were recruited in PR. Male to female ratio was 36:4. Mean age was 70.3 years old (53–90). Comparing pre and post PR outcomes, significant improvements in puff technique from 5 to 7.5/10 score; CAT score 12.4 to 5.9/40 with the minimal clinically important difference ((MCID)) -1.6; 6MWD improved from 345 m to 377 m with MCID +30 m, CRQ fatigue domain from 5.4 to 6.2 points and CRQ mastery domain 6.0 to 6.5 points with both MCID 0.5 points were observed.

Conclusion: PR was beneficial in improving drugs administration, relieving symptoms, enhancing health-related quality of life and increasing exercise capacity of COPD patients being identified in primary care clinics.

AP113

NO₂ INHALATION CAUSES IMPAIRED PULMONARY FUNCTION AND HAEMATOLOGICAL DERANGEMENT IN RATS AND INTERVENTION STUDY

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Background and Aims: Inhalation of air pollutant NO₂ leads to progressive airflow limitation and emphysema-like lesions, but the underlying mechanisms were not fully understood.

Methods: Male SD rats were continuously exposed to NO₂ at a concentration of 20 ppm or normal air on fixed occasion. During the rest periods, all rats breathed normal air. Pulmonary function (PF), haematological parameters, and biochemical tests were examined at the 14th, 45th, and 75th days of NO₂ exposure in anesthetized rats. After 75 days of NO₂ inhalation, NaHS, 5-AZA(5-Azacytidine) or NaCl treatment were carried out for one month (day 76th to 105th) to evaluate their effect on the rats.

Results: Compared with normal air exposure control, at 75th days of NO₂ exposure, a significant decrease in FEV1/FVC% as well histologic evidence of emphysema were found in the rats; NO₂ could led to increased GLU (Glucose), Triglyceride (TG), RBC (Red blood cell), HGB (Haemoglobin), and HCT (Haematocrit). After NO₂ cessation, PF test showed no further deterioration in all three treatments compared to controls, respectively. Compared with NaCl, 5-AZA treatment had the ability to increase levels of GLUv and PLT (Platelets) significantly, and decrease HGB and HCT; with NaHS, Granulocyte and Lymphocyte together with HDL-C levels were greatly elevated.

Conclusion: These findings suggested that NO₂ exposure caused emphysema, PF decline and blood increase of GLU in rats. All three treatments could prevent PF decline further. In addition, demethylation therapy with 5-AZA inhibited the increase of blood GLU; whereas, antioxidative stress therapy with NaHS could reinforce immune function of rats but not increase of blood GLU.

ENVIRONMENTAL FACTORS AND COPD IN THE DEVELOPMENT OF LUNG CANCER

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Background and Aims: COPD is a well-known risk factor for the development of lung cancer, independent of smoking behaviour. However, the environmental risk factors contributing to the development of lung cancer is not well researched except for smoking history and COPD. Therefore, we attempted to examine the prevalence of lung cancer in COPD and the environmental factors associated with the development of lung cancer in National Health Insurance Service–National Sample Cohort (NHIS-NSC).

Methods: NHIS-NSC is a population-based cohort established by NHIS in South Korea. Among 514,866 subjects of NHIS-NSC, 23,506 patients who were diagnosed with any cancer from 2002 to 2003 were excluded. We enlisted 324,621 never-smokers (male = 31.3%), 46,802 ex-smokers (male = 93.4%), and 120,056 smokers (male = 89.6%) and investigated the prevalence and factors associated with the development of lung cancer for 12 year observation period.

Results: Lung cancer developed in 2.83% of never-smokers with COPD, 5.16 % of former smokers of COPD, and 7.04% of smokers with COPD for 12 year period. Age, male gender, history of diabetes, exercise level, and COPD in smokers and never smokers were independent risk factors associated with the development of lung cancer ($P < 0.05$).

Conclusion: Our data suggest that age, male gender, history of diabetes, exercise level, and COPD in smokers and never smokers were independent risk factors associated with the development of lung cancer.

AP115

THE SNP RS61758360 LOCI REDUCING THE RISK OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: To find out relevant locus and genes related with COPD in Chinese Han population.

Methods: We collected COPD families to do the whole genome sequencing and performed SNP detection and annotation on the whole genome sequencing data. Then filtered through the database to select the missense sites located in exons were shared between two or more families for subsequent verification. COPD and non-COPD groups based on pulmonary function, inclusion, and exclusion criteria were recruited. We did the validation by doing the association analysis. Western blotting was used to detect the protein level and real time-PCR was used to detect the mRNA level; Small interfering RNA (siRNA) was used to silence Cbl-b gene expression, and lentiviral gene expression vector was used to over-express Cbl-b gene.

Results: We collected a total of 11 COPD patients from 5 COPD families. The average sequencing depth was more than 30x and the coverage was over 99% of the total genome length. After the advanced analysis, 18 SNP candidate sites were finally obtained.

A total of 1589 subjects were recruited (COPD 656, non-COPD 933). There was no significant difference in gender and age between the two groups. The smoking index, lung function, and body mass index were

significantly different; after genetic models and smoking stratification analysis, we found that the rs61758360 (Cbl-b) locus was associated with COPD.

Cigarette up-regulated Cbl-b protein level and silence of Cbl-b blocked CSE-induced down-regulation of TIMP1 and CSE-induced up-regulation of MMP9 in 16BBE; Over-expression of wild-type Cbl-b down-regulated TIMP1 expression and up-regulated MMP9 expression in 16BBE; Compared with the wild-type Cbl-b group, the mutation Cbl-b group up-regulated the expression of TIMP1 and down-regulated the expression of MMP9.

Conclusion: The rs61758360 is a functional site which can reduce the risk of chronic obstructive pulmonary disease through regulating MMP9/TIMP1 balance.

AP116

GLYCOPYRROLATE IN HIGH-RISK COPD, A DRUG UTILIZATION SURVEILLANCE STUDY IN INDIA (GOAAL): POST-HOC ANALYSES

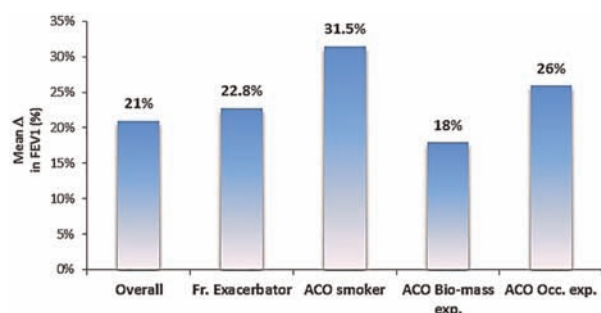
KRISHNAPRASAD K¹, MAHASHUR ASHOK^{2*}, SAGAR C³, HIMANSHU POPHALE⁴, GYANENDRA AGARWAL⁵, AARATRIKA DAS⁶, PRASHANT KATKE¹

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Background and Aims: Exacerbations remain a distinct clinical challenge in Asthma COPD Overlap (ACO-)/Non-ACO COPD cases of India. LAMAs remain the backbone of COPD therapy that provides incremental benefits in preventing disease progression and associated mortality rates. Glycopyrrrolate, an Ultra LAMA offers quick, selective & persistent bronchodilatory effects for superior MCID benefits at 24th h when administered alone or in combination

To assess Clinical utility & Safety of Glycopyrrrolate combination over 12 weeks in High risk COPD cases with/without frequent exacerbations.

Methods: A National, retrospective, case cohort analyses as Drug Utilization Surveillance study was conducted as per ICH-GCP @ 128 centres during Sept '17 with local Ethics committee approval & CTRI notification. Statistical analyses was carried out by QuickCalcs GraphPad Prism ver. 7 software with $P < 0.05$ considered statistically significant



Results: Per protocol analyses of 1117 consecutive Glycopyrrrolate/ICS/LABA combination COPD cases with follow-up visit for at least 12 weeks were analysed. Baseline demographics included Male/Female (76/24%); mean Age 59.5 years; FEV1 (48.9%), FEV1/FVC (58.7%); Reversibility (13.7%), Exacerbation (≥ 1 /year; 728, 65%; 32/years, 389, 35%), CAT (22), Smoke/Bio-mass/Occupation hazard cases with 12.5, 6.3 & 4.4 pack years exposure respectively. Overall group (1117) showed post-bronchodilatory FEV1 & CAT score change of 21% & 5.1 respectively ($p \leq 0.0001$) at 12 weeks. Post-hoc analyses with test of

interaction for Frequent exacerbator & ACO sub-group/s with exposure to smoking or non-smoking risk factors were further assessed. FEV1 (%) change in Frequent exacerbators (398), ACO-smoker (146), ACO-Bio-mass exposure (49), ACO-Occupational exposure (39) were 22.8% ($P < 0.0001$), 31.5% ($P < 0.0001$), 18% ($P < 0.03$) & 26% ($P < 0.0001$) respectively. TEAEs included Dry mouth (42, 3.8%), Headache (5, 0.4%), Constipation (4, 0.4%) of mild to moderate intensity with exacerbation in 2 (0.2%) cases

Conclusion: Glycopyrrrolate & ICS/LABA combination offers Synergistic control of symptoms in High-risk COPD cases with frequent exacerbations or ACO before reassessment for ICS continuation

AP117

STUDY ON THE EFFECTS OF PULMONARY REHABILITATION EXERCISE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN STABLE PERIOD

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Background and Aims: To investigate the effects of pulmonary function exercise on the pulmonary function, dyspnea, quality of life, movement functional ability and anxiety and depression in patients with stable chronic obstructive pulmonary disease (COPD).

Methods: 60 patients with COPD in stable period were recruited as research samples and were divided into 2 groups randomly. The control group was received routine treatments, while the experimental group was treated with regular respiratory exercise, including abdominal lip-shrinking breathing and body exercises on the base of the conventional treatments. Pulmonary function test (FEV1% pred and FEV1/FVC%) and 6-Min Walking Test (6MWT) were used to evaluate pulmonary function and movement functional ability of COPD patients. Dyspnea was assessed by the medical research council (MRC). The St. George's respiratory questionnaire (SGRQ) scale and Hospital anxiety and depression (HAD) scale were used to evaluate the quality-of-life, anxiety and depression of these patients. All patients were followed up and monitored quality of life, dyspnea, pulmonary function, 6-Min Walking Test, anxiety and depression at 4 months.

Results: Both FEV1%pred and FEV1/FVC% were statistically improved in the intervention group compared with the control group. There was obvious difference in MRC score between the two groups. There were markedly difference in 6-minute walking distance and the total scores of SGRQ between the two groups. The anxiety and depression scores showed significantly declined in the intervention group compared with the control group.

Conclusion: This study found that positive effects of pulmonary rehabilitation exercise in stable COPD patients on pulmonary function, quality of life, dyspnea, anxiety and movement functional ability. It was worthy of clinical application.

AP118

COMPOSITE INDEX FOR RECENT MORTALITY IN COPD PATIENTS

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Background and Aims: Multidimensional assessment of chronic obstructive pulmonary disease (COPD) was recommended by the Global Initiative for Chronic Obstruction Lung Disease, and many composite indices had been used to predict general prognosis in COPD patients. We

conducted a study to establish a composite index for recent mortality in COPD patients, which will be helpful for physicians to make a decision to give palliative care in terminal COPD patients.

Methods: Many physiological and laboratory parameters were recorded in COPD patients, and all these patients were followed up at least for one year. Multivariable analysis for one year mortality was conducted, and we used the independent variables to construct a composite index, a multidimensional 11-point scale in which higher scores indicate a higher risk of death.

Results: A total of 558 patients were finally included in the analysis. Thirty seven patients died within one year after enrolment. mMRC score and SaO₂ level were independent variables for predictors of one year mortality. The 11-point scale of this DO index showed that one year mortality in groups with scale 0–3, 4–7, 8–11 were 96.9%, 83.1%, and 37.5% respectively, and two year mortality in groups with scale 0–3, 4–7, 8–11 were 92.3%, 66.7%, and 25% respectively. Validation of this DO index in another cohort is still ongoing.

Conclusion: Composite DO index with 11-point scale may be a useful tool for predicting recent mortality, which will be helpful for physicians to make a decision for palliative care in terminal COPD patients

AP119

ASSOCIATION OF VITAMIN D₃ WITH LUNG FUNCTION AND EXERCISE TOLERANCE IN STABLE COPD PATIENTS: A CROSS-SECTIONAL STUDY

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Background and Aims: As the classic role of Vitamin-D3 in skeletal health is established, new aspect of it has been discovered in tissue and organs other than bones. Vitamin-D3 deficiency has been found in patients with various morbid disorders, such as cardiovascular diseases, autoimmune diseases, infectious diseases, Diabetes mellitus and malignancies including respiratory ailments.

This cross sectional study was designed to evaluate the status of fat soluble vitamin-D3 and its association with lung functions and exercise tolerance in stable COPD patients of Bangladesh.

Methods: 47 male, smoker (>4 pack years), stable (who has not experienced any acute exacerbation, hospitalizations, urgent care visits, or changes in routine medications within 4 weeks prior to study), COPD patients (post bronchodilator FEV1/FVC<0.70; duration >4 years) of >40 years of age, were selected from the OPD of National Institute of Diseases of Chest and Hospital (NIDCH), Dhaka. For the assessment of vitamin-D3 status, their serum 25-hydroxycholecalciferol [25(OH)D]; for lung function, [FEV1] and for exercise tolerance, 6 minute walk distance and level of dyspnea were measured. Results were expressed as percentage and absolute values. The data were statistically analyzed by Graphpad prism (Version 7) using Pearson's correlation coefficient test, where $P < 0.05$ was accepted as significant.

Results: Out of 47 stable COPD patients, 46 (97.8%) were vitamin D deficient (<30 ng/mL). Though severity of COPD (assessed by FEV1) was negatively correlated, but 6 MWD ($P < 0.05$) as well as dyspneic score were positively correlated with serum 25(OH)D level.

Conclusion: This study reveals that, vitamin-D3 deficiency may be significantly related to the decrement of exercise tolerance but not to the severity in stable COPD patients. Further study with larger sample size is recommended to explore the exact relationship of this vitamin with other

aspects of lung function and exercise tolerance in this group of morbid patients.

AP120

EFFICACY AND SAFETY OF ONCE-DAILY INHALED UMECLIDINIUM IN ASIAN PATIENTS WITH COPD: RESULTS FROM A RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Background and Aims: Inhaled long-acting muscarinic antagonist umeclidinium (UMEC) is an approved maintenance treatment for COPD in the US and EU. This is a regional phase III, randomized, double-blind, placebo-controlled, parallel group multicenter study with 24 weeks treatment period to evaluate the efficacy and safety of UMEC with placebo in patients with COPD of Asian ancestry.

Methods: Symptomatic COPD subjects were randomized to UMEC 62.5 mcg or placebo with 2:1 ratio. The primary efficacy endpoint was change from baseline in trough forced expiratory volume in 1 second (FEV1) on day 169; secondary end points were Transition Dyspnea Index (TDI) focal score at week 24 and weighted mean (WM) FEV1 over 0–6 h postdose on day 1. Safety was also assessed.

Results: 440 Asian subjects were enrolled from China and the Republic of Korea: 101 subjects were randomized to placebo and 205 to UMEC group and treated for 24 weeks. A clinically meaningful and statistically significant improvement in trough FEV1 was observed with UMEC compared with placebo at Day 169 (treatment difference 0.154 L, 95% confidence interval [CI] 0.113–0.194, $P < 0.001$). Statistically significant improvements in TDI score were observed for UMEC vs placebo (0.9, 95% CI 0.3–1.5, $P = 0.004$). The difference in weighted mean FEV1 over 0 to 6 h post dose on Day 1 was 125 mL (95% CI 0.103–0.147) in favour of UMEC, was also statistically significant ($P < 0.001$). The incidence of adverse events was similar across groups.

Conclusion: The efficacy of UMEC 62.5 mcg over placebo was demonstrated when administered once-daily via the Ellipta inhaler over a 24-week treatment period in Asian subjects with COPD. The difference in lung function endpoints and TDI were statistically significantly in favour of UMEC over placebo. No new safety concerns were observed.

Funding: GSK (117410; NCT02184611)

AP121

INVESTIGATION OF FRACTIONAL EXHALED NITRIC OXIDE LEVELS IN THE DIFFERENTIATION OF ASTHMA, COPD AND ASTHMA-COPD OVERLAP

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Background and Aims: Fractional exhaled nitric oxide (FeNO) is an easy, sensitive and noninvasive marker of eosinophilic airway inflammation and extensively used to diagnose and manage asthma. Less understood is the differentiation between FeNO level of asthma from chronic obstructive pulmonary disease (COPD) and asthma-COPD overlap (ACO). The aim of this study is to clarify the feasibility of using FeNO to differentiate ACO from asthma and COPD.

Methods: We enrolled 50 subjects (60.0% were male, the mean age was 64. ± 4.4) who were diagnosed with Asthma, ACO and COPD without history of exacerbation within one year. All patients was measured FeNO level using the NIOX VERO[®], pulmonary functional test (PFT) and

blood examination between October 2017 and May 2018. Association of FeNO level with the characteristics of all patients, PFT and blood examination were evaluated.

Results: There were the 22% of COPD patients who met the criteria of ACO. There was no significant difference in the FeNO level between ACO and asthma (30.0ppb vs 29.6ppb, $P = 0.945$). And the FeNO level of ACO was higher compared with COPD (30.0ppb vs 24.7 ppb). Although there was no significant difference between ACO and COPD.

Conclusion: In this study, it was suggested that the FeNO level of ACO and asthma were comparable. And because it seems that there were undiagnosed ACO in the COPD group, FeNO level of COPD tended to be higher.

AP122

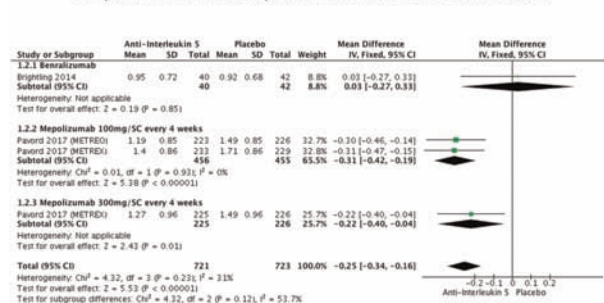
ANTI-INTERLEUKIN 5 AGENTS IN THE TREATMENT OF EOSINOPHILIC CHRONIC OBSTRUCTIVE PULMONARY DISEASE - A SYSTEMATIC REVIEW AND META-ANALYSIS **IRENE ROSELLEN TAN^{1*}, RALPH ELVI VILLALOBOS¹, ANJULI MAY JAEN¹, AILEEN DAVID-WANG¹**

¹University of the Philippines, Philippine General Hospital, Philippines

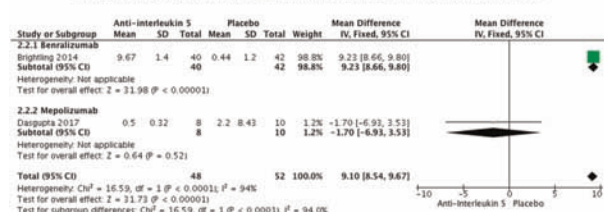
Background and Aims: Chronic obstructive pulmonary disease manifests with neutrophilic airway inflammation but approximately 20–40% of patients have elevated airway eosinophils presenting as >3% sputum eosinophilia. Benefits of newer biologic therapies such as anti-interleukin 5 agents (Mepolizumab and Benralizumab) have been studied in few randomized controlled trials but with contrasting results. At the time of conceptualization, there is no meta-analysis assessing the efficacy and safety of these agents in the eosinophilic phenotype of COPD.

Methods: We did a review and meta-analysis of randomized controlled trials on anti-interleukin 5 therapy in moderate to severe patients with eosinophilic COPD vs placebo. The primary outcome is annual exacerbation rate. Secondary outcomes include reduction of blood and sputum eosinophilia, improvement in lung function, change in symptom and quality of life scores and adverse events.

Comparison of anti-IL5 versus placebo in terms of number of exacerbations



Comparison of anti-IL5 versus placebo in terms of annual exacerbation rate



Results: This analysis included 4 RCTs (3 for Mepolizumab and 1 for Benralizumab) with a total patient population of 1,236 eosinophilic COPD patients. Compared with placebo, patients on anti-IL5 had a significant reduction in the annual exacerbation rate (mean difference -0.24 [-0.35 to

-0.13]) and sputum eosinophilia (mean difference 4.09 [-6.61 to 14.78]). There is a significant improvement in COPD Assessment Test (CAT) scores (mean difference -0.79 [-1.37, -0.21]). Anti-IL5 therapy showed a trend toward longer time-to-exacerbations (HR 2.18 [0.71–6.70]). There is no significant difference in lung function and Saint George's Respiratory Questionnaire scores. There is a trend toward increased overall adverse events (AEs) with anti-IL5 treatment and a trend toward decreased serious AEs and AEs leading to discontinuation of therapy.

Conclusion: Anti-IL5 agents clearly reduce exacerbation rates and sputum eosinophilia and improve quality of life in patients with eosinophilic COPD. Treatment shows equivocal findings regarding time to exacerbation and safety. Additional trials on other anti-IL5 agents such as Reslizumab may be done to further assess the benefit and safety of these novel agents for COPD.

AP123

PULMONARY EMPHYSEMA AND LIPID DYSFUNCTION IN MICE LACKING FATTY ACID SYNTHASE IN ALVEOLAR EPITHELIAL CELLS

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Background and Aims: Chronic obstructive pulmonary disease (COPD), a highly prevalent disease predominantly caused by exposed to cigarette smoke, with no effective treatments. Despite an increased understanding of the pathogenesis of COPD, mechanisms that drive these processes remain incompletely understood.

Methods: To investigate the mechanisms that initiate the COPD, we used a well characterized cigarette smoke exposure mouse model. In vitro, cigarette smoke extract (CSE) was exposed to MLE-12 cells. Mass spectrometry was used to determine the lipid metabolism. To identify the role of fatty acid synthesis (FASN) in the lung, we conditionally deleted FASN in type II cells (AEC2s) in mice.

Results: We found that cigarette smoke exposure for 6 months led to lipid composition altered in the whole lung as well as in AEC2s. FASN is down-regulated by cigarette smoke in AEC2 and cultured cells. mRNA isolated from AEC2s demonstrated that 64% of AEC2s lacked FASN in conditional deleted mice. AEC2s Cells lacking FASN had increased expression of mRNAs associated with lipid synthesis and transport. Lipidomic data indicated that mice deficient in AEC2s led to lipid content changes in the whole lung and AEC2s. Conditional deletion of FASN in AEC2s developed emphysema in aged mice.

Conclusion: Our results suggest lipid alteration and damaged surfactant is a central mechanism that drives cigarette smoke-induced COPD. Further investigation identify the FASN is a key enzyme regulated lipid homeostasis. Lack of FASN led to the development of emphysema.

AP124

A STUDY ON THE PERCEPTION AND REAL WORLD DATA ABOUT LONG TERM OXYGEN THERAPY IN PATIENTS WITH CHRONIC LUNG DISEASES IN KOREA

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Background and Aims: Patients with chronic lung disease who require long term oxygen therapy are increasing. Some patients have a good adherence to oxygen, but some patients are reluctant or unwilling to use it because of several reasons. So, we conducted the survey about

oxygen therapy to investigate the patient's perception and real world data about oxygen therapy.

Methods: Between December 1, 2017 and April 30, 2018, a total of 30 patients responded to the questionnaire on long term oxygen therapy. Included subjects are patients who are currently using oxygen therapy or are expected to use oxygen in the near future. We also collected medical records of these patients.

Results: Among 30 patients, 20 (67%) were men and mean age was 68.6 years. Underlying disease were COPD ($n = 15$), bronchial asthma ($n = 4$), ILD ($n = 4$), bronchiectasis ($n = 3$), TB destroyed lung ($n = 3$), and others. In patients using home oxygen therapy, mean duration per day was 7.7 h. In 19 out of 25 patients, patients were reported to have improved symptoms and quality of life after using oxygen. The most uncomfortable aspects of using oxygen were as follows: noise ($n = 14$), restriction of ambulation ($n = 11$), cost ($n = 6$), dryness in the nose ($n = 6$). The reasons for avoiding use when recommended for oxygen were as follows: the eyes of others ($n = 8$), fear of permanent use ($n = 5$). A total of 10 out of 30 patients refused portable oxygen therapy. The reasons for avoiding use were as follows: the eyes of others ($n = 14$), heaviness when ambulation or moving ($n = 13$).

Conclusion: We found that most patients with chronic lung diseases who used long term oxygen felt beneficial effects, but there were still obstacles that we have to overcome such as technical problems and too much consciousness of the eyes of others. In order to improve the patient's adherence to oxygen therapy, continuous monitoring and education on awareness about oxygen therapy and technical innovation are necessary.

AP125

METFORMIN USE REVERSES THE ADVERSE PROGNOSTIC EFFECT OF DIABETES MELLITUS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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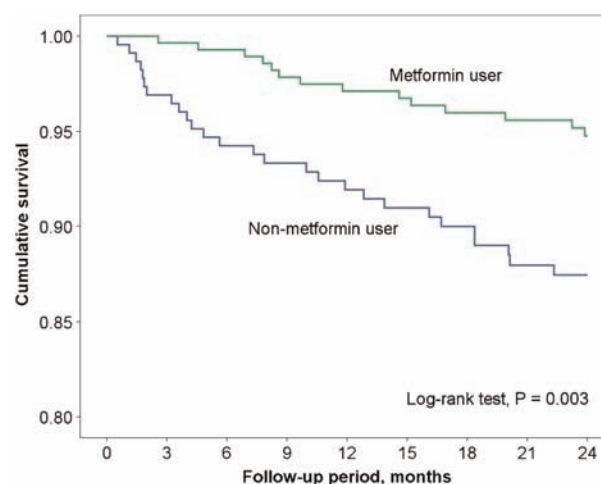
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Background and Aims: Diabetes mellitus (DM) is a common comorbidity among patients with chronic obstructive pulmonary disease (COPD) and is probably associated with increased systemic inflammation and worse prognosis. Metformin, with its pleiotropic anti-inflammatory and antioxidant actions, may offer theoretical benefits in COPD patients with DM. Thus, this study aimed to investigate the effects of DM and metformin use on mortality in the clinical trajectory of COPD.

Methods: We conducted a retrospective cohort study comprising patients with spirometry-confirmed COPD and an age of ≥ 40 years during the period 2008–2014. The primary outcome of interest was all-cause mortality. We evaluated the effect of DM on mortality through the clinical course of COPD and we also assessed the impact of metformin use on survival of the COPD population.

Results: Among 4231 COPD patients, 556 (13%) had comorbid DM and these patients had 1.62 times higher hazards of 2-year mortality than those without DM (95% confidence interval [CI], 1.15–2.28) after adjusting for age, gender, COPD stage, comorbidities and prior COPD hospitalization. Over a 2-year period, metformin users had a significantly lower risk of death (hazard ratio, 0.45; 95% CI, 0.23–0.88) compared to non-metformin users in patients with coexistent COPD and DM (Figure 1). Moreover, metformin users had similar survival to COPD patients without DM.

Conclusion: This study suggests that DM ties to an increased risk of death in COPD patients and the use of metformin seems to mitigate the hazard. Our findings support a pivotal role of metformin in the management of DM in COPD.



AP126

PRELIMINARY APPLICATION OF INTELLIGENT WRISTBANDS IN COPD PATIENTS

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Background and Aims: To observe the daily activities and sleeping tracking of COPD patients with intelligent wristbands., and to explore the correlation between the indexes of pulmonary function, CAT score, mMRC score and six minute walk distance.

Methods: Selected COPD patients for long-term follow-up since on June 2016. The subjects were required to fill out the related journal of the disease and wear a specific intelligent wristbands to recorded the daily activities and sleeping , Regular pulmonary function tracking, CAT, MMRC and six minute walk test were followed up.

Results: Until May 201 years, 46 subjects were temporarily met, with an average age of 65.96 ± 6.09 years, GOLD group: I: 5 (11%), II: 20 (44.4%), III: 14 (31.1%), IV class: 4 (13.3%). After 37.11 ± 27.68 weeks, the daily activities and sleeping records of COPD patients were obtained for a total of 11948 days; The daily and mileage were positively correlated with FVC before and after bronchodilation test, FEV1 before and after bronchodilation test, FEV1/FVC after bronchodilation test, FEV1/ predicted value after bronchodilation test, MMEF after bronchodilation test, and total distance of 6 minutes walking test ($r = 0.166-0.503$, $P = 0.000-0.044$), showing a negative correlation with CAT table score and mMRC classification ($r = -0.355 \sim -0.401$). There was no significant correlation between MMEF and FEV1/FVC after bronchodilation test. The total sleeping was positively correlated with FVC before and after bronchodilation test ($r = 0.180$, 0.166 , $P = 0.031$, 0.047), deep sleeping and six minute walk distance, FVC before and after bronchodilation test, FEV1, FEV1/ predicted value before and after bronchodilation test, FEV1/FVC after bronchodilation test, MMEF significant before and after bronchodilation test ($r = 0.3.10-0.167$, $P = 0.00-0.045$), deep sleeping .

Conclusion: intelligent wristbands can track the steps and sleep of patients with COPD, which can be used to guide the tracking and management of patients.

AP127

EFFICACY AND SAFETY OF SWITCH FROM TIOTROPIUM TO INDACATEROL/GLYCOPYRRONIUM IN SYMPTOMATIC MILD-TO-MODERATE COPD PATIENTS FROM KOREA: A RANDOMIZED, OPEN-LABEL, 12-WEEK TRIAL

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Background and Aims: Bronchodilators are the cornerstone of pharmacological management of COPD. Once-daily (q.d.) indacaterol/glycopyrronium 110/50 µg (IND/GLY) is approved in over 90 countries, including South Korea, for the maintenance treatment of adult patients with symptomatic COPD. This study evaluates the efficacy and safety of a switch from tiotropium 18 µg q.d. (TIO) to IND/GLY 110/50 µg q.d. in symptomatic COPD patients with mild-to-moderate airflow limitation.

Methods: This is a randomized, multicentre, open-label, parallel group, 12-week, trial in mild-to-moderate COPD patients who received TIO 18 µg q.d. for at least 12 weeks prior to study initiation. COPD patients, aged ≥ 40 years, with post-bronchodilator forced expiratory volume in 1 second (FEV₁) ≥ 50% of predicted normal value and post-bronchodilator FEV₁/force vital capacity (FVC) < 0.7, and a smoking history of at least 10 pack-years were included. The primary objective of this study is to demonstrate the superiority of IND/GLY 110/50 µg q.d. over TIO 18 µg q.d. in terms of pre-dose trough FEV₁ following 12 weeks of treatment. Secondary endpoints include the pre-dose trough FEV₁ after 4 weeks of treatment, transition dyspnea index (TDI) total score, COPD assessment test (CAT) total score, and rescue medication use following the 12-week treatment, and safety assessment over the 12-week treatment.

Results: In total, 442 patients were screened; of these, 378 patients were randomized to IND/GLY 110/50 µg q.d. and TIO 18 µg q.d. A total of 347 patients completed the study. The study is expected to demonstrate the superiority of IND/GLY 110/50 µg q.d. over TIO 18 µg q.d. in COPD patients with mild-to-moderate airflow limitation.

Conclusion: Results from this study will add to the existing evidence supporting the greater efficacy of IND/GLY over TIO in patients with COPD.

AP128

NOVEL BENZOXAZIN DERIVATIVE AS NEUTROPHIL ELASTASE INHIBITOR FOR TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Neutrophil elastase is an aggressive cytotoxic protease and plays a vital role in the development of Chronic

Obstructive Pulmonary Disease (COPD) by degrading a wide range of extracellular matrix proteins and thereby causing emphysema. Inhibition of neutrophil elastase by small molecule would prevent the severe tissue damage which might be useful to manage COPD. The aim of the present study is to screen small molecules for their anti-elastase activity and characterize them in vitro.

Methods: Synthetic molecules were screened on the basis of enzyme-substrate kinetic reactions for 2 h in the absence or presence of a known inhibitor. Potential inhibitors were sorted and IC₅₀ values were determined. In vitro assays were carried out to evaluate binding kinetics, potency, enzyme selectivity and bioavailability. In vitro morphological studies were conducted and cell toxicity was determined by MTT assay while cardiac toxicity by automated patch clamp method (hERG).

Results: Out of 50 small molecules, initial screening showed a benzoxazin derivative as good potential inhibitor with an IC₅₀ value of 150 nM as compared to control drug. The lead compound was found to be a reversible and competitive neutrophil elastase inhibitor. The compound was bioavailable and selective towards neutrophil elastase as compared to other endogenous enzymes. The compound prevented cellular desquamation and also showed protective effect against elastase induced cellular morphological changes and toxicity.

Conclusion: Based on the present study a benzoxazin group containing novel synthetic compound is found to be a selective inhibitor of human neutrophil elastase with good efficacy in in-vitro models and has the potential to be effective against neutrophil driven inflammatory lung diseases such as COPD.

AP129

APPRAISAL VALUE OF PERIPHERAL BLOOD EOSINOPHILS IN THE PROGNOSIS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: The aim of was to evaluate the predictive value and prognostic value of peripheral blood eosinophils for acute exacerbation risk in patients with chronic obstructive pulmonary disease (COPD).

Methods: This study was designed as an observational project in hospitalized COPD patients with acute exacerbation. They were divided into the eosinophil group (peripheral blood eosinophil continue no less than 2%) and the non-eosinophil group (eosinophil continue less than 2%). Their hospital stay, dosage of intravenous use of corticosteroids, neutral lymphocyte to lymphocyte ratio (NLR), eosinophil to basophil ratio (EBR), number of exacerbations that occurred during one year's follow-up were compared.

Results: The eosinophil group involved 25 cases, the other group involved 33 cases. Age, gender, BMI, smoking history, hs-CRP, peripheral white blood cell count, FEV₁% predicted had no statistical difference. The eosinophil group had shorter hospitalization days in acute exacerbations (7.68 ± 1.70 vs 9.00 ± 2.67, *P* < 0.05) and less dosage of intravenous use of corticosteroids (105.6 ± 123.90 mg vs 225.76 ± 76.77 mg, *P* < 0.05) compared with non-eosinophil group. The eosinophil group had significantly lower NLR and percentage of peripheral blood neutrophils (both *P* < 0.05). The percentage of peripheral blood lymphocytes and EBR were higher in the eosinophil group than those in the non-eosinophil group (both *P* < 0.05). We observed higher numbers of exacerbations occurred during one year's follow-up in the non-eosinophil group (2.13 ± 1.46) compared to the eosinophil group (1.11 ± 1.05). Only one patient died within one year's follow-up after discharge in the eosinophil group, and the other group had eight deaths (4.0% vs 24.2%, *P* < 0.05).

Conclusion: Our data support that high level of peripheral blood eosinophils result in shorter hospitalization days, better therapeutic response to corticosteroids, higher percentage of peripheral blood lymphocytes, lower numbers of exacerbations and deaths within one year's follow-up after discharge, which suggests the level of peripheral blood eosinophils can assess acute exacerbation risk and prognosis in patients with COPD.

Table 1. Clinical characteristics of patients in the eosinophil group and non-eosinophil group

	eosinophil group (n=22)	non-eosinophil group (n=32)	P
Gender (n, male/female)	22/0	25/7	0.34
Age (mean)	71.32 ± 8.43	71.79 ± 8.76	0.90
Smoking (n)	21/10 ± 2.76	21/40 ± 4.76	0.04
Smoking history (n, %)	18 (77)	87 (33.7)	0.01
In COPD (n)	34/48 ± 40.44	30/31 ± 40.48	0.81
Posterior-spiral blood cell count (10 ⁹ /L)	7.17 ± 1.24	9.90 ± 1.28	0.01
FEV1 (percentage)	43.48 ± 11.37	41.33 ± 11.98	0.39
FEV1/PVC (%)	53.44 ± 12.83	51.80 ± 14.32	0.53

Table 2. Comparison of hospitalization days and dosage of corticosteroids in the eosinophil group and non-eosinophil group

	eosinophil group (n=22)	non-eosinophil group (n=32)	t	P
Length of hospitalization (days)	7.46 ± 1.30	9.50 ± 2.47	-3.28	0.001
Dosage of corticosteroids (mg)	161.60 ± 125.90	225.79 ± 76.77	-4.27	0.0001
Daily dosage of corticosteroids (mg/day)	13.38 ± 15.58	28.33 ± 9.89	-3.76	0.0006

Table 3. Comparison of peripheral blood cell division ratios

	eosinophil group (n=22)	non-eosinophil group (n=32)	t	P
Percentage of peripheral blood eosinophils (%)	41.81 ± 8.46	34.03 ± 9.32	-3.46	0.0009
Percentage of peripheral blood neutrophils (%)	22.79 ± 8.06	17.91 ± 7.70	2.10*	0.0400
IL-6 (%)	3.49 ± 1.11	6.20 ± 4.40	-2.38	0.0276
IL-8 (%)	18.79 ± 17.76	2.39 ± 3.04	6.40	0.0003

Table 4. Comparison of prognosis in two groups within one year's follow-up

	eosinophil group (n=22)	non-eosinophil group (n=32)	Statistic	P
Number of exacerbations	8.11 ± 1.03	2.13 ± 1.46	t = -2.38	0.0238
Death ratio (%)	0/0 (0%)	9 (28.1%)	32 ± 4.045	0.0001

APL003

ANALYZING PATIENTS' CHARACTERISTICS ASSOCIATED WITH SLEEP DISTURBANCE IN COPD PATIENTS

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Background and Aims: Chronic obstructive pulmonary disease (COPD) patients have high prevalence of sleep disturbance. Chronic sleep interruption may compromise patients' quality of life and survival rate. However, patients' characteristic associated with sleep disturbance is still controversial. Our study aims to identify factors which correlate with sleep disturbance in COPD patients in Taiwan.

Methods: This was a randomized, cross-sectional study conducted between 2011 and 2012. This study successfully recruited 180 COPD patients over forty years of age. Each participant had to fill out a questionnaire to answer whether they had sleep disruption due to cough and difficulty breathing. The participants were divided into the two groups with or without sleep disturbance. Analyzing parameters included participants' demographics, co-morbidities, COPD Assessment Test (CAT) and lung function test.

Results: Mean age of patients was 71.72 ± 8.31 years of age, predominantly male who have moderate to severe COPD. The average CAT score of patients with and without sleep disturbance were 15.9 ± 0.51 and 9.4 ± .98 ($P < 0.05$). Multivariate analysis revealed that CAT was associated with sleep disturbance (odd ratio 1.12, 95% confidence interval 1.05–1.19). However, we did not find physical parameter such as high body mass index (BMI), lung function test, or medical co-morbidities (diabetes mellitus, hypertension, hyperlipidemia, and health failure) have correlation with sleep disturbance.

Conclusion: CAT score can be a predictor correlated with self-reported sleep disturbance in patients with COPD in Taiwan.

A PREDICTION MODEL FOR HOSPITALIZED COPD EXACERBATIONS BASED ON "TREATABLE TRAITS"

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Background and Aims: Assessing risk of future exacerbations is an important component in chronic obstructive pulmonary disease (COPD) management. Our aim was to develop and validate a novel model for predicting risk of hospitalized COPD exacerbations based on modifiable factors ("treatable traits") known to contribute to increased exacerbation risk.

Methods: Retrospective observational study of COPD patients followed-up at a tertiary care specialist COPD Clinic between January 2008 and January 2018. Demographics, smoking history, symptoms, comorbidities, spirometry, sputum cultures and healthcare utilization were recorded. Zero-inflated negative binomial regression was used to model the number of hospitalizations for COPD exacerbation in the year prior to death, or 31 January 2018 if alive. Predictive accuracy of the model was compared with several published risk indices.

Results: 237 and 169 patients formed the derivation and validation cohorts respectively. Mean age in the derivation cohort was 7 ± years, 222(93.7%) were male, mean postbronchodilator forced expiratory volume in one second (FEV1) was 6 ± 0% predicted, 209(88.2%) had mMRC ≥ 2 or CAT ≥ 10, and 106(44.7%) experienced ≥ 1 hospitalized exacerbation in the past year. The following factors were found to be independently associated with annual hospitalized exacerbation rate: COPD hospitalization rate in previous year (incidence rate ratio [IRR]: 1.52, 95% confidence interval [CI]: 1.38–1.68, $P < 0.001$), history of invasive/noninvasive ventilation (IRR: 1.60, 95% CI: 1.38–1.68, $P = 0.02$), coronary artery disease (IRR: 1.90, 95% CI: 1.36–2.66, $P < 0.001$), bronchiectasis (IRR: 1.93, 95% CI: 1.20–3.01, $P = 0.006$), and nontuberculous mycobacteria (IRR: 2.04, 95% CI: 1.19–3.48, $P = 0.009$). Predictive accuracy was good in both derivation and validation (area under the receiver operating characteristics curve 0.789 and 0.723 respectively) cohorts. Our model significantly outperformed the GOLD risk assessment criterion and several other published risk prediction models.

Conclusion: We have derived and validated a novel risk prediction model for COPD hospitalizations which outperforms several other risk indices. Our model incorporates several treatable traits which can be targeted for intervention to reduce risk of future hospitalized exacerbations.

APL005

2 MINUTE WALK TEST AS A SCREENING TOOL FOR COPD

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Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease eventually leading to considerable disability in affected patients. COPD is still a disease that is grossly underdiagnosed. India being a high burden and resource poor country, assessing the severity of the disease using currently available guidelines is more often very difficult in daily clinical practice. This study was conducted to find out if 2 minute walk test - a relatively simple test - can be used to screen and assess the severity of the disease.

Aim: To compare 2 Minute Walk Distance with the components of Refined COPD Assessment tool.

Methods: 211 adult patients with Stable COPD were recruited in this study. Spirometry was done to assess the FEV1 and patients were subjected to 2 Minute Walk Test (2MWT) according to standard protocols.

Patients were classified according to the GOLD guideline using the refined ABCD criteria.

Ethical consideration: Clearance of the Institutional Ethics Committee was obtained prior to commencement of the study.

Statistical Analysis: The results were analysed using statistical software SPSS Version 19.0.

Results: The mean distance covered in 2 min (2MWD) by males was 117.10 m and females was 106.96 m and the difference was statistically significant.

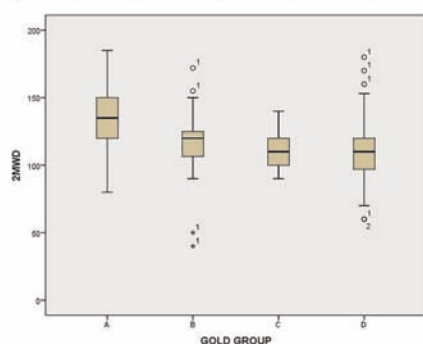
The 2 MWD was compared with the refined ABCD assessment tool. Each component of ABCD assessment both individually and combined showed statistically significant correlation with 2 MWD.

A positive correlation was found between FEV1 and 2 MWD ($P < 0.001$).

Negative correlation was found between 2MWD and each component of Refined COPD assessment tool like GOLD Grading, MMRC, CAT Score, Hospital admissions and GOLD Grouping ($P < 0.001$).

Conclusion: 2 Minute Walk test can be used as an effective tool in screening COPD and also to assess severity of the disease in areas where access to spirometry is restricted.

	Sex	N	Mean	C.I		df	Sig
				L	U		
2MWD	M	165	117.10	2.678	17.615	209	0.008
	F	46	106.96	3.611	16.682		



Critical Care Medicine 1

AP130

RARE PRESENTATION OF ACUTE B-LYMPHOBLASTIC LEUKAEMIA MIMICS GUILLAIN-BARRE SYNDROME: A CASE REPORT

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Background and Aims: Progressive symmetric muscle weakness in an ascending fashion is the classic manifestation of Guillain-Barre syndrome (GBS), which may result in respiratory muscle weakness and need the ventilator support. Some malignancies have been reported in association, but GBS-like symptoms as the initial presentation of the acute B-lymphoblastic leukaemia has not been reported.

Methods: We reported a 76-year-old man who was admitted with presentation of progressive muscle weakness for one week.

Results: Two weeks before admission, he had cough and rhinorrhoea. One week later, he was brought to local hospital because of progressive muscle weakness, which was started from the legs, and then was proceeded to the arms. Intubation for respiratory support was done three days later. Because of fever and limbs weakness, central nervous system infection was suspected, ceftriaxone and vancomycin were used after lumbar puncture. Cerebrospinal fluid (CSF) data revealed albuminocytologic dissociation (protein 395 mg/dL, white cell count (WBC) 3/mm³).

He was transferred to Medical center with suspicion of GBS, where neurologic exam showed powerful movement of head, tetraplegia, and absence of deep tendon reflex. Leukocytosis and blast cell 10.9% were noted. Repeated CSF data showed protein 978 mg/dL, WBC 26/mm³ and some blast cell. Bone marrow biopsy showed moderately hypercellular marrow with diffuse infiltration of blasts. Immunohistochemical study shows positive CD 10, CD 19, and CD 20, and negative CD3, CD33, and TdT. There was no lymph node enlargement or mass on computed tomography. Acute B lymphoblastic leukaemia was diagnosed. Intravenous Rituximab and intrathecal chemotherapy were done. Although imipenem was used, patient died from the Klebsiella pneumoniae bacteremia with septic shock.

Conclusion: It is important for critical care doctor to recognize that the insidiously rapid progression of weakness in an ascending fashion could be the initial presentation of the B-lymphoblastic leukaemia. Delayed diagnosis may result in the death of the patient.

AP131

PREVENTION AND TREATMENT OF EARLY COMPLICATIONS AFTER DCD LUNG TRANSPLANTATION: A CASE SERIES

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Background and Aims: To discuss how to optimize the prevention and treatment of lung transplant complications by reporting 26 patients who underwent lung transplantation diagnosed with end-stage lung disease.

Methods: From October 1, 2015 to January 1, 2018, 26 patients with end-stage lung disease in our hospital were successfully transplanted. Donor lungs were classified as the third categories (Maastricht classification IV) by Chinese Donor Classification. Donor's lungs were perfused and preserved with cotton-sugar-hypokalaemia dextran solution. Methylprednisolone were administered during transplant operation, and tacrolimus, mycophenolate mofetil, prednisone triple immunosuppression were applied after the transplant operation. We adopted a general antimicrobial strategy to prevent early CMV infection, bacterial infection and fungal infection after transplantation. Complications were monitored, managed, and recorded in detail.

Results: Among the 26 patients, 24 were male and 2 were female with an average age of 47.9 years. Bilateral lung transplantation was performed in 2 cases and single lung transplantation in 24 cases. Ten urgent operation and fourteen elective operation were conducted. Twenty-three patients survived more than 30 days after surgery and eighteen patients survived more than 90 days after surgery. Twenty-one cases of lower respiratory tract infection happened in the early postoperative period (within thirty days), and the pathogens were pan-resistant or multi-resistant gram-negative bacteria. Co-infection was common in these cases. Primary graft dysfunction (PGD) occurred in 12 cases. Anastomotic stenosis was found in 5 patients with severe airway infection in the early postoperative period, and bronchoscopic intervention therapy were administered to treat the complications effectively. Acute rejection occurred in 5 cases and all were relieved by using high dose methylprednisolone.

Conclusion: Lower respiratory tract infection, PGD, anastomotic stenosis and acute rejection were commonly complicated to lung transplantation in the early postoperative period. Prevention, monitoring and treatment for these complications were important to improve the clinical outcome of the lung transplant patients.

AP132

DERIVATION OF WEANSNOW SCORE TO ASSESS THE PROBABILITY OF SUCCESSFUL EXTUBATION AND VENTILATOR LIBERATION: AN ANALYSIS AT THE INTENSIVE CARE UNIT OF A MEDICAL CENTER

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Background and Aims: The probability of extubation success in patients with mechanical ventilation (MV) might be related to several factors not limited to the conventional weaning parameters. However, there lacked an application of a composite scoring methods in the setting.

Methods: We retrospectively analyzed 85 patients who had received MV for acute respiratory failure and tried extubation trial at the medical intensive care unit (ICU) of a medical center. We proposed a composite WEANSNOW scoring system and assigned each of the item (Weaning parameters, Endotracheal tube, Arterial blood gas analysis, Nutrition, Secretions, Neuromuscular-affecting agents, Obstructive airway problem, and Wakefulness) with 0 point or 1 point if the item was assessed as low risk or high risk, by pre-determined definitions. Data on the WEANSNOW scores and patients' demographic and clinical features were analyzed, among other variables, to determine the association of this scoring with extubation outcome.

Results: Of the patients, 49 (57.6%) were male, with an age of 67.1 ± 13.5 [24–97] years. Reasons for initiation of MV included acute pulmonary condition in 47.1% patients, acute heart condition in 18.6%, and acute neurologic condition in 17.6%. Main comorbidities included neurologic diseases (48.2%), cardiovascular diseases (35.3%), chronic pulmonary disease (31.8%), and diabetes (31.8%). Of the patients, 21 (24.7%) failed extubation and were reconnected to the ventilator. The average WEANSNOW score was 0.29 ± 0.50 [0–2] for all patients. The mean WEANSNOW scores between the success and failure groups were 0.20 ± 0.06 and 0.52 ± 0.11 , respectively

($P = 0.01$). Using a score of higher than 0 to predict extubation failure, the sensitivity and specificity were 52.2% and 83.6%, respectively.

Conclusion: The pre-extubation assessment with the WEANSNOW scoring method provides valuable insights in the prediction of extubation success in patients with acute respiratory failure.

AP133

RISK OF RECURRENT RESPIRATORY FAILURE SUBSEQUENT TO SUCCESSFUL WEANING FROM INVASIVE MECHANICAL VENTILATION INITIATED FOR NON-SURGICAL REASONS: A NATIONWIDE COHORT STUDY

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Background and Aims: Numerous patients survive respiratory failure and subsequently separate from mechanical ventilation every year. Nevertheless, it remains elusive how the clinical course evolves after

successful ventilator liberation. This study aimed to estimate the risk levels of recurrent respiratory failure and death after weaning success.

Methods: This nationwide cohort study used the entire population database of Taiwan's National Health Insurance (NHI). We included patients who were eventually separated from invasive mechanical ventilation successfully among those were newly placed on such care for at least two days for non-surgical reasons from March 1, 2010, through September 30, 2011. We estimated the probabilities of reinstituting invasive mechanical ventilation by the Kaplan–Meier estimator, and depicted the risk distribution over time on the basis of the hazard function.

Results: There were 56,394 patients newly initiating invasive mechanical ventilation for non-surgical reasons during the study period. Of them, 34,550 patients (61.3%) were successfully weaned from ventilators. The median age of the study cohort was 74 years (IQR, 60–82 years), and 36.3% were women. The median duration for the index mechanical ventilation episode was 8 days (IQR, 5–16 days). After a successful weaning, the subsequent risks of reinstituting invasive mechanical ventilation were 29.5% (95% CI, 29–30%) by six months and 36.8% (95% CI, 36.2–37.4%) by 12 months. The risks for a composite outcome combining reinstitution of invasive mechanical ventilation and death were 45.2% (95% CI, 44.7–45.7%) by six months and 55.0% (95% CI, 54.5–55.6%) by 12 months. The risk of reinstituting invasive mechanical ventilation was trending downwards over time and levelled off on the 30th day after ventilator liberation.

Conclusion: The patients just recovering from respiratory failure were at high risks for recurrent respiratory failure and death. The risks were particularly remarkable within 30 days after ventilator liberation.

AP134

LONG-TERM OUTCOME OF VERY ELDERLY (≥ 80 YEARS) CRITICAL-ILL PATIENTS IN MEDICAL INTENSIVE CARE UNIT IN A TERTIARY HOSPITAL OF KOREA

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Background and Aims: This study evaluated the long-term outcomes of very elderly (age ≥ 80 years) critically ill patients admitted to a medical intensive care unit (MICU) in a regional single tertiary hospital.

Methods: We retrospectively analyzed MICU data obtained from December 2011 to May 2014. The 90-day and 1-, 2-, and 3-year survival rates were assessed among very elderly patients who survived after hospital discharge. Survival was assessed using National Health Insurance Corporation medical insurance standard records. Patient death was defined as a discontinuation of medical insurance; accordingly, the date of death was defined as the day of discontinuation.

Results: Among the 468 patients admitted during the study period, 286 (male:female = 179:107, mean age = 70.9 ± 13.2 years) survived and were discharged. In this latter group, 69 (24.1%) were aged ≥ 80 years while 217 (75.9%) were aged < 80 years. The respective 90-day and 1-, 2-, and 3-year survival rates were 50.7%, 31.9%, 15.9%, and 14.5% among patients aged ≥ 80 years and 68.3%, 54.4%, 45.6%, and 40.1% among those aged < 80 years ($P < 0.05$). We further compared the clinical characteristics between survivors and non-survivors at 1-year post-discharge among the 69 patients aged ≥ 80 years. In this group, non-survivors had a higher proportion of patients with a body mass index ≤ 18 and longer duration of mechanical ventilation, relative to survivors (5.7 ± 4.5 vs 9.6 ± 8.5 days). In multiple logistic regression analyses, an age ≥ 80 years and longer MICU stay were significantly associated with non-survival at 1-year post-discharge.

Conclusion: Very elderly patients have a low long-term mortality rate after admission to the MICU.

AP135

LONG-TERM OUTCOME OF SURVIVORS WITH SEPSIS AFTER INTENSIVE CARE

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Background and Aims: There are few studies in Taiwan analyzing the long-term outcome in patients with sepsis after survival from intensive care unit (ICU) admission. Thus, we designed a study to determine the 5-year mortality in survivors with sepsis.

Methods: The patients from a database of our previous prospective study admitted into the Keelung Chang Gung Memorial hospital medical ICU were followed. Mortality rates of the survivors after ICU discharge and factors that affect long-term mortality were analyzed.

Results: Of the 494 patients, 204 survivors from ICU discharge were found. Their 5-year mortality rate was 85.3%, while the 1st and the 2nd-year mortality rate was 60.3% and 71.1% respectively. Age, history of diabetes mellitus and history of stroke were positively associated with long-term mortality.

Conclusion: Five years after ICU discharge, the survival rate was only 14.7%. Five-year mortality was positively associated with old age, diabetes and stroke history. Older survivors with diabetes and stroke history after surviving sepsis should be closely followed up.

Table 1: Multivariate Cox regression analysis to determine independent factors of patient mortality

Variables	HR	95% CI	P value
Sex	0.941	0.699-1.322	0.724
Age	1.022	1.008-1.037	0.002
APACHE II Score	1.018	0.993-1.043	0.157
Medical history			
COPD	1.273	0.817-1.983	0.286
Arrhythmia			
Malignancy	1.799	1.177-2.750	0.007
Heart failure	0.510	0.291-0.893	0.018
Hypertension	1.282	0.919-1.787	0.143
Liver cirrhosis	1.084	0.580-2.025	0.801
ESRD	1.150	0.547-2.241	0.712
Diabetes mellitus	1.547	1.058-2.262	0.024
Stroke	1.707	1.182-2.465	0.004
Co-morbidities			
Thrombocytopenia	1.097	0.739-1.631	0.645
Bacteremia	0.436	0.225-0.845	0.014
Jaundice	1.080	0.501-2.328	0.845
Shock	1.685	0.953-2.978	0.073
Acute renal failure	1.108	0.760-1.615	0.595
AMI	2.345	0.281-19.555	0.431
Nature of infection			
Pneumonia	1.337	0.785-2.278	0.285
UTI	1.569	0.882-2.790	0.125
Others, as reference			
Acute respiratory failure	1.550	0.910-2.640	0.107
Renal replacement therapy	0.675	0.363-1.255	0.215
Use of low-dose steroid	0.654	0.383-1.116	0.120

HR = hazard ratio; CI = confidence interval; APACHE = Acute Physiology and Chronic Health Evaluation; COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease; AMI = Acute myocardial infarction

AP136

DELAYED ADMISSION TO ICU OVER 6 HOURS WAS ASSOCIATED WITH HIGHER HOSPITAL MORTALITY IN PATIENTS WITH SEPSIS

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Background and Aims: To determine whether delayed admission to ICU with waiting time over 6 h affects outcomes in patients with severe sepsis.

Methods: This study evaluated adult medical ICU patients (18 y/o) with sepsis in Kaohsiung Chang Gung Memorial Hospital. 797 consecutive patients who met the criteria of sepsis-3 were enrolled. All possible clinical factors were prospectively recorded. Cytokine expressions were measured with a MILLIPLEX MAP Human Cytokine/Chemokine Panel (Merck Millipore, Billerica, MA, USA) in 166 patients enrolled to biomarker study. Expression of cell surface TLR4 MFI and HLADR MFI on monocytes was measured by flow cytometry (Cytomics FC500; Beckman Coulter, Inc., Fullerton, CA, USA).

Results: Patients were defined as delayed (waiting time over 6 h) group ($n = 467$) and not-delayed (waiting time less than 6 h) group ($n = 330$). With compatible age, sex, APACHE II score, Charlson comorbidity index, BMI, and initial oxygen index, the prevalence of underlying comorbidity of ESRD was higher in delayed group (13.31% vs 7.14%, $P < 0.05$), possibly suggesting more waiting time needed to arrange ICU bed for haemodialysis. The short-term outcomes regarding 7, 14, 28 days, ICU survival were comparable between the 2 groups. However, there were higher hospital mortality in patient with waiting time over 6 h. The vital signs, SOFA scores, lactate, procalcitonin and oxygen index were almost comparable between the 2 groups over day 1, day 3 and day 7. Inflammatory and anti-inflammatory cytokine concentration and HLA DR expression on monocyte within 7 days were comparable, indicating the immune profile were similar between the 2 groups.

Conclusion: Waiting time over 6 h was associated with higher hospital mortality in patients with sepsis admitted to ICU.

AP137

RISK FACTORS FOR MORTALITY ON PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN VIETNAM

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Background and Aims: Prediction of outcomes in patients with acute respiratory distress syndrome (ARDS) is of major importance for appropriate clinical management decisions. The aim of the study was to elucidate the risk factors of mortality on hospitalized patients with ARDS in Vietnam.

Methods: The retrospective observational study was performed in a national central hospital in Hanoi, Vietnam. Subjects were adult patients (≥ 18 years) who admitted and were diagnosed ARDS at the emergency department or ICU in the study site. The data on patients' general and clinical backgrounds and conditions, radiographic findings, ventilator

settings, gas exchange, and treatments were collected and compared between survivors and non-survivors. The risk factor for mortality was assessed using a logistic regression analysis.

Results: Total 126 patients (mortality, 57.1%) were eligible. In all patients, 94.4% were transferred to the study site from other hospitals in the north part of Vietnam. In the conditions of gas exchange, mean ($\pm$ SD) of PaO₂/FiO₂ between non-survivors (102.1 ± 52.5) and survivors (120.0 ± 66.7) on Day 1 was not significant ($P = 0.079$); however, PaO₂/FiO₂ on Day 3 was improved both on Non-survivors (126.3 ± 79.9) and Survivors (183.9 ± 98.9) with the significant difference ($P = 0.002$). A multivariate logistic regression analysis resulted that PaO₂/FiO₂ [odds ratio (OR), 1.010; 95% confidence interval (CI), 1.003–1.017] and length of pre-hospitalization before admission (OR, 1.122; 95%CI, 1.042–1.210) were independent risk factors for hospital mortality.

Conclusion: The present study revealed that hospitalized patients with ARDS were admitted to the central hospital with severe respiratory conditions. In the central hospital, if pathophysiological conditions does not improve (PaO₂/FiO₂ on Day 3 is 150 or less), the clinical outcome would getting worth. In the treatment of ARDS in Vietnam, the early transfer to the central hospital that can get the early diagnosis and the early initiation of appropriate treatments would contribute to the better outcome.

AP138

A CALCULOUS CHOLECYSTITIS: A FATAL COMPLICATION IN POST-LUNG TRANSPLANTATION PATIENT—A CASE REPORT

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Background and Aims: Gastrointestinal complications are common and result high mortality and morbidity for the post-lung transplantation patient. The acalculous cholecystitis is a severe complication that may happen after major medical or surgical conditions. The relationship between lung transplantation and acalculous cholecystitis had not been well studies.

Methods: We report a 60-year-old male who had diagnosed with idiopathic pulmonary fibrosis 11 years ago and received bilateral lung transplantation in 2017.

Results: The extracorporeal membrane oxygenation (ECMO) was placed during the operation for severe cardiopulmonary failure, and it was removed 3 days later. The extubation was done 7 days post-operation. The pulmonary rehabilitation was arranged after then, and the patient's condition was stable that the discharge plan was made. However, he suffered from the symptoms of mild right upper quadrate abdominal pain at first, and the plain film showed only distended bowel at that time. The shock status was developed on postoperative day 43. CT scan showed massive ascites with enlarged gallbladder. Emergent laparotomy revealed gangrenous change of gallbladder with rupture, and the cholecystectomy was performed. No positive culture data was got during this period except a positive bronchoalveolar lavage cytomegalovirus shell vial culture 60 days post-transplantation. However, due to profound shock status even under high dose of inotropic agent usage, the patient was dead on the postoperative day 71.

Conclusion: Acalculous cholecystitis is a serious complication in post-lung transplantation patient with occult symptoms and signs. Only one case report mentioned about acalculous cholecystitis in lung transplant patient previous, and the cytomegalovirus induced cholecystitis was diagnosed. For this group of patients, aggressive and early detection and intervention is necessary.

PREDICTION OF PRONE POSITION VENTILATION RESPONSE FOR ACUTE RESPIRATORY DISTRESS SYNDROME WITH HIGH-RESOLUTION COMPUTED TOMOGRAPHY

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Background and Aims: Prone positioning is likely to reduce mortality among patients with severe acute respiratory distress syndrome when applied for at least 12 h daily. We aim to evaluate whether the high resolution computed tomographic (HRCT) appearance has predictive value for prone positioning response and its role in prone positioning patients selection

Methods: This observational study was conducted in a medical center in northern Taiwan from October 2014 to June 2016. We evaluated patients with moderate to severe acute respiratory distress syndrome who received invasive mechanical ventilation and prone-positioning sessions of at least 12 h. Each lung was divided into three parts (apex, hilar and basal lung) and each part was divided into three zones (ventral, middle and dorsal part). Each zone was rated on a six-point scale of 0–5 for the extent of consolidation, ground glass opacity, bronchiectasis or pleural effusion.

Results: Among 43 analyzed patients, 26 (60%) patients was prone responsive and 17 (40%) patients was prone non-responsive. Prone response rate (56% vs 66.7%, $P = 0.492$) did not significantly differ between bacterial infection associated acute respiratory distress syndrome group ($n = 25$, 58.2%) and non-bacterial group ($n = 18$, 41.8%). Within bacterial pneumonia group, the consolidation score difference between dorsal and ventral zone at basal lung was higher in prone responder than non-responder (4.5 vs 2.2, $P = 0.068$; AUC of ROC curve = 71.75%, $P = 0.014$). If the basal lung had >3 points of consolidation score than ventral zone, the Sensitivity/Specificity/PPV/NPV for predicting prone responder were 71.4%/72.7%/76.9%/66.6%, respectively. Neither combining the other two parts lung score nor using the other three pattern extent can provide extra predictive power.

Conclusion: The results indicate that consolidation extent difference >3 points between dorsal and ventral part in basal lung field is potentially helpful in predicting prone response in patients with bacterial pneumonia associated acute respiratory distress syndrome.

AP140

CROSS SECTIONAL PREVALENCE STUDY ON PAEDIATRIC PATIENTS DIAGNOSED WITH SEVERE DENGUE AT A TERTIARY HOSPITAL IN CEBU CITY GIVEN NON INVASIVE VENTILATION VS MECHANICAL INTUBATION

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Background and Aims: Non Invasive Ventilation (NIV), is a new form of ventilatory management for respiratory failure using an external interface and positive pressure ventilation. Dengue fever, when severe, may cause acute respiratory failure after initial fluid resuscitation. Although invasive ventilation through an endotracheal tube, has been a mainstay for ventilator management, its inherent risks like upper airway trauma and ventilator associated pneumonia may cause more problems to complicated cases of dengue. The paucity of randomized

controlled trials supporting NIV in paediatric patients with respiratory failure in complicated dengue cases makes this mode of ventilation underutilized. To the author's knowledge, only one study has been conducted on dengue patients with pleural effusion utilizing non-invasive ventilation (Alarcon). In our local setting, there has not been a study on complicated dengue cases utilizing non-invasive ventilation nor a study comparing the outcomes of dengue patients between NIV and those intubated.

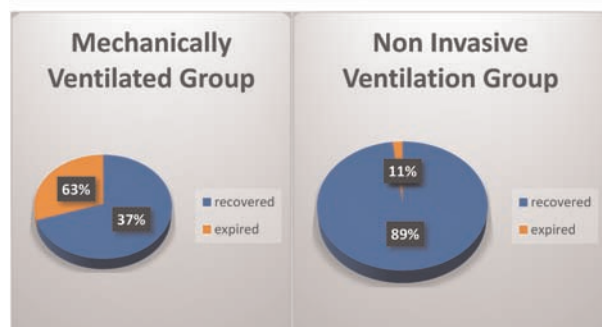
This study aims to compare the outcome of paediatric patients diagnosed as severe dengue with acute respiratory distress or failure that have used NIV to those who were mechanically ventilated due to unavailability of NIV at their time of admission.

Methods: Retrospective cross sectional prevalence study

Results: Results showed dengue patients receiving invasive ventilation had longer hospital stay, higher mortality (63% vs 11%) and more complications related to ventilation. However, they have higher PEWS score at the time of intervention as compared to those in the NIV group.

Conclusion: Non-invasive ventilation, given its advantages, could be a first line of ventilatory support in severe dengue, provided that the patient is cooperative, and hemodynamic ally stable. Patient selection is therefore important. However, this new modality, is not meant to replace invasive ventilation whenever it is clearly indicated. Further controlled studies, perhaps with a larger sample size, is recommended.

	Treatment Used	N	Mean	Std. Deviation
Patient Early Warning Score System	Mechanically Ventilated	19	5.47	1.74
	Non-invasive Ventilation	9	2.67	2.12



AP141

MIGRATING ORTHOPAEDIC PIN PRESENTING AS HAEMOPTYSIS IN A 10 YEAR OLD MALE: A CASE REPORT WIVINA BANCORO¹

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Background and Aims: A 10-year-old child diagnosed with Ewing Sarcoma s/p chemotherapy and limb salvage procedure presented with haemoptysis. Work up then showed an orthopaedic pin migrating through the lung parenchyma which was eventually lodge in the left ventricle.

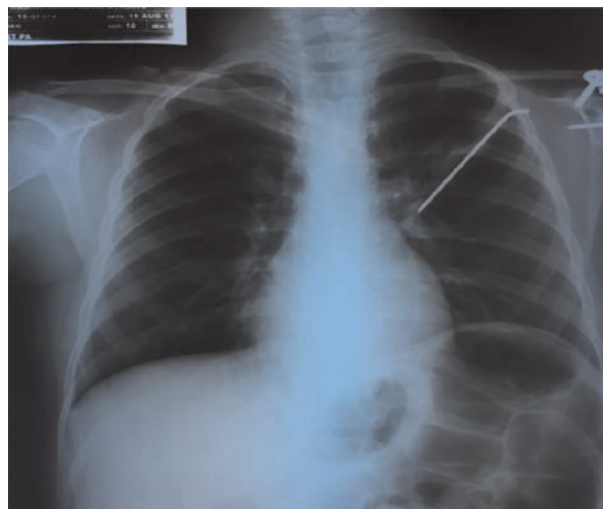
Migrating foreign bodies especially in orthopaedic fixation devices has been reported numerous times. It is a rare occurrence that can have devastating consequences. They usually present with pulmonary manifestations like cough, shortness of breath, chest pain, and in rare instances, syncope, in cases where the foreign body punctures the heart. causing hemopericardium. Its incidence is unknown but there have been several cases reported in children and adults.

Methods: This is a case report.

Results: The patient was admitted for removal of foreign body (orthopaedic pin) eventually lodge in the left ventricle. Patient underwent cardiopulmonary bypass, evacuation of hemopericardium and removal of

foreign body in the left ventricle. A lung parenchymal exploration was attempted. Patient was eventually discharged from post anaesthesia care unit and extubated. A pericardiostomy tube and chest tube thoracostomy was attached which was eventually removed. Patient was eventually discharged improved

Conclusion: Migrating foreign body traversing the lung parenchyma can cause fatal complications especially in children. In patients with history of orthopaedic fixation surgery, constant follow ups should be advised. Any pulmonary symptoms should therefore alert th physician since delayed removal can have devastating consequences.



AP142

FACTORS ASSOCIATED WITH POOR OUTCOME IN SEPSIS PATIENTS WITH LIVER CIRRHOSIS

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Background and Aims: To determine factors associated with poor outcome in sepsis patients with liver cirrhosis.

Methods: This study evaluated 628 adult sepsis patients admitted into the medical intensive care units of Kaohsiung Chang Gung Memorial Hospital during 2013 to 2016. These patients were evaluated according to the criteria for sepsis. Sepsis patients were divided into two group, with liver cirrhosis group and without liver cirrhosis group. Sequential Organ Failure Assessment (SOFA) score and factors associated with poor outcome were collected for analysis. Propensity scoring was also used for control of selection bias. Variables included in the propensity model were age, sex, presence of diabetes mellitus, hypertension, chronic kidney disease, malignancy, and APACHE II score during this admission. After correcting these confounding factors, ICU and hospital mortality analyses were repeated.

Results: Of the 628 sepsis patients in the study, 380 patients survived, and yielding mortality rate of 39.5 %. Only 51 sepsis patients with liver cirrhosis (8.1 %). After propensity score used to correcting confounding factors, short-term mortality, ICU and hospital mortality were analyzed. We found sepsis patients with liver cirrhosis had higher mortality rate up to 60.8 % than without liver cirrhosis. Short-term mortality, including 7 days mortality, 14 days mortality, 28 days mortality, and ICU mortality were also had significant difference than without liver cirrhosis group. ($P <$

0.05) SOFA score at ER, on admission day 1, day 3 and day 7 and platelet amount at ER, on admission day 1, day 3 and day 7 were associated with mortality in liver cirrhosis group.

Conclusion: We found sepsis patients with liver cirrhosis had higher mortality in short-term mortality and hospital mortality, even after propensity score matching. Factors associated with poor outcome were related to patient's SOFA score and platelet amount, even at ER or on admission day 1, day 3, and day 7.

AP143

WEANING PRACTICES AMONG PATIENTS WITH PNEUMONIA ON VENTILATORY SUPPORT AT CHINESE GENERAL HOSPITAL AND MEDICAL CENTER

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Background and Aims: The objective of this study is to evaluate the different weaning strategies performed among patients with pneumonia on ventilatory support admitted in the critical care units of the Chinese General Hospital and Medical Center in terms of success rate, identifying factors for weaning failure and determining the most effective weaning strategy.

Methods: This study was conducted by reviewing records of patients diagnosed with pneumonia that required mechanical ventilator support from August 2013 to July 2016. The demography of the patients including the primary diagnosis, reasons for intubation, Glasgow Coma Scale, mode of weaning, length of critical unit stay, serologic and biochemical profile, mechanical ventilator profile and weaning outcome was collected. Three preferred strategies for weaning was observed during the data collection and grouped namely as: A (SIMV + PSV), B (SIMV + PSV then Tpiece) and C (Tpiece alone).

Results: The mean number of days on ventilator prior to weaning was significantly shorter for Group C (1.7 days). Additionally, the average length of ICU stay of only 6 days among group C was significantly shorter. The mean number of days needed to wean was likewise shorter for group C. (2.3 days). In terms of success rate, results showed that Group C has 88.6% success however, its difference with the other groups turned out to be non-significant ($P = .1266$). The most common reason for weaning failure was the inability to protect the airway forms secretions.

Conclusion: In this study, patients weaning with T piece alone was significantly found to decrease length of ventilator days and ICU stay. Although the success rate seemed to be high as compared to the other two strategies, we have insufficient evidence to demonstrate significance. The most common reason for weaning failure in this study is due to the inability to protect the airway from secretions.

AP144

NEUTROPHIL-TO-LYMPHOCYTE RATIO AND BLOOD PLATELET COUNT CAN BE PROGNOSTIC MARKERS IN ACUTE RESPIRATORY DISTRESS SYNDROME PATIENTS OF DIFFERENT IMMUNE STATES

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Background and Aims: Acute respiratory distress syndrome (ARDS) is the leading cause of high mortality in intensive care units (ICUs) worldwide. An effective marker for prognosis in ARDS is particularly important. In this study, we explored the prognostic and predictive value of the neutrophil-to-lymphocyte ratio (NLR) and blood platelet count (PLT) in ARDS patients of different immune states.

Methods: We retrospectively included 307 ARDS patients treated at a single institute from 2008 to 2017, of which 141 patients were in immunocompromised state. Clinical characteristics and experimental test data, including the NLR, PLT were collected from medical records at 24 h after the ARDS diagnosis. Independent prognostic factors were determined by multivariate Cox regression analysis. Subgroup stratification was performed according to different factors, and the continuous factors were divided according to the median values.

Results: The immunocompromised group had a higher mortality risk than the normal group (HR, 1.440, 95%CI, 1.048–1.977). In the immunocompromised group, The PLT in survivors was significantly higher than that in non-survivors ($P < 0.001$). We took the median PLT value as the cut-off point and further divided all patients into a high PLT group (PLT $> 130 \times 10^9/L$) and a low PLT group (PLT $\leq 130 \times 10^9/L$). In the multivariate Cox regression model, we identified PLT $\leq 130 \times 10^9/L$ as an independent prognostic factor for OS [hazard ratio (HR) 1.550, (95% CI, 1.047–2.293)]. In the normal group. The NLR in survivors was significantly lower than that in non-survivors ($P < 0.001$). We took NLR = 15 as the cut-off point and further divided all patients into a high NLR group (NLR > 15) and a low NLR group (NLR ≤ 15). In the multivariate Cox regression model, we identified NLR > 15 as an independent prognostic factor for OS [hazard ratio (HR) 1.659, (95% CI, 1.073–2.565)].

Conclusion: The PLT is potentially a predictive prognostic biomarker in immunocompromised ARDS patients while NLR is significant in non-immunocompromised ARDS patients.

AP145

HYPERCAPNIA DURING WEANING FROM PROLONGED VENOVENOUS EXTRACORPOREAL MEMBRANE OXYGENATION IN ACUTE RESPIRATORY DISTRESS SYNDROME

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Background and Aims: In patients with acute respiratory distress syndrome (ARDS) failing mechanical ventilation (MV), prolonged venovenous extracorporeal membrane oxygenation (VV-ECMO) as a bridge to recovery is feasible. However, weaning from VV-ECMO is challenging when CO₂ clearance is impaired due to severe lung injury. Here we demonstrate a weaning strategy of allowing gradual tolerance of hypercapnia in this difficult situation.

Methods: We present a 52-year-old man with sudden collapse after ARDS caused by liver abscess. He received temporary venoarterial ECMO and then prolonged VV-ECMO since day 11 of admission. Methylprednisolone was given for persistent ARDS since day 23. A significant improvement in oxygenation and lung compliance was observed.

Results: ECMO weaning was postponed until day 40 due to a small pneumothorax, which was not drained. Bradycardia and hypotension occurred when gas flow was reduced from 2 to 1 L/min with blood flow maintained at 2.6 L/min. Oxygenation was adequate under FiO₂ 30%. The hemodynamic change was associated with acute hypercapnia. Because the minute ventilation was already relatively high, we chose to reduce gas flow slowly over several days to allow metabolic compensation and tolerance of hypercapnia. On day 50, he was successfully weaned from ECMO. During the 40 days of ECMO, the oxygenator was changed thrice for one haemolysis and two leakages. He received tracheostomy on day 71, was successfully weaned from MV on day 80, and transferred to the ward 2 days later. He was decannulated on day 98, and discharged home on day 103. One month later, a lung function test showed a restrictive pattern with a FVC of 1.34 L (36% of predicted) and a FEV₁ of 1.32 L (44% of predicted).

Conclusion: This case report suggests that VV-ECMO weaning can still be proceeded by allowing gradual tolerance of hypercapnia in patients with impaired CO₂ clearance after recovering from ARDS.

AP146

IMPACT OF PATIENT- AND FAMILY-CENTRED CARE MEETINGS ON INTENSIVE CARE RESOURCE UTILISATION IN TERMINALLY ILL PATIENTS: A SINGLE-CENTRE RETROSPECTIVE OBSERVATIONAL STUDY IN TAIWAN

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Background and Aims: Shared decision-making is essential for patients and their families when facing serious and life-threatening diseases. This study aimed to evaluate the impact of patient- and family-centred care meetings (PFCCM) on intensive measures and resource utilisation during end-of-life (EOL) hospitalisation among terminally ill patients.

Methods: A cross-sectional study using retrospective electronic medical record review was conducted in a tertiary referral medical centre in Taiwan. We identified 6843 deceased patients with terminal illness who did or did not receive PFCCM during EOL hospitalisation between January 2013 and December 2015. The primary outcomes were the intensive care unit (ICU) transfer, invasive or non-invasive mechanical ventilation, tracheostomy, haemodialysis, and surgical intervention during the last hospitalisation; The secondary outcomes were total and daily medical expenditure per patient. A generalized estimating equation model was used to compare the differences between the two groups. Odds ratios (OR) with 95% confidence intervals (CI) were estimated.

Table. Odds ratios of intensive care measures and medical expenditure of patients with receiving patient- and family-centered care meetings

	Univariate analysis			Multivariate analysis ^a		
	OR	(95% CI)	p Value	OR	(95% CI)	p Value
ICU admission	0.36	(0.29 to 0.45)	<0.001	0.44	(0.34 to 0.57)	<0.001
Surgery	0.72	(0.58 to 0.89)	0.003	0.74	(0.58 to 0.95)	0.020
Invasive mechanical ventilation	0.40	(0.32 to 0.51)	<0.001	0.50	(0.38 to 0.66)	<0.001
Non-invasive ventilation	0.85	(0.63 to 1.14)	0.269	0.96	(0.70 to 1.31)	0.785
Tracheostomy	0.98	(0.60 to 1.59)	0.930	1.06	(0.62 to 1.83)	0.821
Hemodialysis	0.75	(0.55 to 1.01)	0.062	0.84	(0.59 to 1.17)	0.302
Total medical expenditure (NT\$)	0.89	(0.77 to 1.03)	0.117	0.88	(0.82 to 0.95)	<0.001
Daily medical expenditure (NT\$)	0.63	(0.59 to 0.68)	<0.001	0.83	(0.77 to 0.89)	<0.001

CI, confidence interval; ICU, intensive care unit; NT\$, new Taiwan dollars; OR, odds ratio.

^a Adjusted for patient's age, gender, catastrophic diseases, main diagnoses, Charlson comorbidity index score, LOS, disposition status and year of admission as compared with patients without receiving patient- and family-centered care meetings during end-of-life hospitalisation.

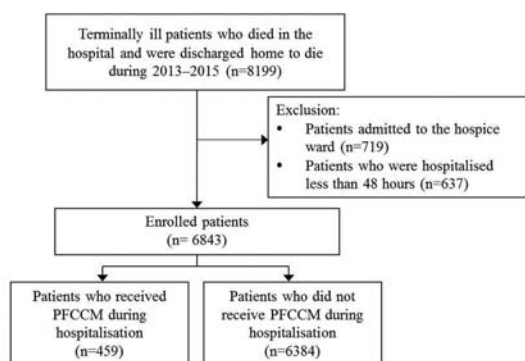


Figure. Flow chart for study inclusion

Results: This study identified 459 patients (6.7%) who received PFCCM during EOL hospitalisation. Multivariate analyses showed that patients who received PFCCM were less likely to have ICU admissions (OR 0.44, 95% CI 0.34 to 0.57), and to undergo surgical interventions (OR 0.74, 95% CI 0.58 to

0.95) and invasive mechanical ventilation (OR 0.50, 95% CI 0.38 to 0.66) during the last hospitalisation, compared with those who did not, after adjusting for patient demographics and clinical conditions and year of admission. Additionally, PFCCM patients also had significantly lower total medical expenditures (OR 0.88, 95% CI 0.82 to 0.95) than non-PFCCM patients.

Conclusion: Patient–physician discussion through PFCCM is associated with less intensive care utilisation and medical expenditure during EOL hospitalisation in terminally ill patients.

AP147

FACTORS ASSOCIATED WITH HIGH FLOW OXYGEN THERAPY FAILURE IN ACUTE HYPOXEMIC RESPIRATORY FAILURE PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: The aim of this study was to identify factors associated with the failure of high-flow oxygen therapy (HFOT) for acute respiratory failure in idiopathic pulmonary fibrosis (IPF) patients.

Methods: We identified 46 patients with acute respiratory failure, excluding DNI (Do Not Intubate), among 79 IPF-diagnosed patients who received HFOT from October 2013 to March 2018. We retrospectively analyzed the patients' medical records and looked for factors related to HFOT failure.

Results: Of the 46 patients, 13 (28%) were successfully recovered, and 33 (72%) had invasive mechanical ventilation due to HFOT failure. Among the parameters analyzed, HFOT flow setting and heart rate (HR) were significantly higher in the HFOT failure group at 24 h and 48 h after the start of HFOT (Flow setting at 24 h: 44.4 ± 8.7 vs 36.4 ± 5.5, *P* = .008, Flow setting at 48 h: 41.7 ± 6.6 vs 35.9 ± 5.4, *P* = .022, HR at 24 h: 97 ± 15.3 vs 85.3 ± 11.9, *P* = .032, HR at 48 h: 96 ± 17.1 vs 79.6 ± 13.6, *P* = .012). In addition, estimated PaO₂/FiO₂ ratio before HFOT initiation were significantly lower in HFOT failure group compared with the success group (70.8 ± 29.9 vs 139.7 ± 64.0, *P* = .003). There were 20 patients (43%) with lung transplantation, and the proportion was significantly higher in HFOT failure group (54.5% vs 15.4%, *P* = .016).

Conclusion: Estimated PaO₂/FiO₂ ratio before HFOT initiation and higher HFOT flow setting and HR at 24 and 48 h after initiation may be used as a predictor of HFOT failure. A large-scale study of various parameters to predict HFOT failure is needed.

AP148

FIRST CASE OF ACUTE RESPIRATORY DISTRESS SYNDROME AND ALIMENTARY TRACT HAEMORRHAGE FOLLOWING MASS INGESTION OF METHYLISOTHIAZOLINONE

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Background and Aims: Methylisothiazolinone (MIT) is one kind of widely used broad-spectrum biocides. Since its extensive use in the 80s as a preservative, the frequency of MIT-related health concerns is increasingly rising. To our knowledge, there is little evidences supporting the environmentally acute and mass exposure to MIT resulting in acute respiratory distress syndrome.

Methods: Here, we report the first case of acute respiratory distress syndrome (ARDS) and alimentary tract haemorrhage following mass ingestion of methylisothiazolinone.

Results: A 42-year man emergently presented with burning throat and abdominal pain after accidental ingestion of about 10 mL MIT with concentration of 14%. Gastric lavage was immediately operated. The patient felt severe progressive respiratory distress and had to undergo an emergency tracheotomy and receive ventilator care. The physical examination revealed conjunctival haemorrhage (Figure 1) and abdominal distention. The CT revealed pleural effusion and oropharynx constriction (Figure 2). APACHE2 score equals 7 and SOFA score 2. The patient received a diagnosis of acute respiratory distress syndrome (ARDS) and alimentary tract haemorrhage based on the data (symptoms, signs, and laboratory tests), which showed the rapidly deteriorating condition following mass ingestion of MIT. Symptomatic treatments were continued and the patient prognosed well.

Conclusion: Though the patient in our case recovered from ARDS and alimentary tract haemorrhage, long-term follow-up is necessary because experimental evidences showed that peripheral airway dysfunction following only exposure to a mixture of CMIT/MIT is irreversible, suggesting a possibility of pulmonary damage that was expected to be considerably severe. This notable case also helps clinicians, patients, families, and other workers to better understand the importance of norm in regulating MIT use in practice.



Figure 1. The physical examination revealed conjunctival hemorrhage.

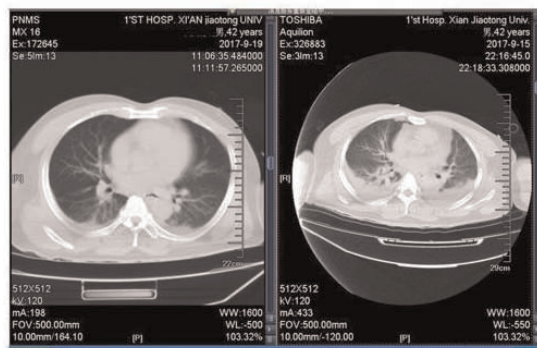


Figure 2. The computed tomography revealed pleural effusion and oropharynx constriction (left) and improvement after treatment (right).

Background and Aims: Studies evaluating the impact of physical function on weaning outcome and survival in patients requiring prolonged mechanical ventilation (PMV) for post-intensive care are scarce.

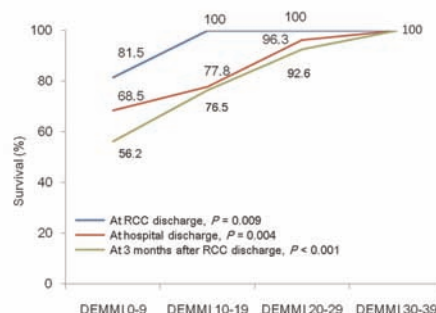
Methods: We retrospectively enrolled patients requiring PMV support who were admitted to the respiratory care center (RCC), a specialized post-intensive care weaning facility with structured pulmonary rehabilitation program, from January 2017 through December 2017. Physical function was assessed repeatedly with the de Morton Mobility Index (DEMMI), at RCC admission and before RCC discharge, respectively. Multivariate regression analyses were used to identify significant, independent parameters associated with weaning outcome. The survival status at RCC discharge, hospital discharge, and 3 months after RCC discharge were compared between different DEMMI groups.

Table 1. Multivariate logistic regression models for significant clinical characteristics associated with weaning success*

Parameters	β	SE	Odds ratio (95% CI)	P
COPD (yes vs. no)	-1.510	0.587	0.211 (0.070–0.698)	.010
ICU category (medical vs. surgical)	-0.922	0.475	0.398 (0.157–1.008)	.052
DEMMI score before RCC discharge	0.062	0.025	1.064 (1.013–1.117)	.013
Albumin (g/dL) at RCC admission	0.910	0.460	2.483 (1.008–6.118)	.048
RSBI (≤ 105 vs. > 105)	1.136	0.496	3.115 (1.177–8.243)	.022

CI, confidence interval; COPD, Chronic obstructive pulmonary disease; DEMMI, the de Morton Mobility Index; ICU, intensive care unit; RCC, respiratory care center; RSBI, rapid shallow breathing index; SE, standard error.

*Variables with statistical significance ($P < .05$) in the univariate analyses were included in the multivariate logistic regression models. Backward variable selection was performed, and the criteria of P values for entry and stay were set at .05 and .10, respectively.



Results: In total, 146 patients were enrolled. The weaning success rate was 69.2%, and survival rates at RCC discharge, hospital discharge and 3 months after RCC discharge were 88.4%, 76.7% and 68.3%, respectively. Multivariate logistic regression models showed that DEMMI scores before RCC discharge, in addition to rapid shallow breathing index ≥ 105 before RCC discharge, albumin level, and lack of diagnosis of chronic obstructive pulmonary disease, was significantly associated with weaning success (odds ratio, 1.064; 95% confidence interval, 1.013–1.117; $P = 0.013$). Patients who had higher DEMMI scores before RCC discharge had a higher probability of survival at RCC discharge ($P = 0.009$), hospital discharge ($P = 0.004$), and 3 months after RCC discharge ($P < 0.001$), and all patients with DEMMI scores ≥ 30 survived at 3 months after RCC discharge.

Conclusion: Physical function assessed with DEMMI after pulmonary rehabilitation was an independent determinant associated with weaning success in patients requiring PMV. Patient with higher DEMMI scores had a higher probability of short-term and mid-term survival.

AP149

PHYSICAL FUNCTION AFTER PULMONARY REHABILITATION AS A PREDICTOR OF WEANING SUCCESS AND SHORT-TERM AND MID-TERM SURVIVAL IN PATIENTS REQUIRING PROLONGED MECHANICAL VENTILATION

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AP150

AN OPTIMIZING MEDICAL MANAGEMENT FOR ACUTE HYPERCAPNIC RESPIRATORY FAILURE DUE TO ACUTE EXACERBATION COPD

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Background and Aims: An acute hypercapnic respiratory failure (AHRF) due to acute exacerbation chronic obstructive pulmonary disease (AECOPD) causing a life-threatening. Initial treatment by optimizing medical management and supplemental oxygen were better than mechanical ventilation.

Methods: We present a 58-year-old ambulatory patient having a COPD exacerbation, conscious, tachypneic with respiratory rate (RR) of 48/min, increasing cough and purulence sputum production, no history of hypertension. Pulse of 137/min, blood pressure (BP) was 190/140 mmHg, and pulse oxygen saturation (SpO₂) was 68%. His breath sounds were wheezes and fine crackles at bilateral lung bases. Arterial blood gas analysis (ABG) and electrolytes showed pH of 7.29, pO₂ = 0 mmHg, pCO₂ = 64.3 mmHg, HCO₃ = 30.1 meq/L, and bilateral fine infiltrates on chest x-ray. Management AHRF was conducted including a supplemental oxygen - non rebreathing mask (NRM) 10 L/m, repeated combination of short-acting inhaled β_2 agonists (SABA) and short-acting muscarinic antagonist (SAMA), inhaled long-acting muscarinic antagonists (LAMA), two puffs respimat inhaler of tiotropium bromide, i.v methylprednisolone, aminophylline infusion, quinolone, i.v furosemid and amlodipine besylate.

Results: The symptoms were reduced after 2 h observation and was being stabil condition, RR of 24/min, BP was 140/90 mmHg, AGD results were improving by pH of 7.47, pO₂ = 86 mmHg, pCO₂ = 32.7 mmHg, HCO₃ = 23.6 meq/L after 24 h observation.

Conclusion: An optimizing medical management of AHRF can prevent a life-threatening and death. We reported the using of tiotropium bromide or LAMA for hypercapnic respiratory failure. A very slow dissociation of tiotropium bromide from muscarinic receptors (M₁ and M₃) cause long broncodilation and a faster dissociation from M₂-receptors cause vasoconstriction immediately to overcome vasodilatation caused by hypercapnia or CO₂ retention. The clinical studies are needed to investigate the use of inhaled LAMA especially tiotropium bromide during hypercapnic respiratory failure.

AP151

CLINICAL PARAMETERS AND SERUM BIOMARKER FOR INFLUENCING ICU MORTALITY IN SEVERE SEPSIS PATIENTS

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Background and Aims: The ICU mortality in severe sepsis patient is still high. In this study, we wish to know that which clinical parameter and serum biomarker over time will influence ICU mortality in sepsis patients mostly.

Methods: A combined retrospective and prospective observational study from a cohort of adult sepsis patients admitted to three medical ICUs at Kaohsiung Chang Gung Memorial Hospital in Taiwan between August 2013 and June 2016. At each sepsis patients admitted to medical ICU, clinical parameters such as Apache II score, SOFA score, PaO₂/FIO₂ values, and serum biomarkers such as CRP, albumin, lactate, procalcitonin were studied on day 1, day 3, day 7 after ICU admission for severity evaluation.

Results: A total 782 severe sepsis patients admitted to medical ICU in this period. We found that 210 patients were ICU non-survivors and 572 patients were ICU survivors. In this study, we can see the level of serum biomarkers such as CRP3, CRP7, PCT7, lactate 1, lactate 3, lactate 7 were higher and albumin 1, albumin 3 were lower for ICU mortality in severe sepsis. Clinical parameter scoring such as Apache II score, SOFA 1, SOFA 3, SOFA 7 were higher for ICU mortality and the values of PaO₂/FIO₂ 1, PaO₂/FIO₂ 3, PaO₂/FIO₂ 7 were lower for ICU mortality in severe sepsis patients. By multivariate analysis, we can see CRP

7, SOFA 7, PaO₂/FIO₂ 1 values were the independent factors for predicting ICU mortality.

Conclusion: Severe sepsis is a complex disease and little clinical parameters and serum biomarkers would predict ICU mortality. In this retrospective cohort, we set much clinical parameters and serum biomarkers over time and use multivariate analysis method to search possible factors for ICU mortality. Finally, we find that CRP 7, SOFA 7, PaO₂/FIO₂ 1 values were the independent factors for predicting ICU mortality in severe sepsis patients.

Table 1: Clinical parameters between ICU non-survivors and ICU survivors

	ICU non-survivors n=210	ICU survivors n=572	P-value
Age	66.77±14.70	62.55±15.65	0.072
Sex			0.218
Male	77 (36.7%)	278 (48.6%)	
Female	133 (63.3%)	294 (51.4%)	
APACHE II	27.36±4.64	23.93±4.15	0.023
SOFA	1.51±0.43	1.10±0.29	0.186
SOFA 1	21.42±2.24	22.23±2.19	0.163
SOFA 3	25.54±2.3	23.63±2.02	0.003
SOFA 7	10.51±4.81	8.32±3.91	<0.001
SOFA 1	8.91±5.55	6.51±3.98	<0.001
SOFA 3	7.47±5.99	5.29±3.32	<0.001
SOFA 7	1.88±1.42	1.06±0.55	<0.001
SOFA 1	1.91±0.92	1.06±0.47	<0.001
SOFA 3	1.81±0.92	1.04±0.45	<0.001
SOFA 7	1.81±0.92	1.04±0.45	<0.001
CRP	28.85±19.3	10.99±12.07	0.009
CRP 1	24.81±19.3	10.99±12.07	0.168
CRP 3	104.44±59.3	33.11±27.07	0.042
CRP 7	58.91±19.3	10.99±12.07	0.004
Albumin	2.92±0.39	3.31±0.37	<0.001
Albumin 1	2.92±0.39	3.31±0.37	<0.001
Albumin 3	2.92±0.39	3.31±0.37	<0.001
Albumin 7	2.92±0.39	3.31±0.37	<0.001
Lactate	1.81±0.92	1.04±0.45	<0.001
Lactate 1	1.81±0.92	1.04±0.45	<0.001
Lactate 3	1.81±0.92	1.04±0.45	<0.001
Lactate 7	1.81±0.92	1.04±0.45	<0.001

Table 2: Serum biomarkers correlation between ICU non-survivors and ICU survivors

	ICU non-survivors n=210	ICU survivors n=572	P-value
CRP 1	143.41±18.32	141.01±13.35	0.486
CRP 3	143.32±15.42	140.89±13.72	0.024
CRP 7	133.10±9.70	137.00±12.44	<0.001
Albumin 1	2.88±0.71	2.88±1.38	0.038
Albumin 3	2.48±0.51	2.91±0.89	0.049
Albumin 7	2.48±0.51	2.91±0.89	0.005
PCT 1	26.47±5.51	23.67±4.80	0.005
PCT 3	26.47±5.51	15.53±4.98	0.136
PCT 7	18.71±4.13	4.95±1.84	0.021
Lactate 1	12.35±5.85	27.65±24.07	<0.001
Lactate 3	28.73±30.42	13.28±9.75	<0.001
Lactate 7	29.44±32.84	13.65±8.53	<0.001

Table 3: Predictors of ICU mortality in severe sepsis patients by multivariate logistic regression analysis

	OR (95% CI)	P-value
CRP 7	1.001 (1.000-1.002)	0.001
SOFA 7	1.001 (1.000-1.002)	0.001
PaO ₂ /FIO ₂ 1	0.999 (0.998-1.000)	0.001

AP152

SINGLE-CENTRE RETROSPECTIVE STUDY OF ADMISSIONS TO THE MEDICAL INTENSIVE CARE UNIT (MICU) AND THE UTILITY OF LACTATE PROCALCITONIN PRODUCT IN PREDICTING MORTALITY

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Background and Aims: Literature regarding 90-day mortality in MICU patients is limited. Lactate and procalcitonin are used worldwide as markers for sepsis and shock, however their use as a predictor of mortality in sepsis has not been assessed. This study aims to examine the clinical profile and determinants of 90-day mortality in MICU admissions, and ability of lactate*procalcitonin product on admission to predict mortality in a subgroup with sepsis.

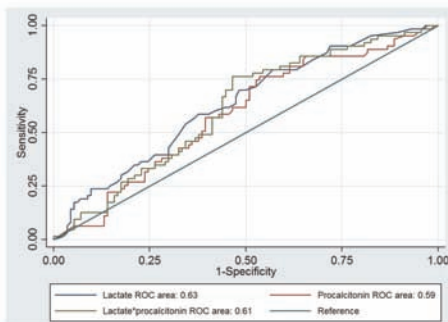
Methods: Data from 538 consecutive MICU admissions to Tan Tock Seng Hospital, Singapore, in 2015 was analyzed using multivariable logistic regression to evaluate independent predictors of 90-day mortality. The ability of lactate, procalcitonin and lactate*procalcitonin to predict mortality was assessed using area under the receiver operating characteristic curve (AUROC).

Results: The 90-day mortality was 45.5%. Mean age was 65 (SD 15) years. Sequential organ failure assessment (SOFA) score, lactate on admission, and Pulseless Electrical Activity (PEA) on arrival were independent predictors of mortality (Table 1). In sepsis subgroup, lactate was a significant predictor of mortality ($P = 0.006$) AUROC 0.63, while the lactate*procalcitonin product did not show significant association with mortality. A history of Chronic Obstructive Pulmonary Disease (COPD) was not associated with an increased mortality.

Conclusion: High SOFA, raised lactate levels, and PEA presentation predicted mortality in our cohort. Lactate*procalcitonin product needs further studies to evaluate its utility as a predictor of mortality.

Table 1: Predictors of 90-day MICU mortality

Variable	Adjusted ¹ OR (95% CI)	P-value
Age	0.99 (0.97-1.03)	0.935
History of Chronic Obstructive Pulmonary Disease	0.11 (0.01-0.84)	0.034
History of Asthma	0.96 (0.26-3.56)	0.951
SOFA score at admission	1.20 (1.03-1.41)	0.019
Lactate at admission	1.19 (1.02-1.41)	0.024
Procalcitonin	1.00 (0.98-1.01)	0.732
PEA arrest	12.14 (1.11-132.86)	0.041



AP153

EXTRACORPOREAL MEMBRANE OXYGENATION APPLICATION IN PREGNANT PATIENT WITH UROSEPSIS ASSOCIATED ACUTE RESPIRATORY DISTRESS SYNDROME – A CASE REPORT

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Background and Aims: Acute Respiratory Distress Syndrome (ARDS) is an uncommon condition during pregnancy. The common causes of ARDS during pregnancy are sepsis from pulmonary or non-pulmonary aetiologies, amniotic fluid embolism, preeclampsia, complications from tocolytic therapy, major trauma, transfusion with multiple-unit blood products, and aspiration of gastric content.

Methods: We report a case of a 19-year-old woman, primipara, with pregnancy 21+2 weeks, who was admitted due to urosepsis with progression to ARDS. The diagnosis was supported by urine culture with *Escherichia coli* without pathogen yielded from sputum and bronchial lavage. And high-resolution computed tomography revealed bilateral symmetrical consolidation.

Results: Transient fetal heart rate decrease noted during admission and hypoxemic respiratory failure developed on the next day. In spite of the application of lung protective ventilation with high level of positive end-expiratory pressure (PEEP) up to 16 mmHg and adequate sedation, refractory hypoxemia (PaO₂: 78.5 mmHg, FiO₂: 100%, PaO₂/FiO₂: 78.5) persisted still. Extracorporeal membrane oxygenation (ECMO) was then applied, and arterial oxygenation improved gradually. ECMO was removed four days later and then she was extubated on the next day. She was discharged with pregnancy 23+2 weeks, without other organs failure.

Conclusion: According to reported studies and our case's experience, extracorporeal life support may be beneficial in the management of the pregnant patient with severe ARDS.

THE EFFECTIVENESS OF BRONCHOSCOPY IN RESPIRATORY FAILURE PATIENTS

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Background and Aims: Respiratory failure is caused by a variety of factors, depending on the patient's background. Sometimes, non-invasive examination alone may not be able to clarify the cause of respiratory failure. In such a case, we often perform bronchoscopy, but its safety and effectiveness are not clear.

Methods: Between April 1, 2014 and March 31, 2017, We extracted patients entering the ICU/emergency ward of our hospital who underwent bronchoscopy and analyzed basic diseases, test results, diagnosis, and outcome etc.

Results: Bronchoscopic examination was performed on 54 cases (36 males, 18 females, average age 70.1 years). The underlying diseases were 9 autoimmune diseases, 7 blood disorders, 1 HIV infection, etc.

In 49 cases, it was considered that the results contributed to the determination of the treatment policy, of which 38 patients improved. No complications were observed. Results were as follows: interstitial pneumonia 7 cases (drug induced pneumonia, acute eosinophilic pneumonia, interstitial pneumonia associated with collagen disease, idiopathic pulmonary fibrosis), ARDS 6 cases, diffuse alveolar haemorrhage 11 cases, excessive sputum 5 cases, respiratory infection 10 cases, respiratory tract bleeding 4 cases, chemical pneumonia 1 case. In 5 cases, the cause of respiratory failure could not be identified, and four of whom died.

Conclusion: Bronchoscopy on respiratory failure patients is useful for determining the treatment policy. It was considered to lead to improvement in patient's prognosis.

AP155

SEVERE INFLUENZA IN THE INTENSIVE CARE UNITS IN 2018: EXPERIENCE OF A REGIONAL HOSPITAL WEI-SHENG CHUNG¹

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Background and Aims: Seasonal influenza can devastate people's health due to frequent emergence of antigen variants. Severe influenza is defined as acute influenza with a syndrome of respiratory distress, altered consciousness, or accompanying a severe heart complication. We reported the patients with severe influenza in the intensive care units in a regional teaching hospital in 2018.

Methods: We enrolled patients with severe influenza illness complicated with respiratory failure requiring admission to the intensive care unit from Jan 1 2018 to March 31, 2018 in a regional hospital.

Results: In total, 7 patients (4 men and 3 women) with severe influenza illness complicated with respiratory failure were admitted at the intensive care unit in a regional teaching hospital from Jan 1 2018 to March 31, 2018. Most of patients (71.4%) were older adults. Their mean age was 79.0 ± 15.3 years (range from 58 y to 94 y). Two patients (28.6%) have received influenza vaccine in 2016. All patients were infected with influenza B. The average days from URI symptoms to ICU admission were 3.6 ± 3.1 days. Five patients (71.4%) received endotracheal tube with ventilator support, one patient (14.3%) received a non-invasive ventilator, and one patient (14.3%) received a venturi mask. The mean days from URI symptoms to prescribing antiviral therapy were 6.6

± 3.8 days. Five of them (71.4%) received peramivir therapy and survived the severe influenza events. Two patients (28.6%) died and their APACH II scores were more than 30. The dead patients have comorbidity of schizophrenia and chronic obstructive pulmonary disease. All patients have received concomitant use of broad spectrum antibiotics (ampicillin/subactam and clarithromycin, amoxicillin/clavulanate and clarithromycin, or levofloxacin).

Conclusion: The case fatality rate for severe influenza B with respiratory failure was 28.6% in a regional teaching hospital in 2018. Patients with High APACH II scores need aggressive treatment.

AP156

INCIDENCE AND CLINICAL OUTCOMES OF DELIRIUM IN CRITICALLY ILL MEDICAL PATIENTS IN A TERTIARY UNIVERSITY TEACHING HOSPITAL

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Background and Aims: Delirium is a common complication in hospitalized patients. Its incidence varies from 20 to 40%. However, data in Thai patients were limited. This study aimed to determine the incidence, risk factors and clinical outcomes of delirium in critically ill medical patients.

Methods: A prospective observational study was conducted in our medical intensive care units (ICUs) between October 2016 and March 2017. Delirium was daily diagnosed by Confusion Assessment Method for the ICU (CAM-ICU), Thai version. Baseline characteristics, medications used in ICUs and clinical outcomes were collected. Risk factors of delirium were identified by using logistic regression.

Results: Totally, 270 patients participated in our study. The majority of them (58.5%) were male with mean age of 63.3 years and mean APACHE II score of 15.68. The overall incidence of delirium in our ICUs was 47.4%. Factors of delirium were male (adjusted OR 2.36, $P = 0.015$), norepinephrine (adjusted OR 7.37, $P < 0.001$), midazolam (adjusted OR 5.44, $P = 0.006$) and fentanyl (OR 2.82, $P = 0.01$). The delirious patients significantly had longer median length of ICU stay (5.5 vs 2 days, $P < 0.001$) and lower median number of ventilator free-day in 28 days (0 vs 27 days, $P < 0.001$) than non-delirious patients. The hospital mortality rate of delirious patients tended to be higher than that of non-delirious patients (53.1 % vs 18.4%, $P = 0.005$). However, after adjusting for age, sex, APACHE II score and medications, delirium was not associated with mortality (OR 2.08, $P = 0.058$).

Conclusion: The incidence of delirium in the patients admitted to our ICUs was high. According to significant factors of delirium including the use of norepinephrine, midazolam and fentanyl, minimizing the use of sedative drugs potentially reduces delirium and its complications. Delirious patients had significantly longer length of ICU stay and duration of mechanical ventilation. The interventions for delirium prevention and treatment should be studied to reduce these morbidities.

AP157

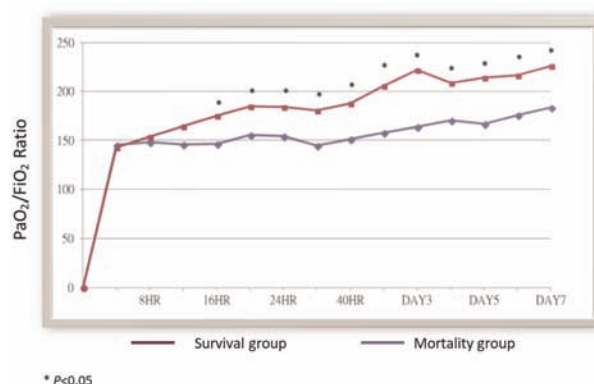
DIFFERENT PAO₂/FIO₂ MEASURING TIME CATEGORIZES DIFFERENT SEVERITY OF LUNG INJURY IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME: A PROSPECTIVE STUDY

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Background and Aims: The definitions of lung severity of acute respiratory distress syndrome (ARDS) patients depend on the PaO₂/FIO₂ ratio. The PaO₂/FIO₂ in most patients can be easily manipulated by altering PEEP, FIO₂, and measuring time. This prospective study was designed to assess different PaO₂/FIO₂ measuring time affects the categorizing the severity of lung injury.

* $P < 0.05$

Methods: Patients were enrolled when they met the American-European Consensus Conference definitions for ARDS from May 2012 to April 2014 in five medical and surgical ICUs of a regional hospital in Taiwan. After enrolment, all patients were put on a standard lung protective ventilatory strategy, including a tidal volume of 6–8 mL/kg predicted body weight, a plateau pressure not exceeded 32 cm H₂O, at a ventilatory rate to maintain PaCO₂ at 35–50 mm Hg, and a combination of PEEP >10 and FIO₂ >0.5 to maintain PaO₂ >60 mm Hg or SpO₂ >90%. Arterial blood gases were obtained 30 min later after standard lung protective ventilatory strategy settings, and then at 4 h, 8 h, 12 h, 16 h, 20 h, 24 h on day 1, and 32 h, 40 h, 48 h on day 2, then once a day from day 3 to day 7.

Results: We enrolled 102 patients and the overall 28-day mortality rate was 51.0%. After analyzing different measuring time, the survival group had significantly better PaO₂/FIO₂ ratio since 16 h after the time meeting ARDS criteria (181.4 ± 3.5 vs 141.5 ± 62.7 ; $P = 0.009$), and at 20 h (184.9 ± 9.9 vs 155.7 ± 10 , $P = 0.039$), 24 h (185.4 ± 9.9 vs 151.7 ± 10.1 , $P = 0.018$), 32 h (183.0 ± 9.9 vs 142.0 ± 10.2 , $P = 0.004$), 40 h (186.9 ± 9.9 vs 152.6 ± 10.4 , $P = 0.017$), 48 h (208.6 ± 10.0 vs 153.8 ± 10.7 , $P < 0.001$), and on day 3 to day 7 ($P < 0.001$) (Figure 1).

Conclusion: In order to categorize lung severity of ARDS patients, PaO₂/FIO₂ ratio criteria should be reassessing at least 16 h after the timing meeting ARDS criteria.

AP158

COMPARISON OF REINTUBATION RATE AND MORTALITY BY HIGH FLOW NASAL CANNULA AND CONVENTIONAL OXYGEN THERAPY IN POST-EXTUBATION PATIENT : A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: High-flow nasal cannula (HFNC) oxygen therapy comprises an air/oxygen blender, an active humidifier, a single heated circuit, and a nasal cannula. It reduction of anatomical dead space, PEEP effect, constant fraction of inspired oxygen, and good humidification. While there have been no big randomized clinical trials comparing reintubation rate in HFNC and conventional oxygen therapy.

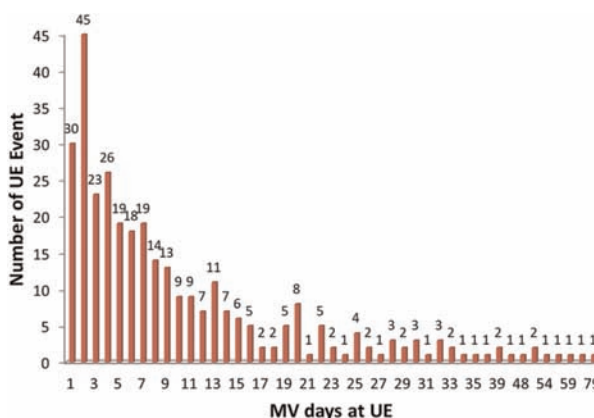
Methods: We identified and collected randomized controlled trials (RCTs) which reported the using HFNC and conventional oxygen therapy with reintubation rate from 2009 Jan. to 2017 Dec. in Cochrane Library, PubMed and Clinical Key. We used the keywords of High flow nasal cannula, oxygen therapy and post-extubation. According to risk level to evaluate the validity of studies and so as to Review Manager 5.3 to calculate for risk ratio, mean and standard deviation.

Results: There were 5 RCTs trials with 1117 patients were included to our systematic review. First, HFNC group was associated with decrease the rate of overall reintubation (RR = 1.09, 95% CI = 1.05–1.14, $P = 0.45$), compared with conventional oxygenation therapy. Second, HFNC group was associated with decrease the rate of overall hypoxemia (RR = 1.36, 95% CI = 0.92–2.00, $P = 0.16$) and decrease the rate of overall mortality (RR = 1.19, 95% CI = 0.67–2.11, $P = 0.89$).

Conclusion: Using high flow nasal cannula compare with general oxygen treatment equipment after extubation, which can significant reduce overall reintubation rate, mortality rate and improve oxygenation.

(72.5% vs 70.9%; $P = .762$), and in-hospital mortality rate (27.5% vs 24.1%; $P = .518$).

Conclusion: The overall weaning rate and in-hospital mortality rates of the UE and non-UE patients were similar. UE occurred in ordinary ward also had similar outcomes to those in ICU.



APL006

OUTCOMES OF UNPLANNED EXTUBATION IN ORDINARY WARD ARE SIMILAR TO THOSE IN INTENSIVE CARE UNIT:

A RETROSPECTIVE CASE-CONTROL STUDY

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Background and Aims: Unplanned extubation (UE) causes considerable adverse effects in patients receiving mechanical ventilation (MV). Previous literature showed inconsistent prognosis in patients with UE. This study aimed to evaluate the clinical implications and outcomes of UE.

Methods: The intubated adult patients with MV support were enrolled and divided into the UE and non-UE groups. Demographic data, admission unit, MV duration, overall weaning rate and mortality rates were compared. The differences in the clinical features and outcomes of UE in patients admitted to ordinary ward and intensive care unit (ICU) were assessed.

Results: Totally 9245 intubated adult patients were included. UE occurred in 303 (3.5%) patients, and occurred 0.27 times/100 MV days. Old age, non-operation related MV cause, and admission out of the ICU were significant factors associated with UE. UE patients showed a trend of better overall weaning rate (71.9% vs 66.7%, $P = .054$) than non-UE. The in-hospital mortality rate (25.7% vs 24.8%, $P = .713$) were similar between the UE and non-UE patients. The reintubation rate of UE patients was 44.1% (142/322). Successful UEs were associated with patients in weaning process (52.8% vs 38.7%, $P = .012$), and patients received non-invasive positive pressure ventilation (NIPPV) support after UE (19.4% vs 3.5%, $P < .001$). Patients with successful UE had significantly shorter MV days, lower APACHE II score, higher overall weaning rate, and lower mortality than those with unsuccessful UE. Outcomes of UE occurred in ordinary ward were not different than those in ICU, with similar reintubation rate (41.2% vs 45.5%; $P = .472$), overall weaning rate

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AP159

PARTICULATE MATTER INCREASES EOSINOPHILIC AIRWAY INFLAMMATION

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Background and Aims: Particulate matter is increasing every year in Asia. And outdoor activities are increasingly difficult and quality of life is diminishing from particulate matter. It is not fully understood how the airway is affected when inhaling particulate matter. We investigated the correlation between particulate matter and fractional exhaled nitric oxide to determine whether particulate matter causes eosinophilic airway inflammation.

Methods: We analyzed fractional exhaled nitric oxide results from January 2016 to December 2017 at the Korea University Guro Hospital. Particulate matter data were provided by the government of the Republic of South Korea. We analyzed the correlation between particulate matter and fractional exhaled nitric oxide by a Pearson correlation analysis and by a multivariate linear regression analysis. To identify the most correlated times, we analyzed the correlation between the fractional exhaled nitric oxide and particulate matter daily average from the day of visit to 4 days before visit.

Results: Fractional exhaled nitric oxide positively correlated with particulate matter at two days before hospital visit in the Pearson correlation (Pearson correlation coefficient = 0.057; P -value = 0.023) and in the multivariate linear regression analysis ($B = 0.062$, P -value = 0.028). If the particulate matter increased by 100, the fractional exhaled nitric oxide value was expected to rise to 6.2 ppb.

Conclusion: There was a positive correlation between particulate matter and fractional exhaled nitric oxide. The positive correlation was

also found in healthy people and asthmatic patients. Therefore, particulate matter can increase eosinophilic airway inflammation.

AP160

THE EFFECTS OF AMBIENT FINE PARTICULATES ON 1-YEAR CHANGES OF LUNG FUNCTION AMONG THE ELDERLY IN TAIWAN

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Background and Aims: Elders have been considered being vulnerable to air pollution, including particulate matters (PM). However, relatively scant attention has been paid for the long-term PM effect on the elder's lung function parameters, especially in Asian population. The study aims to evaluate the association and the potential source related effect of exposure to ambient air pollutants and lung function change in general elders in Taiwan.

Methods: We conducted an elderly cohort study from October 2015 to December 2017. Subjects were enrolled from five hospitals of variant background PM concentrations. Elders aged 65 and didn't have cancer and communication problems were invited to participate in this study. Forced lung function was measured annually by uniform machines in the five hospitals. Long-term (2016 annual mean concentration) exposure to air pollution was estimated by Kriging method at the residential address of each subject. Principle component analysis with varimax rotation was done for six criterion air pollutants to describe the potential sources (factors) and extract the factor scores. We assessed the association between exposures and 1-year lung function change by linear regression modelling with adjustment of demographics, baseline lung function and co-pollutants.

Results: 861 subjects with mean age of 70.3 year old completed baseline and 1-year follow-up lung function studies. After adjustment for confounding factors, per 1 $\mu\text{g}/\text{m}^3$ increase of fine particulates were significantly associated with 1-year decline of FVC (-18.23 mL , -0.75% , $P < 0.0001$) and FEV1 (-15.23 mL , -0.8% , $P < 0.0001$). Factor analysis identified stationary fossil fuel combustion- (PM & sulfur dioxide) and traffic-related (nitric dioxide & carbon monoxide) sources of air pollution. The former was associated with lung function decline.

Conclusion: Long-term exposure to ambient fine particulates and stationary fossil fuel combustion-related air pollution were associated with 1-year lung function decline among the elders in Taiwan.

AUTOPHAGY INVOLVED OXIDATIVE STRESS INDUCED BY ATMOSPHERIC FINE PARTICLES (PM_{2.5}) IN MOUSE ALVEOLAR MACROPHAGES (MH-S)

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Background and Aims: Atmospheric fine particles (PM_{2.5}) are closely related with the morbidity and mortality of acute and chronic inflammatory disease. Although the exact mechanism between PM_{2.5} exposure and its related adverse effects is not clear, PM_{2.5}-induced oxidative stress has been considered as one of the important molecular mechanism during the whole path-physiological process. This work aims to investigate the effect of PM_{2.5} on cell autophagy of mouse alveolar macrophages (MH-S), further explore the effect of the regulating role in the upstream and downstream mechanism and levels of intracellular reactive oxygen species (ROS) of the body in vitro.

Methods: The effects of the PM_{2.5} on morphological of autophagy in MH-S were analyzed by transmission electron microscopy, GFP-LC3 puncta was observed by confocal fluorescence microscope. The cell viability was detected by MTT, the intracellular levels of ROS cells were measured using DCFH-DA. The effects of LC3II and p62 were observed with Western blotting. PM_{2.5}-induced mRNA expression of autophagy-related protein p62 and LC3II was observed with RT-PCR.

Results: Treatment of MH-S cells with PM_{2.5} triggered typical features of autophagy which can be measured by transmission electron microscope. The cell viability showed both time- and concentration-dependent decrease when exposure to PM_{2.5}, which can be attributed to the increased level of ROS. PM_{2.5}-induced autophagy was indicated by an increase in LC3II and a decrease in p62, and accumulation of LC3II and p62 in both time- and concentration-dependent manner. PM_{2.5} 100 $\mu\text{g}/\text{mL}$ treated cells with 24 h showed a marked increase in fluorescence intensity of ROS ($P < 0.05$), and there were obvious autophagic vacuoles around the nucleus.

Conclusion: These results suggest the possibility that PM_{2.5}-induced oxidative stress probably plays a key role in autophagy in MH-S cells.

AP162

DEVELOPMENT OF COMMUNITY PHARMACY TO THE CENTER OF SMOKING CESSATION, INITIATIVE IN THAILAND SUNE LERTSINUDOM^{1*}, PENTIPA KAEWKETTHONG², SIRIRAT TUNPICHART²

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Background and Aims: Smoke free Pharmacy network and Community Pharmacy Association (Thailand) has initiated the development of Community pharmacy to the center of Smoking cessation project for smoker could be accessed smoking cessation service. Therefore, data should be collected and analyzed to assess the outcome of development of Community pharmacy to the center of Smoking cessation project.

Methods: A retrospective study. We collected data from CPA PROJECT database of Community Pharmacy Association (Thailand). The data was gathered from clients who participate during 1 July 2016 to 31 December 2017. We use descriptive statistics by percentages, median, and interquartile range. The data were then analyzed using inferential statistics, including Mann-Whitney U Test, Wilcoxon Signed Rank Test, Pearson Chi-square Test.

Results: There were 58 drug stores and 1,168 clients included in the study. The majority of clients were male (92.0%) with median age of 41 (27.0) years old. The services were provided for 432 (37%) clients in Bangkok and 736 (63%) clients in other provinces. Clients were psychological and behavioural dependence 93.2% and 92.9% respectively. Health was the most important motivation to quit (69.7%). Number of initial cigarettes per day was 13.5 (10.0) and 51.8% of clients had moderate to high nicotine dependence. The results showed that number of cigarettes per day and exhaled CO significantly decreased (15.0 [10.0], 0 [3.0]; $P < 0.001$) and (10.0 [9.0], 5.0 [5.0]; $P < 0.001$) respectively as well as % PEFR significantly increased (86.5 [22.0], 89.3 [24.3]; $P < 0.001$) and the number of people with PEFR < 80% significantly decreased (139 [35.6], 113 [29.0]; $P = 0.047$). Continuous abstinence rate ≥ 30 days were 22.9%.

Conclusion: The development of Community pharmacy to the center of Smoking cessation project provided systematic smoking cessation services by pharmacists which increase the opportunity for smokers to quit and improved lung function. Therefore, the drug stores should be promoted to participate in this project.

AP163

ROLE OF NRF2 IN LUNG INJURY INDUCED BY DIESEL EXHAUST

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Background and Aims: Diesel exhaust (DE) induced oxidative stress play an important role in proinflammatory reaction on airway. Nrf2 is involved in the transcriptional regulation of many antioxidant genes. In the present study, we investigated the role of Nrf2 in the development of DE induced lung injury in both of Nrf2+/+ and Nrf2-/- mice.

Methods: C57BL/6J Nrf2+/+ and Nrf2-/- mice were exposed to DE (DE particle 1 mg/m³) or clean air for 8 h/day and 6 days/week for 4 weeks. The cell populations and the concentration of MIP-2 in bronchoalveolar lavage fluid (BALF) were examined. We also examined the concentration of TNF- α in lung tissues by ELISA. The gene expression of antioxidant enzymes in the lung tissues were examined by real time PCR.

Results: DE particle-laden alveolar macrophages were significantly greater in Nrf2-/- than in Nrf2+/+ mice. Neutrophils number and concentration of MIP-2 in the BALF also significantly increased in Nrf2-/- mice than in Nrf2+/+ mice after DE exposure; however, concentration of TNF- α in the lung tissues decreased in Nrf2-/- mice than in Nrf2+/+ mice after DE exposure. Antioxidant enzyme genes was significantly increased in Nrf2+/+ mice compared with Nrf2-/- mice after exposed to DE.

Conclusion: Our results suggest that alveolar macrophage function was suppressed, and neutrophilic inflammation was induced by DE exposure. Nrf2 is an important protective factor against oxidative stresses, and have a possibility to lower the risk for lung injury induced by DE.

AP164

PREVALENCE, RESPIRATORY SYMPTOMS AND RISK OF COPD AMONG PNEUMOCONIOSIS PATIENTS IN CHINA: A CROSS-SECTIONAL STUDY

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Background and Aims: We sought to evaluate the incidence, risk factors of COPD in pneumoconiosis patients.

Methods: A cross-sectional study was conducted in Hunan Province. Consecutive male underground pneumoconiosis patients employed for at least 1 year were recruited from Hunan Institute of Occupational Disease Prevention. Basic information, respiratory symptoms and clinical scale were evaluated by a structured questionnaire. Pulmonary function test (PFT) and chest X-ray was also conducted.

Results: The prevalence of concomitant COPD in pneumoconiosis patients is 18.65% (119/639). Compared with non-COPD patients, those with COPD have older age, longer exposure duration, lower BMI, more current smoker, higher smoking index, worse pulmonary functions (Pre-FEV₁%, Pre-FVC%, FEV₁/FVC and DLCO%) (all $P < 0.05$). In the five respiratory symptoms (cough, sputum, wheeze, dyspnea, chest tight), only the presence of wheeze and severity score of wheeze and dyspnea showed significant difference between COPD and non-COPD group ($P < 0.01$). The strongest risk of COPD determined by a multiple logistic regression analysis was high pneumoconiosis category (category III compared with category II: (Odds ratio [OR], 10.94; 95% confidence interval [CI], 6.21–19.26; category II compared with category I (OR, 4.37; 95% CI, 2.28–8.38;), followed by the presence of wheeze symptom (OR, 2.94; 95% CI, 1.79–4.83), and per 1 m²/kg reduction of Body Mass Index (BMI) (OR, 1.90; 95% CI, 1.00–1.18), per 1 year older of age (OR, 0.90; 95% CI, 0.87–0.93). No significant association of COPD with smoking, working-related exposure duration, air drill type, exposure type (silicosis or coal), the other respiratory symptoms (cough, sputum, dyspnea and chest tightness).

Conclusion: Pneumoconiosis patients in China are at a high risk of COPD and the combined incidence is beyond our clinician's estimate. Pneumoconiosis patients with COPD may suffer more respiratory symptoms like wheeze and dyspnea than patients without COPD. The high category of pneumoconiosis, wheeze symptom and old age are associated with an increased risk of this combination. We proposed that a routine assessment of lung function and detailed respiratory symptoms evaluation is necessary for timely and adequate clinical management.

AP165

PREVALENCE OF RESPIRATORY DISORDERS IN PILGRIMS TRAVELLING TO INDIA FROM CENTRAL SRI LANKA

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Background and Aims: India is the most popular destination of Sri Lankan Buddhist pilgrims. Increased prevalence of respiratory illnesses has been clinically observed, which has not been formally evaluated.

Our aim was to find out the prevalence of respiratory illnesses in pilgrims visiting to India.

Methods: A cross sectional descriptive study was carried out. Sample was selected randomly. Data were collected using an interviewer administered questionnaire. All subjects were clinically examined and lung functions, relevant biochemical investigations and chest X-ray were obtained prior and post travel. Symptomatic subjects were treated and optimized prior to travel. Data were analyzed by Microsoft Excel and SPSS.

Results: 53 pilgrims including 35 (66%) females were enrolled. Majority ($n = 20$, 37.8%) were in 60–70 year age group. The cohort contained 11 (20.7%) asthma and 2 (3.7%) diagnosed COPD cases. 20 (37.8%) were symptomatic pre-travel, of them 10 (50%) had asthma exacerbations, 4 (20%) acute bronchitis, 2 (10%) COPD exacerbations and 4 (20%) non-specific symptoms. On arrival 19 (35.8%) were symptomatic; 12 (63.1%)

had wheezing and 14 (73.6%) cough. Only 7 out of 20 pre travel symptomatic group continued to have symptoms. 12(63.1%) individuals newly developed symptoms following travel, of which 6(50%) had upper respiratory tract infections, 1(8.3%) asthma exacerbation and 5(41.7%) acute bronchitis. The majority of them ($n = 7$, 58.3%) were in 60–70 year age group and females 8(66.6%). 01(8.3%) was a smoker. 10(83.3%) had chronic exposure to at least one air pollutant, in which 8(80%) for biomass fuel smoke. 6(50%) had co morbidities, of them 4(66.7%) diabetes, 2 (33.3%) ischemic heart disease.

Conclusion: There was a high prevalence of respiratory illness among pilgrims visiting India. Upper respiratory infections were the commonest disease. Elders, females and patients with diabetes were the most prone group. This finding highlights the importance of optimizing preexisting lung diseases prior to travel as well as recognition of high risk groups.

AP166

SCREENING FOR RESPIRATORY DISEASES AMONG BISCUIT FACTORY EMPLOYEES IN CENTRAL SRI LANKA

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Background and Aims: The risks of respiratory diseases due to many occupational exposures are well recognized. However, respiratory diseases among employees of biscuit manufacturing factory have not been evaluated before.

We aimed to describe the respiratory diseases in employees and to assess the work environment.

Methods: A descriptive cross sectional study conducted in May-2018. All employees were enrolled. Spirometry was performed by an experienced technician using Spirolab III. Data were collected using interviewer administered questionnaire and analyzed with Microsoft excel. Symptomatic individuals were further investigated.

Results: 175 employees were screened, of which 159(90.8%) were females. Mean age 32.4 years (range 16–76). 3(18.7%) males were smokers, while 92(57.8%) and 17(10.6%) females were exposed to biomass fuel smoke and passive smoking respectively. 159 employees engaged in activities with high occupational risk, of which 22(13.8%) were not using protective masks. 40(25.1%) females and 10(62.5%) males had one or more comorbidities, of which there were 18(36%) asthma, 6(12%) allergic rhinitis, 6(12%) diabetes, 7(14%) hypertension and 2(4%) epilepsy. 36(22.6%) females and 5(31.2%) males had respiratory symptoms in which 24(58.5%) had cough, 17(41.4%) breathlessness, 15(36.5%) chest pain, and 15(36.5%) wheezing. A case of occupational asthma and a bronchiectasis were diagnosed among them. Mean duration of employment of symptomatic and asymptomatic subjects were 42 and 37 months respectively. Values of Mean FVC, FEV1 and FEV1/FVC ratio were 2.21 L (82.7%), 2.02 L (87.1%), 91.3% in symptomatic and 2.29 L (87.0%), 2.08 L (91.1%) and 89.4% in asymptomatic subjects, which was not statistically significant. Only one subject with asthma had moderately severe obstruction in spirometry. Poor ventilation was observed in factory setting.

Conclusion: Respiratory symptoms were common among employees including one case of occupational asthma. However, difference in lung functions was not observed. Poor ventilation in factory and domiciliary biomass fuel exposure may contribute to symptomatology. However, causal relationship cannot be made from available data.

SOCIOLOGIC ASSESSMENT OF THE DEGREE OF APPLICATION OF LUNG FUNCTION EXAMINATION IN PULMONOLOGICAL PRACTICE

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Background and Aims: The measurement of airflow limitation is necessary for the assessment of the risk of unfavourable events in patients with COPD and asthma. We aimed to study the degree of application of lung function examination in the primary healthcare.

Methods: A sociologic questioning of therapists ($n = 460$) working in the health institutions of the Amur and Yaroslavl regions of Russia was done by a specially developed questionnaire containing 45 questions. For statistic analysis the rank correlation method of Spearman and t-criterion of Student were used.

Results: We found out that within the real clinical practice therapists use the methods of lung function assessment in $87. \pm .0\%$ of cases. Spirometry is used in $65.4 \pm 2.2\%$ of cases "all the time", and in $22. \pm .9\%$ "rarely". The correlation analysis allowed to determine a high degree ($R = 0.98$) of dependence of the use of spirometry in the institutions of the primary healthcare on their placement, work experiences and qualification of physicians. The specialists that have a professional experience of more than 30 years always use spirometry in $84.8 \pm 6.2\%$ cases, and with the professional experience less than 5 years in $54.5 \pm 10.6\%$. The part of physicians who never use spirometry in rural health care institutions reaches $19.5 \pm 3.8\%$, while in urban institutions $5.4 \pm 1.2\%$ ($P < 0.001$). The reasons of such incomplete examination are the absence of diagnostic equipment, in 20.3% cases the over crowdedness, in 13.1% an insufficient qualification of physician. The specific gravity of respondents who have "the absence of necessary conditions" was 35.2% in rural outpatient clinics, and in city policlinics it was 10 times less. Only $15.7 \pm 1.6\%$ of pulmonologic patients are provided with the devices of lung function self-control.

Conclusion: The lung function measurement is not sufficiently used yet in real practice of the primary healthcare. Their wide use at this stage of the medical care is one of the most important tasks.

AP168

RESOURCES OF PULMONOLOGY ON THE TERRITORY OF THE FAR EAST OF RUSSIA: SOCIAL-ECONOMIC STRATIFICATION AND REGIONAL GRADIENTS

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Background and Aims: A developed net of prevention and treatment facilities, provision of medical organizations with qualified personnel in medical institutions make the basis of arrangement and quality of medical care. Aim: To study modern tendencies, regional features of staff and material-technical resources availability in medical institutions that give a specialized pulmonologic care on the territory of the Far-East Federal District (FEFD) of Russia.

Methods: The analysis of the dynamic series of the provision of health care institutions on the territory of FEFD for the period of 2010–2016 was done. For statistical assessment the data base of the Ministry of Health Care, of Federal State Statistic Service, methods of

cluster, comparative and correlation analysis, of prediction modelling were used.

Results: The average ($a = \sum Uf/n$) values of pulmonologists availability are in the range from 0.0600 (Sakhalin region) till 0.2471 per 10000 population (Amur region), and bedspace provision from 0.7242 (Jewish Autonomous Region) till 2.0185 per 10, 000 (Magadan region). Meanwhile the average values of pulmonologists availability on the territory of the FEFD are 6.6% less than on the territory of Russia in general, and bedspace provision is 9.65 more. Cluster analysis of typological distribution of the regions by the levels of pulmonologists and bedspace provision shows that 44.4% and 33.4%, respectively, are in the zone of low and a very low level and 22.2% and 44.4%, respectively, are in the zone of high and a very high level. The levels of resource availability of pulmonology in the regions of Russia are in dependence on the density of population ($r = -0.6416$ and $r = -0.8166$ with the provision, respectively, of doctors and hospital beds) and on the value of the gross regional product ($r = 0.7586$ and $r = 0.4605$, respectively).

Conclusion: On the territory of FEFD of Russia there are significant regional disproportions in the provision of resources for pulmonology, caused by social-demographic and social-economic factors.

AP169

AGE AND GENDER DISTRIBUTIONS AMONG CHRONIC COUGH PATIENTS IN CHINA: COUGH IS NOT A SIMPLE REFLECTION OF COUGH REFLEX SENSITIVITY

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Background and Aims: An older female predominance was found among patients with chronic cough in western countries. Age and gender distributions among patients with chronic cough, as well as its related clinical feature remain unclear in China.

Methods: Since January 2003, a medical record were created for patients who attended our specialist cough clinic and underwent systemic investigations and treatment trials for etiological diagnosis. A retrospective analysis (January 2003-December 2016) of demographic features, cough sensitivity and smoking status of adult patients was conducted in 2017 (Figure 1).

Results: A total of 1822 patients with chronic cough were included (Table 1). The present study found that the most common age of patients with chronic cough was 30–39 years and more than two-thirds of patients aged <50 years in China (Figure 2). Despite an enhanced cough response to capsaicin in female [log C5: 1.5 (0.9, 2.2) vs 2.1 (1.5, 3.0) mM] (Figure 3), the number of female (939, 51.5%) were roughly equal to male (883, 48.5%). No matter in never smokers or patients of all smoking status, an equal gender distribution was shown at the age of 20–49 years whilst a female predominance was presented at the age of 50–89 years (never smokers 1:2.7, all smoking status 1:1.7). Cough reflex sensitivity to capsaicin was not related to age (Figure 4) or smoking status (Figure 5).

Conclusion: Patients with chronic cough had a middle-aged predominant feature, along with a relatively equal gender distribution in China. The demographic features was not consistent with capsaicin cough reflex sensitivity, it suggested enhanced cough response to capsaicin may be a minor feature of chronic cough.

TABLE 1 Clinical characteristics of patients with chronic cough

	All	Female	Male	P value
N	1822 (100)	939 (51.5)	883 (48.5)	-
Age (yr) *	42.9 ± 13.7	45.0 ± 13.8	40.7 ± 13.2	0.000
Cough duration (months)†	24.0 (8.0, 84.0)	24.0 (6.0, 72.0)	36.0 (12.0, 96.0)	0.000
Age of onset (yr)	37.8 ± 14.2	40.2 ± 14.2	35.4 ± 13.7	0.000
Daytime cough scores‡	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.988
Nighttime cough scores‡	1.0 (1.0, 2.0)	2.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.000
Cough VAS§	6.0 (5.0, 7.0)	6 (5.0, 8.0)	6 (5.0, 7.0)	0.006
Laryngeal paresthesia, n (%)	1450 (79.6)	769 (81.9)	681 (77.1)	0.020
Cough triggers, n (%)				
Dust	682 (37.4)	381 (40.6)	301 (34.1)	0.006
Cigarette smoke	778 (42.7)	441 (47.0)	337 (38.2)	0.000
Cooking smell	916 (50.3)	508 (54.1)	408 (46.2)	0.001
Cold air	920 (50.5)	493 (52.5)	427 (48.4)	0.099
Talking	527 (28.9)	305 (32.5)	222 (25.1)	0.000

Comparisons were conducted between female and male. *Data are presented as mean ± SD ; †Data are presented as median (IQR).

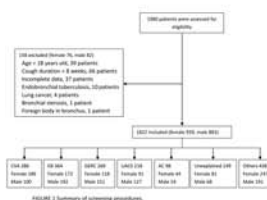


FIGURE 1 Summary of screening procedures.

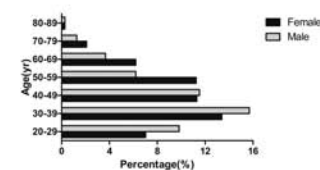


FIGURE 2 Age and gender distribution of patients with chronic cough.

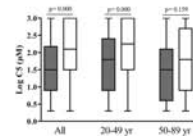


FIGURE 3 Gender difference in cough reflex sensitivity in never smokers. Data are shown as median (IQR). All (208 females, 212 males), 20-49 yr (141 females, 174 males), 50-89 yr (120 females, 95 males).

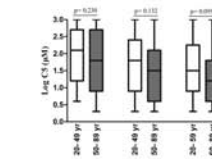


FIGURE 4 Age difference in cough reflex sensitivity in never smokers. Data are shown as median (IQR). Male (20-49 yr, n=89; 50-89 yr, n=86), female (20-49 yr, n=141; 50-89 yr, n=120). 20-49 yr, n=89; 50-89 yr, n=86.

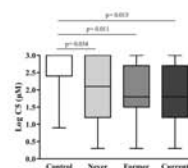


FIGURE 5 Cough reflex sensitivity in male patients with different smoking status. Data are shown as median (IQR). Control (n=86), never smokers (n=41), former smokers (n=89), current smokers (n=18).

AP170

A CASE STUDY OF SILICOSIS ASSOCIATED PROGRESSIVE MASSIVE FIBROSIS AND SCLERODERMA

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Background and Aims: Silica exposure is known to cause silicosis and has been associated with scleroderma. Silicosis can progress to progressive massive fibrosis (PMF). This case study highlights the unusual case of a patient with silicosis, scleroderma and PMF.

Methods: A 45 year old stonemason presented with progressive dyspnoea associated with lethargy, generalised weakness, arthritis, Raynaud's phenomenon and sclerodactyly. He had manufactured kitchen

bench tops for 14 years and had a 30 pack year smoking history. Blood tests showed an IgE level of 297 IU/mL, increased antinuclear antibody (>2560-homogenous pattern) with a positive Scl-70 and Centromere Protein-B. He also had increased serum ACE levels (111 U/L). Full blood count, ESR, electrolytes, calcium and CK were normal and Rheumatoid Factor was negative. Spirometry revealed an FEV1/FVC of 1.95 L/2.1 L with predicted values of 58% and 49%. There was no change post bronchodilator. He had moderate lung restriction with a residual volume and total lung capacity of 35% and 55% predicted respectively. DLCO was 51% predicted, correcting to 88% predicted. Chest x-ray and CT scan of the chest showed multiple randomly distributed nodules within the lungs, some in perilymphatic distribution, associated with significant mediastinal and hilar adenopathy, with mass like areas of opacifications in the upper lobes, consistent with a conglomerate of coalesced nodules. Fine needle aspiration revealed benign reactive lymphadenopathy. Bronchoscopy washings revealed mainly macrophages with 8% eosinophils, and were negative for tuberculosis and bacterial growth. Trans-bronchial biopsy showed a fibrotic nodule of cellular silicosis. In light of his occupational history, this patient likely has silicosis with PMF. His examination findings and immunological results also point to scleroderma associated with silica exposure.

Results: Australia is seeing the re-emergence of diseases like silicosis

Conclusion: This case emphasises the danger of working with engineered granites leading to the unusual and rarely described presentation of PMF and scleroderma.

Interstitial Lung Disease 1

AP171

BEYOND DEPRESSION AND ANXIETY. A COMPREHENSIVE ASSESSMENT OF THE PSYCHOLOGICAL HEALTH OF PEOPLE DIAGNOSED WITH IPF AND THEIR CAREGIVERS

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Background and Aims: The aim of this study was to investigate the psychological health in IPF patients and their caregivers. Disease progression in IPF is variable, however, all patients eventually experience progressive decline in lung function, along with symptom burden. Very little is currently known about the patient's experience, the burden the disease places on family members and caregivers and the needs of both during the disease course.

Methods: A newly designed semi-structured clinical interview plus validated scales was used to investigate the prevalence of preparatory grief, anxiety and depression, in both IPF patients (diagnosed by ATS/ERS/JRS/ALAT criteria) and their caregivers. Within the IPF cohort, we used a validated Type D Personality scale in order to determine the relationship between personality and health-related quality of life outcomes.

Results: Our preliminary results indicate that preparatory grief is experienced by IPF patients and their caregivers around the time of diagnosis and can re-occur when there is an accelerated lung function decline. Patients report that at initial diagnosis, there was little to no psychological support offered, which exacerbated grief reactions.

Conclusion: Our preliminary findings indicate that grief reactions are experienced by IPF patients and their caregivers and significantly contribute to the distress experienced. Based on these findings we will design

and deliver a structured intervention for patient and caregiver support. Early indications are that IPF patients and their caregivers may need immediate support after diagnosis and ongoing access to support services.

AP172

DIFFERENCE OF THE CLINICAL CHARACTERISTICS AND OUTCOME BETWEEN CONNECTIVE TISSUE DISEASES ASSOCIATED INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: This study was in order to understand difference of the clinical characteristics and outcome between connective tissue diseases associated interstitial lung disease (CTD-ILD) and idiopathic pulmonary fibrosis (IPF)

Methods: We performed a retrospective case-control study in patients with CTD-ILD or IPF from January 2003 to December 2017 in the department of respiratory disease, the third affiliated hospital of Sun Yat-sen University. Variables of interest included respiratory symptoms, HRCT features, distribution at CT, ICU stay, 30-day treatment response. The study was approved by the Institutional Review Board of the hospital.

Results: Of the 210 patients (163 CTD-ILD and 47 were IPF), The main HRCT features were subpleural distribution (97.1%), ground-glass opacities (58.1%), patchy attenuation (49.0%), reticular abnormality (46.7%), honeycombing (27.6%). 64.8% were female. The average age was 52.81 ± 13.86 years. The average HRCT score was 6.85 ± 3.85. The 30-day effective therapy rate of all patients was 37.6%. By contrast, CTD-ILD occurs more commonly in females (*P* 0.004). IPF patients were more smokers (*P* 0.000). Cough (*P* 0.002) and sputum (*P* 0.000) were more frequent in IPF group. Reticular abnormality (*P* 0.019) and honeycombing (*P* 0.000) were more frequent in IPF group. Diffuse distribution at CT was more frequent in IPF group. In CTD-ILD group, the lymphocyte rate (*P* 0.006), albumin level (*P* 0.011) in blood and the HRCT score (*P* 0.000) were lower, the neutrophil-to-lymphocyte ratio in blood was higher (*P* 0.005). There was no difference in 30-day treatment response assessment between groups (*P* 0.566).

Conclusion: CTD-ILD occurs more commonly in females. IPF patients were more smokers, often had cough and sputum symptoms. Reticular abnormality and honeycombing were more frequent in IPF group. In CTD-ILD group, the lymphocyte rate, albumin level in blood and the HRCT score were lower, the neutrophil-to-lymphocyte ratio in blood was higher. There was no difference in 30-day treatment response assessment between groups.

AP173

CLINICAL FEATURES OF PATIENTS WITH CLINICALLY AMYOPATHIC DERMATOMYOSITIS WHO HAVE CIRCULATING ANTI-MDA5 AUTOANTIBODIES WITH INTERSTITIAL PNEUMONIA

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Background and Aims: Anti-melanoma differentiation-associated gene 5 (MDA5) autoantibodies have been identified as myositis-specific autoantibodies that are often associated with clinically amyopathic

dermatomyositis (CADM) and a poor prognosis due to rapidly progressive interstitial lung disease (RP-ILD). Recently, combination protocol involving high-dose PSL and biweekly IVCY with a calcineurin inhibitor in RP-ILD was described. However, there are many unclear points in the clinical course in the combination therapy.

Methods: We retrospectively analyzed 24 patients with CADM who had anti-MDA5 autoantibodies. Their clinical phenotypes including laboratory test results, high-resolution lung computed tomography data, response to therapy, and prognosis were compared between those who were survival and dead.

Results: Among 24 patients, 15 patients were complicated with RP-ILD. All patients with RP-ILD were treated with combination protocol and 2 patients were needed to add with rituximab. 6 patients were dead by current disease. There was a tendency of the elderly and high A-aDO₂ at the admission in patients who died. Laboratory and image dates weren't different. The incidence of mediastinal emphysema and bacterial, fungal, or cytomegalovirus (CMV) infection was complicated during treatments.

Conclusion: Combination protocol was effective in patients with RP-ILD. In clinical phenotypes, age and A-aDO₂ were only significantly related to the response to therapy.

AP174

FIVE CASES OF ANTI-MDA-5(ANTI-CADM140) POSITIVE CLINICALLY AMYOPATHIC DERMATOMYOSITIS(CADM) WITH INTERSTITIAL PNEUMONIA

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Background and Aims: Clinically Amyopathic Dermatomyositis (CADM) is classified the dermatomyositis with minimal or no muscular symptoms and often have interstitial lung disease (ILD). Especially Anti-Melanoma Differentiation-Associated Gene5 (MDA-5) antibodies (Anti-CADM140 antibodies) positive CADM is poor prognosis because of rapid progressive ILD. We assessed background, ILD patterns of chest CT, treatments and prognosis of Anti-MDA-5 antibodies positive CADM patients with ILD.

Methods: Since 2011 to 2017, 5 patients of Anti-MDA-5 antibodies positive CADM patients with ILD. We assessed background, ILD patterns of chest CT, treatments and effects.

Results: Male (2 patients), Female (3 patients), median age 63 (53–79 years), ILD patterns of chest CT were Diffuse Alveolar Damage (DAD) 2 patients, Nonspecific Interstitial Pneumonia (NSIP) 2 patients and Organizing Pneumonia (OP) 1 patient. Treatment regimen were Methylprednisolone (mPSL) pulse + Intravenous cyclophosphamide (CYC) + tacrolimus + intravenous immunoglobulin (IVIG) 3 patients, mPSL pulse+Intravenous CYC + tacrolimus 1 patient, mPSL pulse+tacrolimus 1 patient. 4 patients died within 2 months after treatment, and 3 patients had Ulceration all patients were started treatment after 2 months or more from any symptoms appeared. Only one patient(Female) alive. She had no Ulceration and was started treatment within 12 days from symptoms appeared, and low serum ferritin and neutrophil/lymphocyte ratio (NLR).

Conclusion: Four of five patients died within 2 months after treatment with poor prognosis. We report about prognosis factor of this disease from previous reports.

CLINICAL FEATURES AND PROGNOSTIC FACTORS FOR SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE

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Background and Aims: Interstitial lung disease (ILD) is a frequent complication in patients with systemic sclerosis and is associated with significant morbidity and mortality. However, limited data exist regarding clinical characteristics and prognostic factors in Asian patients with systemic sclerosis related ILD (SSc-ILD). The aim of this study is to evaluate the clinical features, outcome and prognostic factors for SSc-ILD patients in South Korea.

Methods: Clinical data were retrospectively analyzed in 85 patients with SSc-ILD (biopsy proven case, $n = 17$). The Cox proportional hazards regression model was used for analyzing predictors for clinical outcomes.

Results: Median follow-up period was 4.6 years (interquartile range: 2.7–7.4 years). Mean age of the subjects was 53 years, 15% were male, and 21% were smokers. The overall mortality rate was 12.9% during follow-up (1 year = 0%, 3 years = 4.7%, 5 years = 5.9%). Non-survivors showed shorter duration of dyspnea (0.9 years vs 2.1 years., $P = 0.006$) and lower diffusing capacity of carbon monoxide (49.3 ± 23.1 % predicted. vs 60.5 ± 18.7 % predicted. , $P = 0.089$) compared with survivors; however, there were no significant differences in other variables including age, sex, smoking history and exercise capacity (Table 1). In univariate Cox analysis, age (hazard ratio [HR], 1.140), male gender (HR, 3.527), estimated pulmonary artery systolic pressure (HR, 1.102) and Gender-Age-Physiology (GAP) stage (HR, 6.899) were predictors for mortality.

Table1. Comparison of baseline characteristics between survivors and non-survivors in patients

Total (N=85)	Survivor (N=74)	Non-survivor (N=11)	P value
Male	13 (17.6%)	4 (36.4%)	0.294
Follow up duration, years	4.49 $\pm$ 3.40	2.61 $\pm$ 3.07.0	0.088
Age at diagnosis, y	52.6 $\pm$ 11.5	57.5 $\pm$ 10.4	0.183
Duration of dyspnea, years	2.1 $\pm$ 2.0	0.9 $\pm$ 0.6	0.006
Ever smoker	15 (20.3%)	3 (27.3%)	0.893
Body mass index (kg/m ²)	23.5 $\pm$ 3.2	22.1 $\pm$ 4.1	0.222
FVC %	73.1 $\pm$ 19.0	69.4 $\pm$ 20.6	0.567
DLCO %	60.5 $\pm$ 18.7	49.3 $\pm$ 23.1	0.089

Data are expressed as number (%), mean $\pm$ standard deviation, or median (interquartile range), depending on variable distribution

DLCO=diffusion capacity of the lung for carbon monoxide; FVC=forced vital capacity.

Conclusion: Among patients with systemic sclerosis related ILD in South Korea, female was predominant and mean diagnosed age was at 53.3 years old as reported previously. The GAP stage was independently associated with a worse prognosis.

AP176

DIGESTIVE ADVERSE EVENTS FOLLOWING NINTEDANIB ADMINISTRATION IN IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: Digestive adverse events, including nausea and diarrhoea, are the most common adverse effects of nintedanib. When a patient with idiopathic pulmonary fibrosis (IPF) exhibits these adverse effects, nintedanib treatment cannot be continued. However, the clinical features of the development of digestive adverse events during nintedanib administration are unknown. Our aim is to investigate the digestive toxicity of nintedanib and risk factors for development of digestive adverse events following nintedanib administration in patients with IPF.

Methods: We enrolled 64 Japanese patients with IPF who received nintedanib between October 2015 and April 2018. The diagnosis of IPF was based on the ATS/ERS/JRS/ALAT IPF statement in 2011. We retrospectively evaluated clinical characteristics, including body mass index (BMI); performance status (PS); change in forced vital capacity (FVC); and digestive toxicity, especially nausea and diarrhoea.

Results: The mean FVC was 2192 ± 729 mL before the initiation of nintedanib administration. Moreover, the mean annual decline in FVC was -115 mL. Sixteen and 15 patients developed nausea and diarrhoea of above grade 2 in Common Terminology Criteria for Adverse Events, respectively. Of these patients, half of the patients with nausea and 4 patients with diarrhoea could not receive nintedanib owing to the toxicity. The annual decline in FVC in patients with nausea was significantly lower than that in patients without nausea. To predict the risk of developing nausea and diarrhoea, the optimal BMI cut-off value was calculated as 21.6 kg/m² using the receiver operating characteristic curve. Multivariate analysis revealed that poor PS (2–4) and low BMI were significant risk factors for the development of nausea or anorexia due to toxicity of nintedanib. Low BMI trended toward being related to the development of diarrhoea.

Conclusion: Poor PS and low BMI are associated with the development of digestive adverse events during nintedanib treatment in patients with IPF.

AP177

SERUM SOLUBLE IL-2 RECEPTOR IS A POSSIBLE PROGNOSTIC BIOMARKER IN IDIOPATHIC INTERSTITIAL PNEUMONIA

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Background and Aims: Idiopathic interstitial pneumonia (IIP) is a chronic fibrosing lung disease of unknown etiology. Because the natural course of IIP is heterogeneous, the clinical course is unpredictable at the time of diagnosis. Although several biomarkers have been proposed, they are not sufficient to use in the clinical settings. It has been reported that soluble IL-2 receptor (sIL-2R) characterized the activation of T cells and was a useful biomarker for several hematologic disorders, autoimmune diseases and sarcoidosis. However, it has not been clarified the clinical significance of sIL-2R in IIP. The goal of this study was to determine whether sIL-2R is a clinically useful biomarker in patients with IIP.

Methods: Review patients with interstitial pneumonia admitted to our hospital, and retrospective analysis was performed. IIP and interstitial pneumonia associated with connective tissue disease (IP-CTD) were included. IIP was also divided into idiopathic pulmonary fibrosis (IPF) and non-IPF according to the recent international consensus classification. Serum sIL-2R was measured and analyzed the relationship with clinical characteristics in patients with interstitial pneumonia.

Results: 191 patients with interstitial pneumonia were included. 118 and 73 patients were IIP and IP-CTD. Serum sIL-2R were significantly higher in patients with IP-CTD compared to those with IIP. In patients with interstitial pneumonia, serum sIL-2R had a significant positive correlation with CRP, ESR and %inflammatory cells in bronchoalveolar lavage fluid, however, a multivariate analysis revealed serum sIL-2R was the prognostic risk factor in patients with IIP, not IP-CTD. In addition, IPF diagnosis was not related to the prognosis in patients with IIP. In patients with IIP, the survival rate was significantly higher in the high serum sIL-2R group compared to the low serum sIL-2R group.

Conclusion: Serum sIL-2R is a possible prognostic biomarker in patients with IIP.

AP178

PULMONARY LANGERHANS CELL HISTIOCYTOSIS ASSOCIATED WITH SEVERE PULMONARY ARTERIAL HYPERTENSION: REPORT OF A CASE

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Background and Aims: Pulmonary Langerhans cell histiocytosis (PLCH) is a smoking-related interstitial lung disease which tends to occur in young adults. Severe pulmonary arterial hypertension (PAH) complicating PLCH is rare (WHO classification type 5) and optimal management strategies of these patients remain unknown.

Methods: We report a 47-year-old man who was a heavy smoker with two episodes of spontaneous pneumothorax. PLCH was diagnosed after lung biopsy at the age of 32. He was lost to follow-up until 14 years later when he developed progressive exertional dyspnea and hypoxemia. HRCT findings were consistent with advanced PLCH and lung fibrosis. The positron emission tomography did not reveal extrapulmonary involvement. The FVC was 39.1% and DLco was 18.1% predicted. His right heart catheterization (RHC) revealed a mean pulmonary arterial pressure (mPAP) of 61 mmHg and a pulmonary vascular resistance of PVR of 23 Wood units. During the subsequent one year, his management included: (1) long-term oxygen therapy; (2) chemotherapy with vinblastine, cladribine, and prednisolone; (3) sildenafil and macitentan for PAH, and (4) pirfenidone and nintedanib for lung fibrosis.

Results: His WHO functional class improved to III and the follow-up HRCT showed no progression of pulmonary fibrosis. His haemodynamic (Table 1) and PFT also improved (FVC 44.8%, DLco 23.1%). However, exertional hypoxemia persisted and he is currently waiting for lung transplantation.

Conclusion: Severe PAH complicating PLCH is rare and remains a therapeutic challenge. Our experience from this case suggests that chemotherapy, PAH-specific drugs, and novel anti-fibrotic agents may be of benefits in preventing disease progression in these patients.

Table 1. Pulmonary hemodynamics at baseline and after 1-year treatment

Pulmonary hemodynamics	PAWP (mmHg)	PAP (s/d/m) (mmHg)	RAP (mmHg)	CI (L/min/m ²)	PVR (Wood unit)
Baseline	7	89/44/61	16	1.5	23
After 1-year treatment	7	72/38/51	8	2.0	14

Abbreviations. CI, cardiac index; PAWP, pulmonary arterial wedge pressure; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure

AP179

MORPHOLOGICAL ANALYSIS OF ALVEOLAR MACROPHAGE IN PATIENTS WITH PULMONARY ALVEOLAR PROTEINOSIS: LET'S REFLECT THE CELL ON A BRONCHOALVEOLAR FLUID SPECIMEN-PART 1

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Background and Aims: It has been defined the type of pulmonary alveolar proteinosis (PAP) is classified by the existence of anti GM-CSF autoantibody. Most of PAP have serum anti GM-CSF autoantibody and they are named as autoimmune PAP (APAP). On the other hand, the pathogenesis of PAP without anti GM-CSF autoantibody such as secondary PAP (SPAP) has been unclear until now.

We hope to find a clue the determining the etiology of SPAP. Therefore, the aim of this study is to analyze the characteristic cell form of alveolar macrophage (AM) in SPAP compared with APAP.

Methods: We have a hypothesis that AM of SPAP tends to show the aberrant type. Twenty cases of SPAP complicated with myelodysplastic syndrome (MDS) were enrolled in this study. We analyzed the cell area, nuclear area, and NC ratio of AM on bronchoalveolar lavage fluid (BALF) specimen by digital microscope. They were compared those of APAP ($n = 20$).

Results: Median cell area and nuclear area of AM in SPAP was $102 \mu\text{m}^2$ and $36 \mu\text{m}^2$, respectively. These findings were significant smaller than those of APAP. However, NC ratio of AM in SPAP was larger than APAP and there were lots of cells with high NC ratio up to 40%.

Conclusion: AM form in SPAP was clearly difference from APAP. It was suggested that AM in SPAP has aberrant type as same as haematological malignant cell in MDS. Based on these results, it is demonstrated that haematological malignant cell derived from bone marrow may be associated with the onset of SPAP.

AP180

THE PREVALENCE OF "CLINICAL PPFE "IN DAILY MEDICAL PRACTICE: TWO YEARS' EXPERIENCE AT A MEDICAL CENTER IN JAPAN

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Background and Aims: Idiopathic pleuroparenchymal fibroelastosis (PPFE) is recognized as a rare form of idiopathic interstitial pneumonia (IIP). Radiologic feature of PPFE is upper lobe pleural thickening with associated subpleural fibrosis concentrated in the upper lobe on chest computed tomography (CT), and pathological feature is upper zone pleural fibrosis with subjacent intra-alveolar fibrosis accompanied by alveolar septal elastosis. To diagnose PPFE, both radiological and pathological criteria need to be fulfilled.

Our clinical experience suggests not a small number of patients had "PPFE-like" CT findings, symptoms as well as clinical course. Those patients' lung function tends to be too impaired to conduct pathological examination. They do not get diagnosed with PPFE due to lack of pathological evaluation. To understand how prevalent the patients with "clinical

PPFE" which lacks pathological examination in clinical space, we reviewed our hospital's medical records.

Methods: We reviewed all the patients who visited our department at Saitama Medical Center, a branch hospital of Jichi medical University, between April 2016 and March 2018. The patients with pulmonary interstitial lesions proven by CT were enrolled in this study. Patients with the secondary interstitial lung disease, such as collagen-vascular disease, chronic hypersensitivity pneumonitis, and drug-induced lung injury, were excluded.

Results: Chest CT proved 356 patients had pulmonary interstitial lesions among all the patients who visited our department in the past 2 years. We excluded 166 patients with the secondary interstitial lung disease and analyzed 190 patients. Upper-lobe-dominant distribution were observed with 8 patients, and 5 of them had "PPFE-like" CT findings and symptoms. Among those 5 patients, 3 patients developed respiratory failure rapidly and 1 patient died within a year.

Conclusion: We identified 5 patients with "clinical PPFE" which lacked pathological examination among 190 patients with IIPs. One limitation was it was difficult to exclude chronic hypersensitivity pneumonitis completely without conducting pathological examination.

AP181

GOOD LUNG FUNCTION BUT PROGRESSIVE RAYNAUD'S PHENOMENON IN A PATIENT OF SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE AFTER BILATERAL LUNG TRANSPLANTATION

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Background and Aims: Systemic sclerosis (SSc) is one of the major causes of connective tissue disease-related interstitial lung disease (CTD-ILD). SSc can be a progressive and fatal disease in a subset of patients for whom lung transplant represents a life-saving procedure.

Methods: A 58-year-old man was diagnosed of SSc with mild dyspnea on exertion, Raynaud's phenomenon, sclerodactyly, abnormal nail-fold capillary pattern, positive anti-Scl-70 and usual interstitial pneumonia (UIP) pattern on high-resolution computer tomography (HRCT) of chest in 2009. Pulmonary function test revealed mild restrictive lung disease with forced vital capacity (FVC) 2.13 L (63% of prediction) and decreased diffusion capacity of carbon monoxide (DLCO) with 53%. Penicillamine was prescribed since then. In 2012, UIP pattern on HRCT of chest showed progression and 6-minute walking test (6MWT) revealed 546 m with significant post-exercise desaturation (from 97% to 42%). FVC deteriorated to 1.84 L with 52% of prediction. Echocardiography revealed pulmonary hypertension with estimated mean pulmonary artery pressure about 50 mmHg. On May 2017, the FVC decreased to 1.46 L with 47%, DLCO decreased to 12% and 6MWT walking distance decreased to 289 m.

Results: Considering progressively deteriorated lung function and dyspnea symptom, lung transplantation was performed on December 31th in 2017. Three months later, the follow-up pulmonary function tests were significantly improved with FVC 1.72 L (55%), DLCO 63% and 6 MWT walking distance 377 m. Both immunosuppressant (Tacrolimus, mycophenolate mofetil, methylprednisolone) and Penicillamine were prescribed after transplantation. Bilateral lung transplantation seemed to be significantly beneficial in terms of improvement of lung function and quality of life. However, the patient suffered from worsening of Raynaud's phenomenon of bilateral hands with severe pain and gangrene change.

Conclusion: For SSc patients, the Raynaud's phenomenon reminded us the nature of SSc as a progressive disease and the role of anti-SSc agent need more addressed especially after lung transplantation.

AP182

EXPLORING THE RELATIONSHIP BETWEEN THE PATHOPHYSIOLOGY OF PULMONARY HYPERTENSION (PH) AND THE STATUS OF INTERSTITIAL PNEUMONIA (IP) IN IP-ASSOCIATED PH

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Background and Aims: Patients with interstitial pneumonia (IP) are at risk of developing pulmonary hypertension (PH), as the underlying condition worsens or becomes severer, thus further compromising their prognosis.

Methods: To describe three cases of IP-associated PH showing improvements in IP status and to explore the relationship between PH pathophysiology and IP status based on changes observed in PH.

Results: **Case 1.** A patient with collagen-vascular disease (CVD)-IP was diagnosed as having PH associated with anti-synthetase syndrome (ASS) and was started on bosentan therapy, which led to improvements in mPAP as well as in subjective symptoms over time. Indeed, the patient had had no acute exacerbations, with the serum markers of IP remaining low over 6 years following initiation of bosentan therapy. **Case 2.** A patient was diagnosed as having PH due to idiopathic pulmonary fibrosis (IPF) and was started on bosentan therapy, which led to clear improvements in PH, WHO functional class and maximum exercise tolerance on treadmill exercise testing. **Case 3.** A patient was diagnosed as having PH due to idiopathic interstitial pneumonia (IIP) and was started on nintedanib therapy, which led to clear improvements in the pathophysiology of IP and PH.

Conclusion: Improvements in the pathophysiology of IP appear to be accounted for largely by those in IP-associated PH.

AP183

EXTERNAL THERAPY OF TRADITIONAL CHINESE MEDICINE FOR IDIOPATHIC PULMONARY FIBROSIS: A LITERATURE ANALYSIS

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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is a prototype of chronic, progressive and fibrotic lung disease associated with a poor prognosis. Although two drugs for IPF are now available, many gaps are still to be filled. External therapy of traditional Chinese medicine (TCM-ET) has been widely used to treat IPF patients. Therefore, this study aimed to analyze the current status of the development and application of TCM-ET for IPF by a literature analysis.

Methods: PubMed, Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chongqing VIP and Wanfang Data were searched from their inception dates to May 10th, 2018. Literatures on TCM-ET for IPF were included. We extracted from included literatures the information about the first author, year of publication, types and characteristics of intervention.

Results: TCM-ET could dredge the meridians/channels, regulate Qi and activate blood, reinforce the healthy Qi and eliminate the pathogenic factors. The types of intervention include acupoint application, acupuncture and moxibustion, iontophoresis and catgut embedding, etc. TCM-ET

was characteristics by cost-effectiveness, safety, convenience and few adverse effects.

Conclusion: TCM-ET plays an important role in the prevention and treatment of IPF. However, both basic and clinical researches on TCM-ET should be further undertaken, such as mechanism of TCM-ET, standardization of manipulation and therapeutic evaluation.

AP184

ANALYSIS OF CLINICAL FACTORS DECIDING NECESSITY TO TREAT INTERSTITIAL PNEUMONIAS POSITIVE FOR ANTI-AMINOACYL-TRNA SYNTHETASE ANTIBODIES

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Background and Aims: Anti-aminoacyl-tRNA synthetase (ARS) antibodies are representative antibodies of polymyositis (PM) / dermatomyositis (DM). Progression of interstitial pneumonia (IP) strongly affects prognosis and respiratory condition of anti-ARS positive patients. The responsiveness of their IP activities to corticosteroids are considered generally well, but the refractory courses are often experienced. We analysed clinical factors deciding necessity to treat IPs positive for anti-ARS antibodies in our institution.

Methods: We retrospectively reviewed 42 IP patients positive for anti-ARS antibodies in the database of our institution from July 1995 to January 2018. These patients were divided into two groups, untreated group and treatment group. Between the groups, we compared about their backgrounds, findings on physical examination, laboratory data, pulmonary computed tomography (CT) findings and prognosis.

Results: All backgrounds such as age, sex, and smoking history were not statistically different. Seven patients presented with characteristic skin rashes of PM/DM only in treatment group. With regard to laboratory findings, the mean values of lactate dehydrogenase (LDH) and C-reactive protein (CRP) in the first visit were higher in treatment group (LDH: 274.5 vs 201.0, CRP: 1.58 vs 0.06). Analysis of CT findings revealed that the ratio of nonspecific interstitial pneumonia pattern was higher in treatment group than untreated group (85.7% vs 42.9%). Sixteen IP patients were treated only with corticosteroids. The addition of immunosuppressive agents to corticosteroids was needed for remission of IP in 12 patients. Although three patients in treatment group were died of IP, the statistical differences of progression free survival by therapeutic regimens were not confirmed.

Conclusion: The present study revealed that some IP patients positive for anti-ARS antibodies could be followed up without treatment. The value of LDH and CRP, and CT findings may help to decide whether the treatment is needed or not.

AP185

CRYPTOCOCCUS NEOFORMS INDUCED HYPERSENSITIVITY PNEUMONITIS: A CASE REPORT

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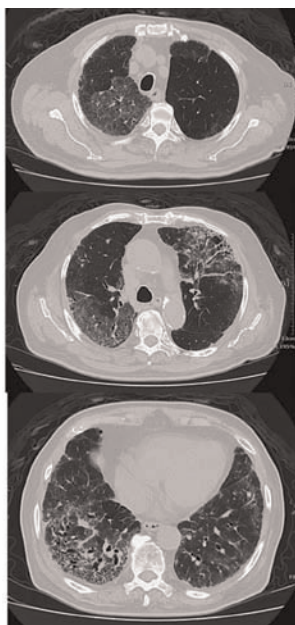
Background and Aims: It is very difficult to find the actual cause of chronic hypersensitivity pneumonitis in clinical practice. Nevertheless, hypersensitivity pneumonitis is a interstitial lung disease resulting from inhalation of variety of antigens.

Methods: Here, we present a case diagnosed with chronic hypersensitivity pneumonitis induced by cryptococcus neoformans.

Results: Mr. Wong, an 81-year-old male, who used to sell herbal tea for living, suffered from chest pain for one month. He also complained progressed dyspnea in recently one week. He denied fever, legs pitting edema, productive cough, and contact or travel history. He visited our clinics on Feb. 6, 2018. His saturation was around 80% in ambient air. Therefore he was admitted for survey. His medical history included asthma, coronary artery disease, hypertension, old pulmonary tuberculosis, gout and old cerebral vascular accident. His current medicine was betaloc, aspirin, MgO, sevikar, tonsaric, vytorin, and acetylcystein. Chest CT showed bilateral ground glass opacity from upper to lower lobe, and fibrotic change over lower lobe bilaterally. His white blood cell counts was 10,200/cumm and CRP 11 mg/dl. Empiric antibiotics tazocin was given. There were negative results including serum mycoplasma IgM, Cryptococcus neoformans antigen, blood culture and sputum culture. DLCO was only 25%. Due to history of coronary artery disease and chest pain persisted, cardiac catheterization was performed and stenting from left anterior descending and left circumflex artery. But his chest pain persisted with persisted low saturation. Methylprednisolone intravenous use was given for suspect hypersensitivity pneumonitis. Therefore we arranged bronchoscopic examination. Bronchoalveolar lavage via RB2 was performed. Fluid analysis showed lymphocytosis (37%). The fungus culture showed cryptococcus neoformans (100 CFU/mL). According to the results, diflucan intravenous was treated. His symptoms improved and saturation was up to 95% without oxygen use.

Conclusion: Exposure to fungus antigen should be keep in mind in clinical evaluation of susceptible patients.

Pulmonary function	Pre	Post	BD
FVC	2.21(69%)	2.36(73%)	7
FEV1	1.68(78%)	1.86(86%)	11
FEV1/FVC	76	79	
TLC	3.13(59%)	3.57(67%)	
DLCO	25%	DLCO/VA	45%



AP186

BLEOMYCIN-INDUCED IPF MODEL IS ASSOCIATED WITH CELL CYCLE ARREST IN LUNG EPITHELIAL CELL

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Background and Aims: Idiopathic Pulmonary Fibrosis (IPF) is chronic inflammatory lung disease accompanied by fibrosis of the interstitium caused leading to declining lung function. Alveolar Epithelial cells (AECs) participate in the maintenance of lung function not only as recovery in response to various stimuli.

So, we determined whether IPF pathogenesis is associated with abnormal cell cycle of AEC.

Methods: IPF mouse model was established using 1 mg/kg Bleomycin (BLM). C57/BL6 mice were injected BLM as intra-tracheal injection (i.t.) for 2 weeks. Mice were sacrificed at 14 day and harvested lung tissue and broncho-alveolar lavage fluid (BALF). Lung tissues were observed by Haematoxylin & Eosin stain (H&E), Masson's trichrome stain (MTS), ELISA, and BALF were observed Wright-Giemsa method, ELISA. Murine alveolar type II epithelial cells (MLE-12) were exposed by 1–10 mg/mL BLM for 24 h. BLM-induced MLE-12 cells were analyzed viability by MTT, pro-inflammatory cytokine by ELISA, gene expression by qRT-PCR, DNA damage by Hoechst 33258 staining, nuclear size by DAPI staining, cell cycle by PI staining.

Results: In IPF mouse model, pulmonary fibrosis was induced in H&E -, MTS- staining, and the protein level of α -SMA was increased while RAGE was slightly decreased in western blot analysis. Moreover, number of macrophages and pro-inflammatory cytokines were increased. In MLE-12 cells, BLM induced the pro-inflammatory cytokine release including TGF- β , TNF- α , IL-6. In real-time PCR analysis, mRNA levels of p21 and p53 which are regulators of cell cycle arrest were increased.

Conclusion: Our findings suggest that the injured AECs are associated with RAGE expression through cell cycle arrest in progression of IPF.

AP187

THE ROLE OF FOLLOW-UP EVALUATION IN THE DIAGNOSTIC ALGORITHM OF IDIOPATHIC INTERSTITIAL PNEUMONIA: A RETROSPECTIVE STUDY

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Background and Aims: The accuracy of multidisciplinary discussion (MDD) in the diagnosis of idiopathic interstitial pneumonia (IIP) may be challenged by the follow-up for a given patient. We aimed to evaluate the alteration of diagnosis of individual expert and MDT as a whole in the longitudinal diagnostic procedure of IIP.

Methods: The retrospective analysis included 56 patients diagnosed as IIP by The First Affiliated Hospital of Guangzhou Medical University with follow-up visits during Jan 1st to Aug 31st 2014. Each expert was provided information in a sequential manner and was asked to assign an individual diagnosis and an MDT diagnosis after group discussion. The level of agreement among individual experts and between different visits was calculated by kappa and the agreement between individual specialist and MDT with different consensus levels was measured by weighted-kappa coefficients.

Results: The follow-up increased the agreement between clinicians (k from 0.349 to 0.620) as well as between radiologist and clinicians (k from 0.369 to 0.615). Follow-up data changed the original MDT diagnosis in 10.7% and consensus level in 25.0% of all cases; it altered the original clinical diagnosis in 25.9% and clinician consensus level in 57.1% of all cases. The diagnostic performance of individual clinicians or radiologist was closer to that of the MDT compared with the pathologist, and follow-up further increased the agreement.

Conclusion: The longitudinal evaluation of patients with IIP improved the inter-observer agreement in a multidisciplinary team. The performance

of individual clinicians or radiologist was approaching to multidisciplinary team when provided with follow-up data.

AP188

INVESTIGATION OF INTRODUCTION OF NINTEDANIB FOR IDIOPATHIC PULMONARY FIBROSIS IN OUR HOSPITAL

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Background and Aims: Nintedanib, an oral tyrosine kinase inhibitor, has been shown to slow down the progression of idiopathic pulmonary fibrosis (IPF) in two randomised placebo-controlled trials by reducing the annual decline in forced vital capacity (FVC). However, data on the efficacy and safety of nintedanib for idiopathic pulmonary fibrosis is not sufficient.

Methods: We investigated, retrospectively, the effects and side effects, and so on, of nintedanib in 6 patients with IPF who were interventionally treated with nintedanib from October 2015 to May 2018.

Results: There are 6 subjects, male/female = 4 cases/2 cases, average age 70.3 years old, GAP index I/II/III/unknown = 0 cases/4 cases/1 case/1 case, %FVC 57.6 ± 12.9%, %DLCO 33.5 ± 11.6%, and KL-6 1399 ± 948 U/mL.

Four cases were discontinued, the reason for stopping was 2 cases of anorexia/1 case of liver function disorder, 1 case of blood sputum, and restarted in 2 cases. In addition, there was one case in which we continued oral administration after weight loss. One case was seen in which Nintedanib's involvement died of onset of kidney failure that cannot be denied. 3 cases improved %FVC, 4 cases showed a decrease in KL-6.

Conclusion: There is a possibility that improvement of %FVC, KL-6 decrease can be expected by Nintedanib in some special cases which is a part of many IPF patients. However, when using nintedanib, adequate caution is required for the occurrence of adverse events. We will analyze and report in more detail at the 23rd Congress of the APSR.

AP189

LUNG TRANSPLANT REFERRALS FOR IDIOPATHIC PULMONARY FIBROSIS PATIENTS IN HONG KONG

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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease with poor prognosis and limited pharmacological treatments. The median survival time from diagnosis is 2 to 3 years. Lung Transplant (LT) is a viable option for selected patients but is limited by scarcity of donors.

Methods: A systematic retrospective review of IPF patients referred for LT in Hong Kong between January 2008 and December 2017 was done.

Results: There were 20 referrals with diagnosis of IPF (M:F = 12:8) with mean age of 53.4 years (range 37 to 62). Majority of patients were referred for LT evaluation in a late stage of disease with 75% being oxygen dependent and 70% in New York Heart Association Class 3 or 4).

One patient went abroad for LT soon after seen. Eleven out of the remaining 19 patients managed to complete evaluation for LT while 8 patients died during evaluation. Two were excluded from LT due to medical reasons. Four received LT ultimately with waiting time ranging

from 1 to 296 days. Mortality on waiting list was 55.5%. All 5 patients who received LT were alive (7 to 40 months from LT) and enjoying good lung functions.

Of the 13 potential recipients who did not receive LT, all but 1 died. The mean time from referral for LT evaluation to death was 6.0 months (range 0.5 to 13). The mean waiting time for LT in Hong Kong was 11.47 months (2007 to 2016, unpublished data).

Conclusion: The high waiting list mortality (55.5%) and short survival from referral to death (mean 6.0 months) for IPF patients in Hong Kong reflected the local contemporary situation of scarcity of donors and late referrals. As LT confers survival benefit, early referral and strategies in expanding the lung donor pool might help the present unfavourable situation.

AP190

RESPIRATORY BRONCHIOLITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (RB-ILD) PRESENTS WITH PROGRESSIVE DYSPNEA- A CASE REPORT

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Background and Aims: Respiratory bronchiolitis-associated interstitial lung disease (RB-ILD) is a syndrome of small airway inflammation and interstitial lung disease occurring in smokers. Most smokers develop a subclinical bronchiolitis but a few patients who develop more severe inflammation with clinically significant interstitial lung disease are said to have RB-ILD. The clinical presentation resembles those of patients with other interstitial lung diseases- cough and dyspnea, with coarse rales on physical examination. Diffuse fine reticulonodular interstitial opacities are found on chest radiograph, usually with normal-appearing volumes. Histologically it is characterized by patchy and non-uniform accumulation of finely pigmented tan brown macrophages within membranous, terminal and respiratory bronchioles.

Methods: We present the case of a 57 year-old, Taiwanese man, a cigarette smoker consuming 1 pack per day for 30 years, with history of chronic obstructive pulmonary disease that presented with productive cough, progressive dyspnea, body weight loss, and generalized weakness for one month. Chest X-ray and chest CT scan were done. Video-assisted thoracic surgery was done with right upper lobe wedge resection.

Results: On lung biopsy, pigment-laden macrophages are found within alveoli, and peribronchial inflammation noted.

Conclusion: Treatment of respiratory bronchiolitis-associated interstitial lung disease is smoking cessation and avoidance of even passive cigarette exposure, which may prevent improvement or lead to recurrence of the illness.

AP191

This abstract has been withdrawn.

AP192

SAFETY OF NINTEDANIB IN IDIOPATHIC PULMONARY FIBROSIS: A REAL-LIFE STUDY AT OUR HOSPITAL

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Background and Aims: Nintedanib represents an antifibrotic compound able to slow down disease progression of patients with idiopathic pulmonary fibrosis (IPF).

The aim of this study is to evaluate the safety of nintedanib in patients with IPF in a real-life setting.

Methods: This study was retrospective, real-life study for patients with IPF receiving nintedanib between October 2015 and August 2017.

Results: We identified 32 patients with IPF receiving nintedanib (23 males, median age: 74.5, mean%FVC $\pm$ SD = 71.1 $\pm$ 20.1).

The most frequent adverse event was liver dysfunction with a rate of 34.4%. Nineteen patients (59.4%) experienced adverse event. In this study, patients were able to manage diarrhoea with anti-diarrheal. Although all adverse events were improved in a short period of time after discontinuation of medication, 11 patients (34.4%) had to permanently discontinue nintedanib due to severe adverse events.

Conclusion: The most common adverse event was liver dysfunction followed by nausea and diarrhoea, which was different from a previous studies.

AP193

REVIEW ANALYSIS FOR CLINICAL CHARACTERISTICS OF INTERSTITIAL LUNG DISEASE ACCOMPANIED WITH LUNG CANCER (ILD-LC)

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Background and Aims: To explore the clinical characteristics of interstitial lung disease accompanied with lung cancer (ILD-LC) thus improving diagnostic technique.

Methods: From January 2016 to December 2017, 35 cases of ILD-LC diagnosed at first visit to the second hospital of Jilin University (all cases with definite history of ILD), were retrospectively analyzed. During the same period, 60 cases of ILD and 60 cases of LC diagnosed at first visit were also collected and grouped. Indices including basic data, tumor marker, imaging characteristics, pathological type and mutation ratio of EGFR from each group were compared to analyze clinical characteristics of ILD-LC.

Results:

ILD-LC group preponderates in male ratio, age and smoking indices than ILD group ($P < 0.05$).

ILD-LC group preponderates in CA19-9, CA125, CYFRA21-1, CEA than ILD group ($P < 0.05$).

In ILD-LC group, tumours were mainly generated within interstitial lesion region, mainly presented as peripheral carcinoma and typically characterized by adenocarcinoma from vitreous lesions and multiple pulmonary metastasis lesions.

LC group preponderates in mutation ration of EGFR than ILD-LC group ($P < 0.05$).

Conclusion: High-risk factors for pathogenesis of ILD-LC include aging, smoking, male preponderance. Expression of tumor markers generally goes in parallel with pathogenesis of tumor. Most lesions are presented as peripheral carcinoma pathologically defined as adenocarcinoma, with limited mutation ratio of EGFR.

AP194

SPORADIC LYMPHANGIOLEIOMYOMATOSIS PRESENTING AS SPONTANEOUS PNEUMOTHORAX: A CASE REPORT

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Background and Aims: Lymphangioleiomyomatosis (LAM) is a rare, diffuse and progressive lung disease that affects young women of childbearing age. It occurs as a sporadic disease or with tuberous sclerosis (TSC).

Methods: A case of a 49-year old female, Asian, no co-morbidities presented with progressive dyspnea. On physical examination, respiratory system showed asymmetric lung expansion, tachypnea, decreased vocal and tactile fremitus in the right base. Hyperresonant on the right base. Decreased breath sounds on the right mid to base lung field. Other systems were unremarkable. Chest radiograph showed pneumothorax on the right and HRCT done showing diffusely varicized thin walled cystic lesions with intervening normal lung. Cranial MRI was unremarkable and abdominal ultrasound showed minimal ascitis. She was subjected for video assisted thoracotomy with biopsy which showed HMB45 and SMA positive, definitive of LAM.

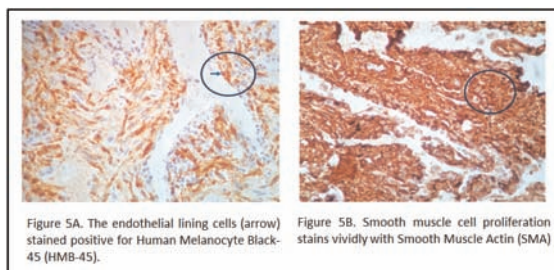


Figure 5A. The endothelial lining cells (arrow) stained positive for Human Melanocyte Black-45 (HMB-45).

Figure 5B. Smooth muscle cell proliferation stains vividly with Smooth Muscle Actin (SMA)

Results: LAM is a rare disease of unknown etiology. Definite diagnosis is characterized by HRCT findings suggestive of LAM and immunostaining positive for HMB45 and SMA. There is no specific treatment for this condition. However, more recently sirolimus have been implied in the management of LAM. Surgical intervention is needed for the management of recurrent pneumothorax. Our patient presented with progressive dyspnea with no other features of tuberous sclerosis. She was diagnosed with definite LAM based on the HRCT findings plus the Immunostaining results.

Conclusion: LAM is a rare disease characterized by the proliferation of unique smooth muscle-like cell involving the small airways, pulmonary microvasculature, and lymphatic structures causing an airway obstruction, cystic changes in the lung parenchyma and pneumothorax.

AP195

HYALURONAN IN BRONCHOALVEOLAR LAVAGE FLUID FROM PATIENTS WITH AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Background and Aims: Hyaluronan (HA), a non-sulfated glycosaminoglycan is a major constituent of the extracellular matrix (ECM), and growing evidence shows its important roles on inflammation, injury and repair in the lung. We have previously demonstrated that serum HA was significantly higher in patients with clinically stable idiopathic interstitial pneumonia (IIP) than healthy controls, and had a positive correlation with CRP and SP-D. In addition, HA was positively correlated with the percentage of inflammatory cells and CXCL8 in bronchoalveolar lavage (BAL) fluid. These results indicate that HA is involved in the pathogenesis of several pulmonary diseases. However, the clinical significance of HA in autoimmune pulmonary alveolar proteinosis (aPAP) has not been clarified. The goal of this study was to determine whether HA is a clinically useful biomarker in patients with aPAP.

Methods: Review patients with aPAP admitted to our hospital, and retrospective analysis was performed. At first, HA in BAL fluid was compared between patients with aPAP and idiopathic pulmonary fibrosis (IPF). Next, the relationship of HA in BAL fluid with clinical parameters was analyzed in patients with aPAP. Finally, we compared HA in BAL fluid between patients with and without therapeutic whole lung lavage.

Results: In patients with aPAP, HA in BAL fluid, which was significantly higher than in those with IPF. In addition, HA in BAL fluid had a significant positive correlation with serum LDH, KL-6, SP-A, and CEA. Furthermore, HA in BAL fluid was significantly higher in patients with therapeutic whole lung lavage than in those without the therapy.

Conclusion: In patients with aPAP, HA in BAL fluid may be a clinically useful biomarker which reflects the disease severity.

AP196

OBSERVATION ON THERAPEUTIC EFFICACY OF GM-CSF INHALATION IN PATIENTS WITH RECURRENT PULMONARY ALVEOLAR PROTEINOSIS

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Background and Aims: To evaluate therapeutic efficacy and safety of the granulocyte-macrophage colony-stimulating factor (GM-CSF) inhalation in patients with recurrent pulmonary alveolar proteinosis (PAP)

Methods: 3 cases were treated by GM-CSF inhalation. Compare the clinical data of the pulmonary function and SPO₂, observe the clinical symptoms and pulmonary lesions.

Results: The pulmonary function test and manifestations were improved obviously, and the ground-glass opacity was improved in high-resolution CT. The average of SPO₂ increased from 53 mmHg to 73 mmHg, FVC/pred increased from 55.4% to 74.9%, FEV₁% increased from 60.9% to 76.4%, DLCO/Pred increased from 35.5% to 52.3% by received GM-CSF inhalation. There were no any adverse reactions in 3 cases.

Conclusion: Inhaled GM-CSF therapy is effective and safe in recurrent PAP. But the long-term effect remains to be seen.

AP197

DISEASE ACTIVITY IN AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS ANALYZED BY A MULTIPLEX IMMUNOASSAY SYSTEM

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Background and Aims: Although serum anti-GM-CSF autoantibody is present in patients with autoimmune pulmonary alveolar proteinosis (aPAP), this autoantibody titer is not related to disease severity or prediction for the prognosis. Even if autoantibody level is extraordinary high, some cases show a spontaneous remission. Furthermore, when treated by whole lung lavage method on hemithorax, other lung which has not washed can be improved. With these facts, we hypothesize that some kind of fluid elements including cytokine/chemokine increase activity of alveolar macrophage in aPAP and may contribute improvement of disease condition.

Methods: Clinical course of each cases including therapy with whole lung lavage and/or GM-CSF inhalation were divided into the progression stage and the remission stage. Comprehensive serum cytokine/chemokine levels were measured at each point in time and analyzed by a multiplex immunoassay system.

Results: The compositions of cytokines were different between the progression stage and the remission stage. In particular of the remission stage, it showed the elevation of the inflammatory cytokine levels concerning the activation of M1 macrophages such as interferon gamma.

Conclusion: In cases of aPAP, there is a possibility of improving the disease activity in accordance of a high serum inflammatory cytokine levels which activate M1 alveolar macrophages.

AP198

CASE OF TUBEROUS SCLEROSIS COMPLEX WITH PULMONARY LYMPHANGIOLEIOMYOMATOSIS AND ANGIOMYOLIPOMAS OF THE LIVER AND KIDNEY

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Background and Aims: Tuberous sclerosis complex (TSC) is a multisystem, genetic disorder often causes neurologic disorders, dermatologic manifestations, renal angiomyolipomas, and pulmonary lymphangioleiomyomatosis. Although most of the affected patients present early in life, some features become more prominent during adulthood.

Methods: In this case report we present a female patient who were diagnosed as TSC at the age of 47.

Results: 47-year-old female patient presented with dyspnea, fatigue and seizure. Although she felt dyspnea for long time she stated that she was healthy until last month. Her creatinine level, liver function tests were high and she had mild hypoxemia. Abdominal ultrasonography revealed renal and hepatic angiomyolipomas (AML). Cranial MRI revealed agenesis of septum pellucidum and in thorax CT there were cysts consistent with lymphangioleiomyomatosis (LAM). She diagnosed as TSC. She denied family history of TSC.

Conclusion: While, seizure and other TSC-associated neuropsychiatric disorders mostly appear during childhood, renal AML and LAM which are the most important causes of morbidity, become significant during adulthood. However in this case, neurological manifestations also became prominent in adulthood. Thus in cases with neurological, pulmonary and renal findings, TSC should be kept in mind even they are in late adulthood.

Lung Cancer 1

AP199

A CASE OF RESECTED LUNG METASTASIS FROM UTERINE LEIOMYOSARCOMA

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Background and Aims: Uterine sarcomas represent 8% of uterine body malignant tumours, about one-third of which are considered leiomyosarcoma. Uterine leiomyosarcoma shows distant metastasis at an early stage, is resistant to chemo- and radiotherapy and displays poor prognosis. Although resection is reportedly effective against pulmonary metastasis, progression is often very fast and the opportunity of resection is frequently missed, and reports of resection cases are extremely few.

Methods: Since we performed surgery for a single lung metastasis occurring after surgery for uterine leiomyosarcoma, we report on the existing literature.

Results: An 81-year-old woman underwent total ablation of the uterus and bilateral adnexectomy due to uterine leiomyosarcoma in our department of gynaecology. Chest X-ray 15 months later revealed a nodular shadow in the right middle lung field. Blood testing showed that concentrations of CEA, SLX, SCC, Cyfra, and ProGRP were all within normal limits. Chest computed tomography revealed a 1.0-cm circular solid nodule with large boundary clarity, near the right border of right lung S2. No other nodular lesions were noted in the other lung lobes, and swelling of the mediastinal and hilar lymph nodes was not observed. On FDG-PET examination, SUVmax was 2.4 in the same lung nodule, and no accumulation was identified in other parts of the whole body. On suspicion of single lung metastasis from uterine sarcoma, thoracoscopic partial resection of the right upper lobe of the lung was performed. The postoperative course was good. Proliferation of spindle cells was found on pathological examination, similar to the histology of the previous uterine lesions, suggesting lung metastasis of leiomyosarcoma. Since surgery, follow-up observation has been carried out on an outpatient basis with no administration of anticancer agent, and no recurrence has been recognized as of 7 months postoperatively.

Conclusion: We successfully performed a surgery for lung metastasis occurring after surgery for uterine leiomyosarcoma.

AP200

FUCOSYLTRANSFERASE 4 PROMOTES CANCER METASTASIS VIA ENHANCING GLYCOSYLATION OF EGFR/TGFBR SIGNALING NETWORK IN NON-SMALL CELL LUNG CANCER

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Background and Aims: Aberrant glycosylation has been known to regulate cancer cell trafficking via promoting intravascular adhesion during metastasis. Clinicopathological studies have also shown a strong correlation between aberrant glycosylation and invasive/metastatic potentials of human cancers. However, the major glycosylation enzymes that drive lung cancer metastases and the signalling networks involved in the process remain incompletely understood.

Methods: We identified fucosyltransferase 4 (FUT4) as a strong predictor of patient prognosis from two independent cohorts of patients with NSCLC (TCGA and NTUH). We analyzed functional roles of FUT4 through over-expression and knock-down studies using lung cancer cell lines in vitro. Metastatic and homing potentials of FUT4-overexpressed and/or knockdown cells were evaluated in vivo in immunodeficient mice. Genome-wide RNA-seq and MS-based immune-precipitation proteomics were performed to study molecular signalling networks.

Results: High expressions of FUT4 were associated with poor survivals in lung adenocarcinomas ($P = 0.000681$). FUT4-overexpressing

lung cancer cells showed significantly increased migration, invasion, and adhesion abilities in vitro, as well as enhanced homing ability to the lungs in vivo. FUT4-overexpressing cells displayed typical characteristics of epithelial-to-mesenchymal transition (EMT) in a protein level-dependent manner. Lewis X and AAL antigens were significantly up-regulated in FUT4-overexpressing cells, which facilitated binding to E- and L-selections. Gene Set Enrichment Analyses of RNA-seq data highlighted metastasis-related signalling, especially EGF and TGF- β pathways. Molecularly, FUT4 enhanced EGFR/TGFBR signalling through glycosylation of multiple pathway proteins.

Conclusion: FUT4 promoted metastasis through enhancing mesenchymal phenotype mediated by glycosylated EGFR/TGFBR signalling, and through increasing binding affinity of cancer cells to selections. High levels of FUT4 in tumor tissues significantly correlated with poor prognosis in NSCLC patients. Our study not only provided new insights into the role of FUT4 on molecular signalling as a potential therapeutic target, but also identified FUT4 as a prognostic marker in NSCLC.

AP201

EXPERIENCE ON HYPERPROGRESSION DISEASE (HPD) BY IMMUNOTHERAPY FOR LUNG CANCER

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Background and Aims: Currently in Japan, three drugs such as nivolumab (NIVO), pembrolizumab (PEMB), atezolizumab can be used for immunotherapy. Although long-term response can be expected as compared with conventional anti-cancer drug therapy, HPD showing rapid disease progression has been reported.

Methods: Between December 2015 and May 2018, 173 patients (pts) was treated with NIVO monotherapy and 43 pts treated with PEMB monotherapy at Sapporo Minami Sanjo Hospital.

The initial treatment effect of 43 pts (NIVO: 33 PEMB:9) was PD

We classified this pts into two groups, HPD group and non-HPD group.

The definition of HPD was defined as a Response Evaluation Criteria in Solid Tumours (RECIST) progression at the first evaluation and a 2-fold or greater increase in tumor growth rate from baseline (before treatment with immunotherapy).

Results: 7 cases (16%) were classified into HPD group.

Median survival of HPD group was 175 days (54–618).

Median survival of non-HPD group was 141 days (22–635).

In the HPD group, the proportion of cases where the tumor growth rate in the prior treatment was 2 times or more was 3 out of 7 cases.

Conclusion: Half of those classified into HPD group have a high rate of tumor growth in the prior treatment.

Both disease progression affected by immunotherapy and disease progression due to characteristics of the tumor itself.

AP202

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR EARLY STAGE OF NON-SMALL CELL LUNG CANCER: A RETROSPECTIVE, SINGLE-INSTITUTIONAL EXPERIENCE

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Background and Aims: Standard treatment of early stage of non-small cell lung cancer (NSCLC) is surgical resection which 5-year overall survival (OS) rate is ranging from 60% to 80%. SBRT has been reported as an alternative effective treatment option for patients with early-stage NSCLC who cannot undergo an operation due to variable cause. But outcome of SBRT was variable. The purposes of this study are reporting the clinical outcomes of SBRT for early-stage NSCLC and looking for factors affecting survival of lung cancer after SBRT.

Methods: From January 2011 to December 2016, total of 64 patients with early-stage NSCLC were treated with SBRT at Soonchunhyang university hospital. Thirty nine patients were inoperable because of poor cardiac or pulmonary function. And 14 of patients refused surgery. Other patients were inoperable due to previous history of malignancy or concurrent cerebrovascular accident. SBRT was given with 48–60 GY in 4–10 fraction.

Results: The median follow up time was 20.5 months (range: 0.5–70). There were a total of 32 Stage IA (T1) tumours, 16 stage 1B (T2a) tumours, 10 stage 2A (T2b) tumours and 6 stage 2B (T3) tumours. A total of 18 of the patients (28%) was failed. Among these, 11 local, 8 regional, and 12 distant failures were observed. At 5-years following, survival rates were 66.7% for cancer specific survival (CSS), 36.1% for OS and progression-free survival (PFS) was 57.7%, respectively. Factor affecting survival of lung cancer after SBRT is tumor size. Fifty of patients experienced radiation pneumonitis of any grade and there's no one experiencing grade 4, 5 pneumonitis.

Conclusion: Our study has shown that SBRT can be an effective and safe treatment modality for early stage NSCLC patients who are medically inoperable or who refuse surgery. Tumor size is the meaningful predictor of response to SBRT and should be considered in treatment planning.

AP203

PRIMARY THYMIC CARCINOMA, CLEAR CELL TYPE: A CASE REPORT

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Background and Aims: Thymic carcinoma is an epithelial tumor with a high degree of histologic anaplasia, obvious cell atypia, and increased proliferative activity and is unassociated with immature T cells. Due to extreme rarity of thymic carcinoma, wide variation of histology and the differences in diagnostic criteria, its exact incidence are usually unknown. The largest series from a single institute is comprised of 20 cases collected over 75 years. The clear cell type of thymic carcinoma are included in the high-grade malignancy group others are lymphoepithelial-like carcinoma, small cell/neuroendocrine carcinoma, sarcomatoid carcinoma, and undifferentiated/anaplastic carcinoma.

Methods: We describe a case of thymic clear cell carcinoma diagnosed by cytology. We report a case of a 47 year old female, non-smoker, who presented with generalized body weakness and fever. Upon work up chest computed tomography (CT) scan revealed bilobed hyperdense mass with irregular inner margins at the right paracardiac area. Patient was initially treated with Anti-Koch's medication but was unable to tolerate due to persistent headache and vomiting. The tumor was eventually resected and biopsy of the mass showed clear cell differentiated, primary thymic carcinoma. Immunostaining results were positive for TTF-1 and CK7 and negative for CK20, CD10, RCC and PAS leading to diagnosis of Clear Cell tumor with glandular differentiation, Primary Thymic Carcinoma. Patient underwent 3 cycles of cisplatin with paclitaxel chemotherapy. Upon follow up there was noted decrease in the size of the mass. Clear cell carcinoma is a rare subtype of thymic carcinoma. Histology of the tumor reveals lobules or sheets of polygonal cells with clear cytoplasm, small nuclei with inconspicuous nucleoli, and a scanty fibrovascular stroma. The clear cytoplasm contains abundant glycogen but no

mucin. Prognostic factors in general include race, sex, age, immunologic status, therapeutic effects, stage, and tumor histology.

Results: Treatment ideally is complete resection but is often impossible, as found in the case due to invasive pericardial extension. Preoperative chemotherapy has been recommended to reduce the volume of a tumor to allow complete resection and to possible increase in the survival rate.

Conclusion: In conclusion, Thymic Clear Cell Carcinoma is difficult to diagnose because of ill-defined symptoms and usually diagnosed incidentally. Treatment for thymic cancer remains to be established. This was the first case of thymic clear cell carcinoma in our institution diagnosed on cytology with help of immunohistochemistry. We aim that with this paper we can contribute to solve challenges in diagnosing and treating patients in the future

AP204

PROGNOSTIC EFFECT OF SERUM OXIDATIVE STRESS LEVEL ACCORDING TO SMOKING STATUS IN PATIENTS WITH CURATIVELY RESECTED STAGE I NON-SMALL CELL LUNG CANCER

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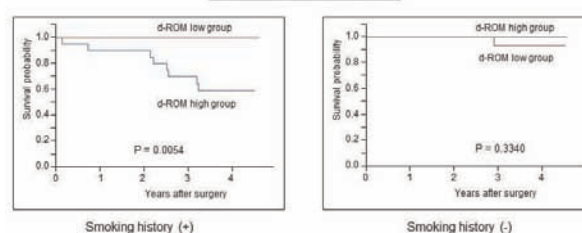
Background and Aims: Since there is a growing body of evidence that suggests reactive oxygen species correlate with various malignant tumours features, preoperative serum oxidative stress level has been recognized as a prognostic biomarker. Smoking is recognized as a significant risk factor for lung cancer development and poor clinical outcomes. Thus, this study aimed to assess the prognostic effect of serum oxidative stress levels according to the smoking status in patients with stage I non-small cell lung cancer (NSCLC).

Methods: In this study, serum reactive oxygen metabolite (ROM) levels were measured in 65 patients who underwent curative resections for pathological stage I NSCLC. Of these enrolled patients, 36 were current or former smokers and 29 never smoked. The clinical relevance of serum ROM levels and smoking statuses with disease outcomes were evaluated.

Results: The Kaplan-Meier method analysis revealed that smoking status and serum ROM levels were significantly associated with overall survival (log rank test; $P = 0.0309$ and $P = 0.0165$, respectively). Among patients with smoking histories ($n = 36$), those with high serum ROM levels showed significantly poorer overall survival than those with low serum ROM levels (log rank test; $P = 0.0054$). Conversely, among patients without smoking histories ($n = 29$), there was no significant difference in overall survival between patients with high and low serum ROM levels (log rank test; $P = 0.3340$).

Conclusion: The prognostic effect of serum ROM levels has a strong association with smoking status. Further studies are required to elucidate the specific mechanism through which serum ROM levels affect clinical outcomes, especially in patients with smoking histories.

Overall survival curves



AP205

THE ROLE OF THE CIRCULATING TUMOR CELLS IN THE SOLITARY PULMONARY NODULES

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Background and Aims: The study aims to determine the sensitive and specific of circulating tumor cell (CTC) in the diagnosis of solitary pulmonary nodules (SPN).

Methods: CTCs were collected from 6 mL of blood based on i-FISH method, which is detected the gene copy number in eight chromosomes and a tumor-associated antigen CK18.

Results: In the evaluation of clinical utility, the results showed that the CTC levels of 85 patients with NSCLC were significantly higher than the controls (46 patients with benign lung diseases). With a threshold of 6 CTC units, the method showed a sensitivity of 75% and a specificity of 80% in the diagnosis of NSCLC, especially in the GGO is higher than the sub-solid nodule (SSN) and solid nodule ($P < 0.05$). Compared with the existing clinical biomarkers such as neuron-specific enolase (NSE), carcinoembryonic antigen (CEA), cancer antigen 125 (CA125), cyfra211, and squamous cell carcinoma antigen (SCC Ag), the method showed the higher diagnostic efficiency (area under the curve, 0.641; 95% confidence interval, 0.508–0.760). CTC, NSE, CEA, CA125, cyfra211 and SCC Ag was the highest diagnostic efficiency (area under the curve, 0.75; 95% confidence interval, 0.622–0.878).

Conclusion: Our results demonstrated that CTCs were feasible diagnostic biomarkers in patients with SPN, especially in grinded glass nodules (GGO). Furthermore, CTC combined with the other tumor marker show the highest diagnostic efficiency.

AP206

A CASE OF OSTEOSARCOMA LUNG METASTASIS WITH LONG-TERM SURVIVAL BY MULTIDISCIPLINARY TREATMENT CENTERED ON MULTIPLE SURGICAL EXCISION

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Background and Aims: Introduction Osteosarcoma often metastasizes to the lung, and the 5-year survival rate of osteosarcoma with pulmonary metastasis is less than 40%. Therefore treatment is considered to be an important factor affecting prognosis.

Methods: We report a case of long-term survival with carrying out local treatment mainly on multiple surgical resection for osteosarcoma multiple lung metastasis.

Results: Case When she was 28 years old, she received a wide-spread resection of right tibial osteosarcoma, and adjuvant chemotherapy after surgery was performed. 4 years later, she underwent resection for bilateral multiple lung metastasis (55 right, 61 left). After that, she underwent multiple surgeries for bilateral lung metastasis. When she was 38, 41, 44, 45, 50 years old, she received removal of 69, 55, 3, 1, 5 metastasis tumor. We resected a total of about 250 tumours. Furthermore, radiofrequency ablation (RFA) and radiotherapy and percutaneous ethanol injection therapy (PEIT) were performed. When she was 51 years old, the remaining another lesion gradually increased, therefore we considered surgery. However, a new lesion was found in the right ventricle by preoperative PET / CT. Although chemotherapy and surgical treatment were considered, she hoped for palliative treatment. She died after 23 years after the removal of the primary lesion.

Conclusion: We experienced a case of long-term survival by multidisciplinary therapy centred on multiple surgical resections.

AP207

ADJUVANT CHEMOTHERAPY FOR PATIENTS WITH NON-SMALL CELL LUNG CANCER –EXPERIENCE FROM TAIWAN

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Background and Aims: Adjuvant chemotherapy is the standard treatment for patients with resectable non-small cell lung cancer. Platinum plus vinorelbine is the regimen with more evidence. However, the best regimen is not clear.

Methods: We retrospectively reviewed the patients of resectable NSCLC and those were treated between 2011 and 2015. Data on age, gender, ECOG performance status, type of tumor, response to treatment, type of adjuvant chemotherapy, and efficacy of different chemotherapy were collected.

Results: In all, 117 patients were enrolled. Sixty patients were stage IIA, 25 patients were stage IIB, and 82 patients were stage IIIA. The PFS of stage IIA patients who received platinum+vinorelbine has a trend to be longer (29.6 months vs 14.9 months, $P = 0.129$). The PFS of stage IIB and IIIA is not reached. Patients received combination chemotherapy seems to have a longer PFS, although not statistically significant (15.6 months vs 8.8 months, $P = 0.657$). Finally, patients who received platinum + vinorelbine is not significantly longer than those received platinum+other chemotherapy (17.9 months vs 12.0 months, $P = 0.24$). According to different N stage, the PFS for N0 is not reached. The PFS of N1 disease was 17.7 months, and of N2 disease was 11.6 months.

Conclusion: Combination chemotherapy is still a preferred treatment choice after surgery before more efficient treatment strategy is found.

AP208

IMMUNOTHERAPY IN NSCLC PATIENTS POSITIVE FOR ANA COULD BE HIGH-RISK AND HIGH-RETURN

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Background and Aims: Immunotherapy in non-small cell lung cancer (NSCLC) patients with diagnosis of autoimmune disease is thought to be high risk of developing immune symptoms. However, little is known about immunotherapy in NSCLC patients positive for antinuclear antibody (ANA), which indicates some type of autoimmune condition. We aimed to clarify the relationship between ANA titer and outcome of immunotherapy in NSCLC.

Methods: We retrospectively reviewed thirty-one patients who were diagnosed with NSCLC and treated with PD-1 inhibitor, either Nivolumab or Pembrolizumab at our hospital from January 2016 to April 2018. We categorized them into three groups by the ANA test (indirect immunofluorescence assay); positive for ANA group (≥ 80), borderline for ANA group ($=40$), negative for ANA group (<40). We investigated the difference of treatment effect and adverse event (AE) among three groups.

Results: According to ANA titer, four patients were categorized as positive for ANA group, ten patients as borderline for ANA group, and seventeen patients as negative for ANA group. Positive for ANA group had high response rates (RR 75%) and good progression-free survival (median PFS 10.65 months), and other two groups had lower RR and worse PFS than positive for ANA group. In addition, all patients of positive for ANA group experienced AEs, while less than 25% patients experienced AEs in other two groups. Two patients in positive for ANA group had to interrupt their treatments because of AEs, in particular interstitial lung diseases which led to respiratory failure and required systemic

corticosteroids, whereas they showed a measurable clinical response and remained in remission for a long time after the last treatment.

Conclusion: Although NSCLC patients positive for ANA tended to experience AEs of immunotherapy, they showed a good response to the treatment. ANA titer could be one of the predictors for AEs and treatment effects with immunotherapy in NSCLC.

AP209

LONG-TERM NICOTINE EXPOSURE IN LUNG CANCER

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Background and Aims: Lung cancer is the leading cause of cancer-related mortality worldwide. Most patients are diagnosed at an advanced stage without noticeable symptoms. Nicotine, as the major addictive component in cigarettes, may be involved in the progression of lung cancer cells after a long term exposure. The present study investigates the potential effectors of long-term nicotine exposure in lung cancer.

Methods: cDNA microarray was firstly used to explore the potential effectors of long-term nicotine exposure in the parental squamous lung cancer cells, H157, and H157N, harvested with nicotine (10 μ M) for 2 years. The bioinformatics platform was used to analyze whether the mRNA expression of various effectors might contribute to patient survival.

Results: There were 5 transcripts (CXCR4, VEGFA, TP73, IL-1 β , WNT5A) (>2-fold intensity) were significantly increased and associated with several pathways (i.e. Activation of MAPK activity, positive regulation of protein phosphorylation, response to hypoxia and ion transport). Accordingly, the Kaplan–Meier survival curves of patient groups with CXCR4, VEGFA, TP73 and IL-1 β significantly predicted a worse overall survival of lung cancer patient. Intriguingly, high WNT5A mRNA levels improved patient survival in 1926 lung cancer cases ($P = 0.003$) but unexpectedly associated with a poor survival rate in those patients with smoking history ($P = 0.005$).

Conclusion: Our results suggested that the interplay of long term nicotine exposure and WNT5A related signalling might play roles in lung cancer. The exact roles and underlying mechanisms of the WNT5A related signalling as well as its interplay with nicotine demand further investigations in particular those lung cancer patients with smoking history.

AP210

RESPIRATORY MUSCLE STRENGTH, EXERCISE CAPACITY, AND DYSPNEA DURING PULMONARY REHABILITATION AFTER LOBECTOMY IN PATIENTS WITH NON-SMALL CELL LUNG CANCER

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Background and Aims: Pulmonary rehabilitation (PR) has been reported to prevent postoperative pulmonary complications and improve reduced pulmonary function after lobectomy. This study aimed to characterize the recovery of respiratory muscle strength, exercise capacity, and dyspnea after lobectomy in patients with non-small cell lung cancer (NSCLC) undergoing PR.

Methods: A total of 37 patients with NSCLC who underwent single lobectomy (15 males and 22 females, mean age $6 \pm$ years, mean hospital stay $1 \pm$ days) were enrolled for this study. They performed protocolized PR, including breathing exercises, endurance and resistance training, from 1–2 weeks before to 3 months after lobectomy. Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁), maximal inspiratory (MIP) and expiratory (MEP) mouth pressures, quadriceps strength (QS), 6-minute walk distance (6MWD), and modified Medical Research Council (mMRC) dyspnea grade were evaluated preoperatively, at discharge, and at 1 and 3 months after lobectomy. This study was approved by the Institutional Review Board for Clinical Research, Tokai University (17R-389).

Results: At discharge, FVC, FEV₁, MIP, MEP and 6MWD were lower than preoperative values (72%, 72%, 79%, 66%, and 87% of preoperative values, respectively) and mMRC grade was impaired (median: 1 [inter-quartile range: 1–2]), but QS did not change. From discharge to 3 months after lobectomy, all parameters improved. At 3 months after lobectomy, MIP, MEP, QS, and 6MWD improved to 114%, 100%, 110%, and 104% of preoperative values, respectively; FVC and FEV₁ did not reach preoperative values (84% and 85%, respectively). mMRC grade at 3 months after lobectomy (0 [0–1]) did not change from preoperative value.

Conclusion: We found that after single lobectomy for patients with NSCLC undergoing protocolized PR, 1) respiratory muscle strength, exercise capacity, and dyspnea recover to preoperative levels by 3 months, and 2) pulmonary function does not reach preoperative levels until at least 3 months.

AP211

THE FREQUENCY OF EGFR MUTATION AND ALK REARRANGEMENT IN PATIENTS WITH LUNG ADENOCARCINOMA: THE EXPERIENCE OF A LOCAL HOSPITAL IN TAIWAN

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Background and Aims: The studies concerning about frequency of driver mutations in patients with lung adenocarcinoma have great population-based diversity. A prospective study of medical centres in Taiwan had showed the frequency of EGFR mutations in lung adenocarcinoma was 55% and ALK rearrangement was 9.8% in EGFR-wild type lung adenocarcinoma. The aim of this study was to analyze these driver mutations among patients diagnosed of lung adenocarcinoma in a local hospital of Taiwan.

Methods: A retrospective cohort study was conducted for the analysis of driver mutations status among patients with newly-diagnosed lung adenocarcinoma in Chen Ching hospital, a local hospital in Taiwan. Two common driver mutations (EGFR mutation and ALK rearrangement) were identified by the pharmacogenomics Lab, National Research Program for Biopharmaceuticals (NRPB), the National Center of Excellence for Clinical Trial and Research of NTUH. EGFR mutations were tested in all patients (Cohort 1) and ALK rearrangement testing were performed in a half of EGFR-wild type patients (Cohort 2).

Results: From January 2013 to December 2017, a total of 322 patients with newly-diagnosed lung adenocarcinoma were enrolled (Cohort 1). EGFR mutations were found in 193 patients (60%). Of the EGFR-positive patients, L858R was the most common (45%) and exon 19 deletion was the second (42%). In Cohort 2 population, 8 of 62 patients (12.9%) were positive for ALK IHC staining. The statistical significance of the presence of EGFR mutations was detected for both gender and smoking status. However, the presence of ALK rearrangement did not show a significant correlation with gender or smoking status.

Conclusion: The frequency of EGFR mutations and ALK rearrangement detected in the local hospital are slightly higher than the data from a prospective study of medical centres in Taiwan.

AP212

RAPID DIAGNOSIS OF THORACIC LYMPH NODE METASTASIS IN PATIENTS WITH LUNG CANCER DURING SURGERY BY DIELECTRIC PROPERTY TEST

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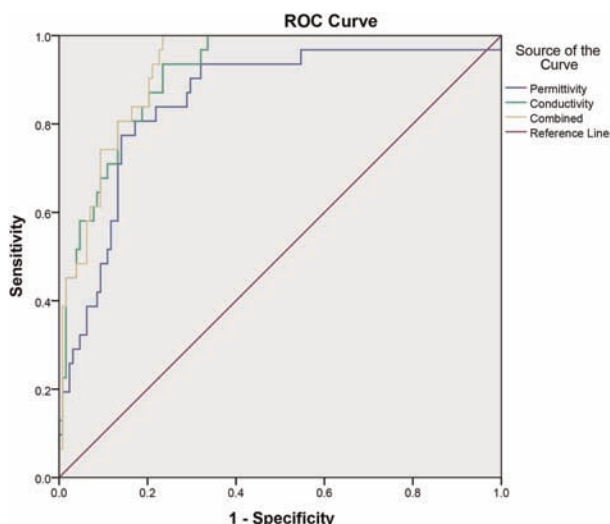
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Background and Aims: For patients with resectable lung cancer less than 2 cm in poor condition such as heart and/or lung dysfunction, segmentectomy may be another alternative option, when no metastasis of the N1 and N2 lymph nodes was confirmed. Frozen section is widely used for rapid diagnosis, but it takes too much time of waiting and its accuracy depends on the pathologists. On the other hand, dielectric property has been proven to be objective and vary among different tissues under different pathophysiological conditions. In this way, this studies aims to investigate the accuracy of dielectric property test in the rapid diagnosis of thoracic lymph nodes metastasis.

Methods: Patients with lung cancer receiving surgery with lymph nodes dissection were recruited. Lymph nodes were tested for dielectric property immediately after dissection before sending to pathologist for frozen section diagnosis, which takes less than 5 min. The informed consents were obtained before surgery. Mann-Whitney Test and multiple variables for ROC curve analysis were used.

Results: 159 thoracic lymph nodes from 51 patients with lung cancer were tested. And according to pathological diagnosis, no metastasis were found in 128 lymph nodes, while metastasis were found in the other 31. For each node, 4000 datasets of dielectric property (permittivity and conductivity) at different frequencies from 1 MHz to 4000 MHz were collected. The differences of mean permittivity and conductivity between the 2 groups were both statistically significant ($P < 0.001$). The AUC of ROC curve with permittivity was 0.917(95% CI: 0.872–0.961), the AUC with conductivity was 0.853(95% CI: 0.776–0.931), and the AUC with the joint of permittivity and conductivity was 0.926 (95% CI: 0.886–0.966).

Conclusion: Dielectric property test could become another rapid way of diagnosing thoracic lymph nodes metastasis with satisfying accuracy in patients with lung cancer.



AP213

EFFICACY AND SAFETY OF ANTI-PD-L1 ANTIBODY IN NSCLC PATIENTS WHO PREVIOUSLY TREATED WITH ANTI PD-1 ANTIBODIES: PRELIMINARY STUDY

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Background and Aims **Background:** Anti-PD-L1 antibody (atezolizumab) was approved for non-small cell lung cancer (NSCLC). Physician can use anti-PD-L1 antibody (atezolizumab) in addition to anti-PD-1 antibodies (nivolumab and pembrolizumab) for the treatment of NSCLC. It is still unclear that efficacy and safety of using anti-PD-L1 antibody for the patients who previously treated with anti-PD-1 antibodies.

Aim: To investigate the efficacy and safety of atezolizumab for the patients who previously treated with nivolumab and/or pembrolizumab.

Methods: We retrospectively reviewed the NSCLC patients who treated with atezolizumab after receiving nivolumab and/or pembrolizumab during the treatment of lung cancer.

Results: Total 14 patients were received atezolizumab for the treatment. Of 14 patients, 9 (64.3%) patients received at least one anti-PD-1 antibody (nivolumab and/or pembrolizumab) treatment. These patients were mean age at 71.6 ± 6.7 year-old. Four (44.4%) patients had adenocarcinoma, 3 (33.3%) patients had squamous cell carcinoma, a (11.1%) patient had adeno-squamous cell carcinoma and a (11.1%) patient had NOS, respectively. PD-L1 expression of the tumor tissues showed TPS $50\% \leq$ for 4 (44.4%) patients, $1\% \leq$ TPS $< 50\%$ for 2 (22.2%) patients, TPS $< 1\%$ for a (11.1%) patient and undetermined for 2 (22.2%) patients, respectively. Median regimens before atezolizumab were three. Patients who received cytotoxic chemotherapy between anti-PD-1 antibody and atezolizumab were five (55.6%). Two patients (22.2%) maintained their best response as stable disease and partial response.

Conclusion **Conclusions:** Total 9 patients received atezolizumab after the treatment with anti-PD-1 antibodies (nivolumab and/or pembrolizumab). Only selected patients could receive the benefits of atezolizumab after anti-PD-1 antibodies therapy in our preliminary study.

AP214

A COMPREHENSIVE ANALYSIS OF PD-L1 EXPRESSION IN LUNG CANCER PATIENTS: WITH EMPHASIS ON THE IMPACT OF ARCHIVAL TISSUE

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Background and Aims: To assess the PD-L1 expression in different histologic types and gene mutation statuses of lung cancer.

Methods: Total 4062 pathology-confirmed lung cancer patients were retrospectively screened at Kaohsiung Chang Gung Memorial Hospital from November 2010 to June 2017. There were 756 lung cancer patients assessed with anti-PD-L1 antibody clone 22C3 by immunohistochemical assay, and finally 655 lung cancer patients with confirmed PD-L1 expression level were retrospectively enrolled in this study, including 21 (3.2%) small cell lung cancer (SCLC) patients and 634 (96.8%) non-small cell lung cancer (NSCLC) patients.

Results: NSCLC had significantly higher PD-L1 expression compared to SCLC ($P = 0.004$). There was significant difference in PD-L1 expression between different histologic types in NSCLC ($P < 0.001$). There was higher PD-L1 expression in EGFR wild type than in EGFR mutation type ($P < 0.001$). There was higher PD-L1 expression in ALK mutation than in EGFR mutation ($P = 0.005$). Longer tumor tissue storage time correlated with lower PD-L1 expression in lung cancer ($P < 0.001$ for linear trend).

Conclusion: Significant differences in PD-L1 expression were found between SCLC and NSCLC and between different histologic types in NSCLC. EGFR and ALK mutation statuses and tumor tissue storage time may influence PD-L1 expression level.

AP215

THE INCIDENCE OF EGFR MUTATIONS IN PATIENTS WITH ADENOCARCINOMA

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Background and Aims: Many clinical trials have shown the effectiveness of tyrosine-kinase inhibitors to lung adenocarcinoma patients with epidermal growth factor (EGFR) mutation. One meta-analysis reported in 2013 (mutMap) shows that 47.9% among Asian patients with lung adenocarcinoma have EGFR mutation. EGFR mutation plays an important role for predicting effectiveness of the treatment, and prognosis in lung adenocarcinoma patients. In this study we investigated the incidence and the types of EGFR mutation among lung adenocarcinoma patients diagnosed by the department of respiratory medicine in our hospital.

Methods: We retrospectively investigated the rate and type of EGFR mutation from medical records of 655 patients with lung cancer diagnosed in the department of respiratory medicine in Ishikawa prefectural central hospital from 2012 to 2016.

Results: There were 335 patients diagnosed as adenocarcinoma among 655 patients. There were 100 patients had EGFR mutations (30.1% among adenocarcinoma patients). There were 48 cases with L858R mutation (47.1%) and 35 cases with Exon 19 deletion (34.3%) in EGFR mutations. Overall survival of EGFR mutation positive patients in stage III and IV is significantly longer (49 cases, 32.3 months) than EGFR mutation negative patients (148 cases, 11.6 months).

Conclusion: About 30% patients with lung adenocarcinoma patients have EGFR mutations in our retrospective investigation from 2012 to 2016, and the prognosis is better than the patients without EGFR mutations.

AP216

EFFECTIVENESS OF TREATMENTS IN ADVANCED NON-SMALL CELL LUNG CANCER WITH EXON 20 INSERTION EPIDERMAL GROWTH FACTOR RECEPTOR MUTATIONS

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Background and Aims: Treatments of advanced non-small cell lung cancer (NSCLC) patients with epidermal growth factor receptor (EGFR) mutations deletions in exon 19 and L858R are well-known, and clinical responses to tyrosine kinase inhibitors (TKIs) are prominent. But the effectiveness of treatments in patients with exon 20 insertion

mutations are not well documented. This study aimed to improve the understanding of the clinical response to various treatments of advanced NSCLC patients with exon 20 insertion mutations.

Methods: Specimens from 3806 NSCLC patients were tested for EGFR mutations. We surveyed the different first-line treatments and their effectiveness in NSCLC patients with exon 20 insertion EGFR mutations.

Results: Of the 3806 patients, 2113 (55.5%) had EGFR mutations, including 85 patients (4.0%) with exon 20 insertion mutations. Effectiveness of different first-line treatments are compared. Pemetrexed-containing regimens were associated with better progression-free survival (6.2 m vs 2.7 m, $P < 0.001$) and overall survival (28.0 m vs 13.9 m, $P = 0.016$) than regimens without pemetrexed. TKIs were related to poor response to patients with exon 20 insertions. However, the mutation A763_Y764 insFQEA was associated with favourable response to TKIs.

Conclusion: Exon 20 insertion EGFR mutations constituted a distinct part of the whole group of EGFR mutations. Different first-line treatments and variants of the mutations may be associated with different outcomes in advanced NSCLC.

AP217

MICRORNA EXPRESSION PROFILING FOR IDENTIFYING MALIGNANT PLEURAL EFFUSION IN PATIENTS WITH LUNG ADENOCARCINOMA

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Background and Aims: Early diagnosis and treatment of malignant pleural effusions (MPE) are important because they improve symptoms, shorten hospitalization stays, and increase cancer-specific survival. MicroRNAs (miRNAs) are a class of short, non-coding RNA molecules, some of whose presence and expressions in samples of biological fluids have been reported to be altered in patients with cancer. Therefore, miRNAs could serve as diagnostic biomarker in cancer. We investigated exosomal miRNA profiles in MPE, including lung adenocarcinoma pleural effusion (Ad-MPE), and benign pleural effusion (BPE).

Methods: A total of 46 PE samples from patients with malignancies (lung adenocarcinoma, $n = 40$; metastatic lung cancer, $n = 6$) and non-neoplastic diseases (BPE, $n = 15$) were collected. Four miRNA expressions in exosomes in PE were evaluated by using real-time reverse transcription quantitative polymerase chain reaction. The area under the receiver operating characteristic curve (AUC) was used to evaluate the diagnostic performance of the identified miRNAs.

Results: The expression levels of miR-182 and miR-210 were found to be significantly higher in the Ad-MPE than the BPE samples. ($P = 0.019$ and $P < 0.001$, respectively). The AUCs of miR-182 and miR-210 for distinguishing Ad-MPE from BPE were 0.82 and 0.84, respectively.

Conclusion: These results suggest that exosomal miR-182 and miR-210 expressions in patients with pleural effusion may have a diagnostic potential for differentiating Ad-MPE from BPE.

AP218

TEXTURE ANALYSIS PREDICTING EGFR MUTATION AND RECURRENCE IN LUNG ADENOCARCINOMA

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Background and Aims: We aimed to investigate the discriminative value of texture feature in EGFR mutation of lung adenocarcinoma and prognostic value of texture features using 18Fluorine-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT).

Methods: Sixty-three lung adenocarcinoma patients with preoperative 18F-FDG PET/CT between January 2010 and December 2014 were included. Texture features are extracted automatically by using LIFEX software (Université Paris Saclay, CEA-SHFJ, Orsay, France), which provided texture features of grey level co-occurrence matrix, neighbourhood grey-level different matrix, grey-level run length matrix, and grey-level zone length matrix.

Results: Contrast ($P = 0.0179$), dissimilarity ($P = 0.024$), entropy ($P = 0.0097$), HGRE ($P = 0.0093$), HGZE ($P = 0.0044$), LRHGE ($P = 0.0076$), RLNU ($P = 0.0249$), SRHGE ($P = 0.0105$), SZHGE ($P = 0.014$), ZLNU ($P = 0.011$), SUVmax ($P = 0.0087$), SUVmean ($P = 0.0084$), SUVpeak ($P = 0.0105$), TLG ($P = 0.0138$) were lower in adenocarcinoma with mutant EGFR, while energy ($P = 0.102$), homogeneity ($P = 0.0318$), LGRE ($P = 0.0079$), LGZE ($P = 0.0055$), LRLGE ($P = 0.0084$), LZLGE ($P = 0.037$), SRLGE ($P = 0.0059$), SZLGE ($P = 0.0417$) were higher in adenocarcinoma of mutant EGFR. Entropy (odds ratio 0.2548, 95% CI 0.09–0.7209, $P = 0.01$) was the independent predictor of EGFR mutation. In addition, LRHGE (hazard ratio 1.0017, 95% CI 1.0008–1.0026, $P = 0.0002$) predicted the recurrence in lung adenocarcinoma.

Conclusion: Texture features predicted EGFR mutation in lung adenocarcinoma. In addition, LRHGE was an independent predictor of recurrence in patients with lung adenocarcinoma.

AP219

DIFFERENCES OF CLINICAL FEATURES BASED ON PD-L1 EXPRESSION IN JAPANESE LUNG CANCER PATIENTS

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Background and Aims: Since immuno-checkpoint inhibitors targeting programmed death-1 receptor (PD-1) and its ligand (PD-L1) have shown their promising effects to non-small cell lung carcinoma (NSCLC), PD-L1 expression has become one of the important factors in deciding treatment strategy of NSCLC. However, differences in clinical characteristics and lung cancer profile depending on tumor proportion score (TPS) of PD-L1 has not been fully clarified yet. The aim of this study was to analyze the clinical features of NSCLC patients in our institute based on TPS.

Methods: We retrospectively evaluated the characteristics of NSCLC patients who had been analyzed their TPS in our institute from February, 2017 to December, 2017.

Results: Total of 146 NSCLC was tested for PD-L1 expression. Average age of patients was 73.5 years-old, and 70.3% were male. 16.1% showed TPS > 50%, 45.9% showed TPS of 149%, and 39.0% were negative. Male patients and smokers were more dominant in higher TPS group (Male: TPS < 1% : 69.6%, 1% < TPS < 49%: 69.7%, TPS > 50%: 77.3%, Smoker: TPS < 1%: 67.9%, 1% < TPS < 49%: 81.8%, TPS >

50%: 90.9%). In terms of histology, 54.5% of TPS > 50% NSCLC were squamous cell carcinoma, while only 14.0% in TPS negative NSCLC. Proportion of advanced NSCLC was higher in TPS > 50% group (TPS < 1% 24.6%, 1% < TPS < 49%: 31.3%, TPS > 50%: 59.0%), and none of the NSCLC patient with TPS > 50% were operable.

Conclusion: High PD-L1 expression was more frequent in males and smokers. More than half of NSCLC with TPS > 50% were squamous cell carcinoma, and tended to be a more advanced stage than lower TPS group.

AP220

NON-SMALL CELL CARCINOMA OF THE LUNG INITIALLY PRESENTING AS LUNG ABSCESS

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Background and Aims Objective: To describe a case of non-small cell lung carcinoma initially presenting as lung abscess.

Methods Methods: We present the clinical, diagnostic and laboratory data in our patient and reviewed the related published literatures.

Results: A 59 year-old male initially presented with productive cough and undocumented fever. Patient was managed as a case of lung abscess and pneumonia treated with antibiotics. Patient was eventually discharged. However, symptoms of productive cough now with associated haemoptysis persisted. Patient was then started on anti-Koch's medications completed for 6 months. On follow-up, repeat chest X-ray revealed pulmonary mass. CT-scan guided biopsy of the lung was done which revealed cell findings compatible with non-small cell carcinoma.

Conclusion: Lung abscesses are usually caused by bacterial infections. The most common components of the mixed bacterial populations in lung abscesses are anaerobic bacteria. Lung abscess may also complicate pulmonary infarction, primary lung cancer (central carcinoma with necrosis) and metastatic malignancies (1). Studies have showed that lung abscess which persisted despite antibiotic therapy most likely is an underlying lung cancer. CT of the chest, fibre optic bronchoscopy and cytological analysis of the abscess fluid are often helpful in diagnosing an underlying lung carcinoma (2). Underlying malignant disease may be overlooked that when eventually malignant nature is apparent, radical treatment is no longer possible (3). Patients presenting with lung abscess secondary to an undiagnosed lung cancer may have recurrent pneumonia (4). As in the case of our patient, a thorough diagnostic work-up was necessary before the underlying lung carcinoma was discovered.

AP221

OSIMERTINIB COMBINED WITH CETUXIMAB FOR NON-SMALL CELL LUNG CANCER (NSCLC) WITH T790M AND C797S MUTATIONS

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Background and Aims: Osimertinib, third generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), is approved to treat non-small cell lung cancer (NSCLC) with T790M mutation. T790M positive lung cancer becomes resistant to osimertinib after acquiring C797S mutation. We want to find effective regimen for T790M and C797S positive NSCLC.

Methods: A retrospective chart review of T790M and C797S mutant NSCLC, treated by osimertinib and cetuximab, was performed.

Results: Four patients were enrolled. EGFR mutations at initial diagnosis were exon 19 deletion in one, exon 19 deletion and T790M in

another and L858R in the others. They were all treated according to guideline including TKIs, chemotherapy and immunotherapy. Three developed acquired T790M after resistance to first or second generation TKIs, and the other had de novo T790M. All four patients received osimertinib. Re-biopsy was performed after acquired resistance to osimertinib. Latest EGFR mutations were all T790M and C797S. Osimertinib and cetuximab were administered for all. Progression-free survival (PFS) was 4.1 months and one month, respectively in case 1 and 2. Status of cancer was stable in the others.

Conclusion: Osimertinib, combined with cetuximab seems to be effective for T790M and C797S positive NSCLC. Further studies are necessary in order to understand the mechanism.

Osimertinib and cetuximab for lung adenocarcinoma, stage IV with T790M and C797S mutation

Case	1	2	3	4
Gender/Sex	64/Female	61/Female	66/Female	85/Male
Initial EGFR mutation	Exon 19 deletion	L858R	exon 19 deletion and T790M	L858R
Prior TKI use	Erlotinib Afatinib Osimertinib	Gefitinib Erlotinib Osimertinib	Erlotinib Narazotinib Osimertinib	Erlotinib Gefitinib Osimertinib
Time of C797S mutation after osimertinib	7.7 months	4.8 months	11.6 months	14.7 months
Line of osimertinib and cetuximab	13 th (2017/11/03)	15 th (2018/03/23)	10 th (2018/01/23)	8 th (2018/02/02)
Status/PFS	PD/4.1 months	PD/one months	SD/under treatment	SD/under treatment

PD: progression disease, SD: stable disease

AP222

NO TIME TO LOSE- UNDERSTANDING HOW VARIATION IN PRACTICE AFFECTS LENGTH OF STAY FOR PATIENTS WITH MALIGNANT PLEURAL EFFUSION

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¹Tan Tock Seng Hospital, Singapore

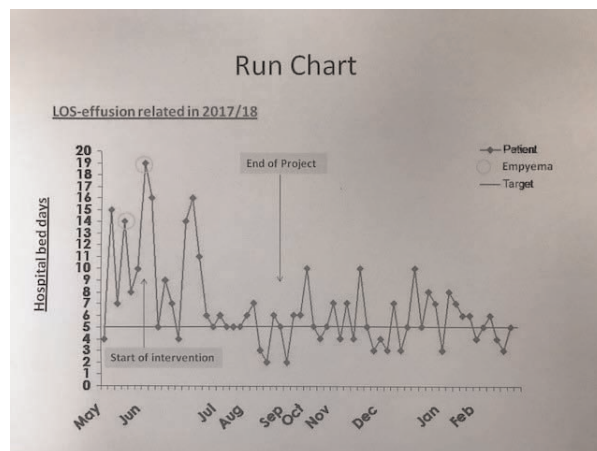
Background and Aims: Malignant pleural effusion (MPE) is a rising healthcare burden requiring inpatient care. Variation in clinical practice results in prolonged length of stay (LOS) for this vulnerable group where life expectancy is already compromised. Chest tube drainage remains the local predominant treatment of symptomatic MPE, and talc pleurodesis performed depends on suitability and patients' preference. An institution-based clinical audit in 2016 revealed a median effusion related LOS of >7 days against 4 days reported from recent published data. This review aims to improve management of MPE by reducing hospital stay whilst maintaining quality care.

Methods: All patients admitted to our institution for symptomatic MPE and managed with chest tube drainage with/without talc pleurodesis from 1 Jan to 31 Dec 2016 were included for baseline data ($n = 53$). We identified factors of delay in chest tube removal and implemented targeted interventions over 3 months (1 Jun to 31 Aug 2017) namely 1. Spreading the word to stakeholders (Respiratory Medicine, Palliative Medicine, General Medicine, Radiology) involved in care of patients with MPE; 2. Collaboration with Pathology/molecular laboratory for timely reporting of results; 3. Regular reminder and education of senior/junior staff regarding evidence-based practice; 4. Implementation of a practical guide/checklist for chest tube management and talc pleurodesis; 5. Talc pleurodesis Procedure Information Sheet.

Results: Data of 61 patients during and post intervention between 1 Jun 2017 and 28 Feb 2018 was analysed. Median effusion related LOS decreased from >7 to 5 days. The effect was sustained after project

completion. Other quality indices included better clinical practice such as compliance of pre-pleurodesis chest imaging check and analgesia (Before: 63%; After: 80%); and reduction in blood cultures/IV antibiotics for post-talc fever (Before: 33%; After: 6%)

Conclusion: Through education and collaborative efforts in building partnerships, we achieved success in improving management of MPE and reducing effusion related LOS.



AP223

DNA DEMETHYLATING AGENTS SENSITIZE IMMUNE-BASED CYTOTOXICITY BY UPREGULATING IMMUNE SYNAPSE MOLECULES ON LUNG CANCER CELLS

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Background and Aims: Cell-based immunotherapy is revolutionizing lung cancer management in the clinic. Enhancement of immunogenicity of cancer cells and their interaction with immune cells still is key to boosting clinical efficacy of immunotherapy. However, it has been known that cancer cells may avoid immune attack via downregulating cancer antigens by aberrant DNA hypermethylation. Therefore, it is critical to reveal which immunogenic molecules on the cancer cell surface can be altered by DNA demethylating agents (e.g. decitabine), and may be key players that sensitize responses to the subsequent combinatorial immune-based therapy.

Methods: We applied stable isotope labelling with amino acids in cell culture (SILAC)-based quantitative proteomics to identify membrane proteins altered in decitabine-treated human lung cancer cells. In order to identify membrane proteins showing in cancer cell surface compartment, the extracellular residues of proteins were biotinylated and then the proteins were isolated by pull down with streptavidin-beads.

Results: Remarkably, we observed that several proteins known to be at the immune synapse between target cells and natural killer (NK) cells or $\gamma\delta$ T cells were upregulated by decitabine. This indicates potential sensitization effects of decitabine to NK cells or $\gamma\delta$ T cell therapy in a major histocompatibility complexes (MHC)-independent manner. Among these decitabine-upregulated immune synapse proteins, intercellular adhesion molecule 1 (ICAM1), a surface glycoprotein and member of the immunoglobulin superfamily, were the mostly enhanced. ICAM1 protein expression level is indeed promoted by decitabine treatment in almost all human

lung cancer cell lines we examined. Overexpression of ICAM1 on cancer cells has been shown to promote interactions between cancer cells and NK cells. We therefore revealed that anti-cancer cytotoxicity by MHC-independent $\gamma\delta$ T cells were also enhanced on decitabine-sensitized lung cancer cells.

Conclusion: These findings have great clinical implications and provide novel molecular basis for coupling DNA demethylation agents with $\gamma\delta$ T cell-based immunotherapy in lung cancer patients.

AP224

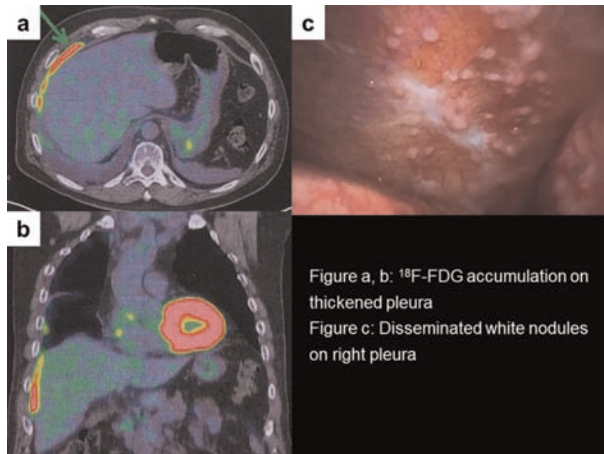
A CASE OF PSEUDOMESOTHELIOMATOUS LUNG CANCER IN PATIENT WITHOUT EXPOSURE TO ASBESTOS

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Background and Aims: Pseudomesotheliomatous carcinoma of the lung (PMCL) is a rare entity accounting for less than 1% incidence among all lung cancer and characterized by extensive pleural growth and minor invasion of lung tissue. Herein, we present a case of PMCL finally diagnosed by histopathological examination in addition to ¹⁸F-FDG PET/CT scan.

Methods: A 64-year-old Japanese male with hypertension and chronic thyroiditis visited our hospital complaining of a 3-day history of respiratory distress. He was current smoker (40-pack-year) and worked at the brewing industry for years. On physical examination, he had weak breath sounds and a chest radiograph revealed massive pleural effusion (PE) in the entire right lung field. Thoracentesis identified bloody and exudative PE, suggesting that the patient developed a lung tumor and malignant PE. However, we could not find primary lesion in pulmonary fields after removing PE. Contrast enhance computed tomography of the chest showed pleural thickening and small nodules on parietal and visceral pleura, and ¹⁸F-FDG PET/CT scan also revealed the pleural spread in the right thorax. Therefore, we conducted surgical biopsy of pleural nodules for definitive diagnosis, and thoracoscope showed disseminated white nodules over the right pleura. Finally, pathological examinations confirmed the presence of malignant cells using surgical specimens, and histochemical and immunohistochemical analysis revealed the tumor was pseudomesotheliomatous adenocarcinoma.



Results: According to the previous studies, major pseudomesotheliomatous tumours were adenocarcinoma, and there was relation between increased asbestos concentration in the lung tissue and the appearance of PMCL although the present case had no history of exposure to

asbestos. This case was unique at the point that we could identify pseudomesotheliomatous lung cancer in a visual way by thoracoscope.

Conclusion: Physicians should consider the possibility of PMCL when seeing the patient with bloody and exudative PE, but no apparent mass lesion in the lung.

AP225

METFORMIN PROLONGS SURVIVAL IN LUNG CANCER EGFR-TKIS PATIENTS

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Background and Aims: Metformin use has been reported to reduce cancer risk, and improve survival in lung cancer patients. This study aimed to investigate the effect of metformin use among patients with lung cancer receiving epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKIs) therapy.

Methods: A nationwide, population-based case-control study was conducted using the Taiwan National Health Insurance Research Database. From January 1, 2004 to December 31, 2012, a total of 373 metformin and 1,260 non-metformin lung cancer cohorts with diabetes mellitus and EGFR-TKIs treatment were studied.

Results: Metformin use was significantly associated with a reduced risk of death (HR: 0.73, 95% CI: 0.62–0.85, $P < 0.001$). In addition, metformin use was associated with a significantly longer median progression-free survival (9.2 months, 95% CI: 8.6–11.7 vs 6.4 months, 95% CI: 5.9–7.2 months, $P < 0.001$) and median overall survival (33.4 months, 95% CI: 29.4–40.2 vs 25.4 months, 95% CI: 23.7–27.2 months, $P < 0.001$).

Conclusion: In conclusion, metformin might potentially enhance the therapeutic effect and increase survival in patients with lung cancer receiving EGFR-TKI therapy.

AP226

NORTHERN MALAYSIA PULMONOLOGY CENTRE EXPERIENCE AND ANALYSIS OF PROGRESSION FREE SURVIVAL RATE WITH TYROSINE KINASE INHIBITORS IN MANAGING ADVANCED ADENOCARCINOMA OF LUNG

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Background and Aims: Pulmonologist plays an inevitable role in diagnosing lung carcinoma and managing it. Specific oncogenes with driver mutations, such as the Epidermal Growth Factor Receptor (EGFR) gene can lead to adenocarcinoma of the lung. Personalized therapy (Tyrosine Kinase Inhibitors) has become an important strategy in combating it under pulmonologist care.

Methods: We retrospectively analyze the treatment and management of adenocarcinoma of the lung in our center. The data analyses were performed using the SPSS Statistics for Windows Version 21.0. In this study, descriptive statistics were employed for selected variables. The findings were presented based on the types and distribution of the data. Categorical data was presented as frequencies and percentages, except age were presented as means and standard deviations.

Comparison of the differences between two sets of radiological measurement within the same group was analyzed using the Wilcoxon Signed-Rank test

The aim of study is to look at outcome of the management of the patients using Targeted therapy

Results: In total, 30 patients were analyzed (12 males, 18 females; median age 58.7 ± 11.17 with 33.3% of them were smokers and 13.3% of them were passive smokers). Tissue biopsies were obtained by pleural biopsy (63.3%), endobronchial biopsy (16.6%), and CT/Ultrasound guided biopsy (23.3%). All of them had EGFR mutations. 19 of them received TKI as the first line chemotherapy where else 6 of them received cisplatin based chemotherapy. Progression free survival (PFS) in the group received TKI were significantly longer (8.4 months) than group which received cisplatin based chemo (6.8 months).

Median target lesions, which treated by TKI's reduced from 48 mm (pretreatment) to 32.5 mm (post treatment). Non target lesions reduced to 15 mm (post treatment) from 23 mm (pretreatment). Many of them develop side effects of skin (46.7%).

Conclusion: There were clinical benefits for patients who received TKI as first line therapy in EGFR mutation patients.

AP227

AN IMMUNE PROFILE OF TUMOR PD-L1 EXPRESSION PLUS CD4 OR CD8 T CELL INFILTRATIONS CORRELATED WITH TREATMENT EFFICACY OF PD-1 BLOCKADE ANTIBODIES IN NSCLC PATIENTS

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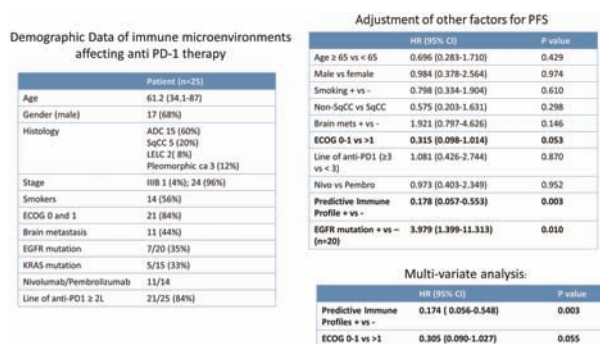
¹National Taiwan University Hospital, Taiwan

Background and Aims: Immunotherapy targeting PD-1/PD-L1 axis result in great success in lung cancer treatment, but only a minority of patients show durable response. Though tumor PD-L1 expressions selects a subset of patients responding to PD-1 blockade, the predictive value is unsatisfied. The incorporation of tumor infiltrating lymphocytes into PD-L1 expression may better correlate the treatment response of anti-PD-1.

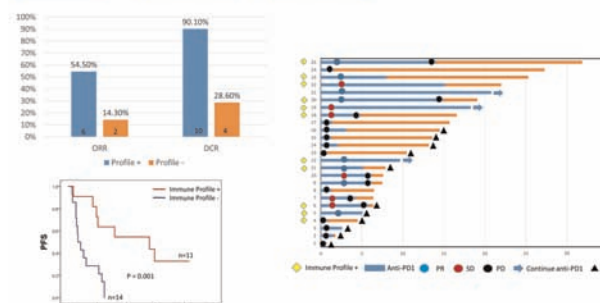
Methods: We retrospectively examined non-small cell lung cancer (NSCLC) patients treated with Nivolumab or Pembrolizumab monotherapy. Using immunohistochemistry (IHC), the pre-anti-PD1 treatment tissue specimens were analyzed for a panel of factors involving immune microenvironments, including immune checkpoints (PD-L1, Galectin-9), immune cells (CD4+ T cells, CD8+ T cells, regulatory T cells, M1 and M2 macrophages), antigen presenting machines (MHC class I), and genetic alterations related to immune cells infiltrations (PTEN, beta-catenin). The results were correlated with the treatment response and survival of patients.

Results: Total 25 NSCLC cases were eligible for this study. We found tumor PD-L1, CD4+ T cells, and CD8+ T cells were associated with better objective response rate (ORR), disease control rate (DCR), and progression free survival (PFS). After incorporation of these biomarkers, an immune profile (PD-L1 >0% and either CD4+ T cell $\geq 10\%$ or CD8+ T cell $\geq 10\%$) showed a better efficacy to predict ORR, DCR, and PFS. For ORR and DCR, the PPV of a positive immune profile was 54.5% and 90.1%, respectively; the NPV of a negative immune profile was 85.7% and 71.4%, respectively. Through multi-variate analysis, a positive immune profile and ECOG ≤ 1 were independently associated with longer PFS.

Conclusion: An immune profile comprising a quantitatively calculation of tumor PD-L1 expression, CD4+ T cell, and CD8+ T cells by simple IHC testing may help predict treatment response and outcomes of PD-1 blockade.



PD-L1 $\geq 1\%$ + CD4 $\geq 10\%$ or CD8 $\geq 10\%$ → Better ORR, DCR, and PFS



AP228

SMALL CELL LUNG CANCER TRANSFORMATION AND T790M MUTATION COEXISTING AFTER SUBSEQUENT FIRST AND THIRD GENERATION EGFR-TKI THERAPY: A RARE CASE REPORT AND LITERATURE REVIEW

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¹The First Affiliated Hospital of Sun Yet-Sen University, China

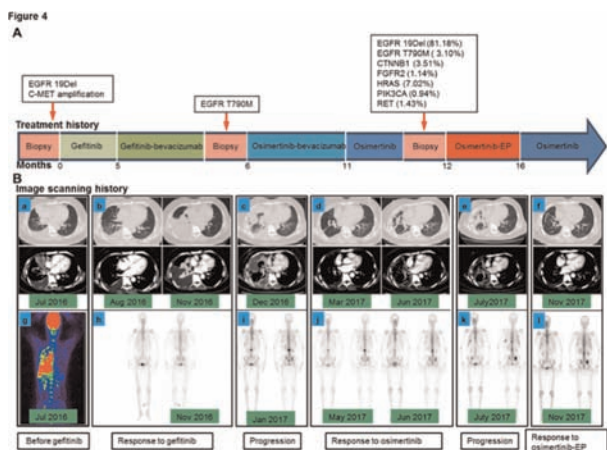
Background and Aims: Despite the proliferation of EGFR-TKIs, patients still face problems with drug resistance and disease progression. So far, no patient has been found to small cell lung cancer (SCLC) transformation with an accompanying T790M mutation. This case was reported to explore the clinical manifestation, mechanism, and treatment of this situation mentioned above in lung adenocarcinoma treated with EGFR-TKIs to increase awareness.

Methods: We retrospectively analyzed the clinical manifestations and pathological data of one case who had undergone subsequent treatment with gefitinib and osimertinib and then received re-biopsy after disease progression. We searched PubMed databases with the keywords "transformation" "SCLC" and "T790M", and review the relevant literatures.

Results: Pleural puncture cytology and EBUS-TBNA was performed and the 45-year-old woman was diagnosed to a EGFR-mutated lung adenocarcinoma. Positron emission tomography-computed tomography and magnetic resonance imaging showed advanced stage IV lung cancer. Then gefitinib was administered at a dose of 250 mg daily which maintained a clinical response for 5 months. After progression, blood NGS showed EGFR T790M mutation, and the patient received osimertinib 80 mg daily. After 5 months, she had a progression again and underwent a re-biopsy, while the results revealed SCLC transformation with an accompanying T790M mutation. She received chemotherapy plus osimertinib, which PFS was 8 months. To our knowledge, this is the first case of SCLC transformation and T790M coexisting after the subsequent first and

third generation EGFR-TKI therapy. The combination of chemotherapy and osimertinib may be the appropriate choice.

Conclusion: Re-biopsy plays a very important role in the management while progression after EGFR-TKI treatment, which helps to understand the mechanism of drug resistance and develop the next treatment strategy. Re-biopsy plays a very important role in the management while progression after EGFR-TKI treatment, which helps to understand the mechanism of drug resistance and develop the next treatment strategy.



AP229

PULMONARY SCLEROSING PNEUMOCYTOMA IN AN ASYMPTOMATIC YOUNG ASIAN MAN: A CLINICOPATHOLOGIC CASE REPORT

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Background and Aims: Pulmonary sclerosing pneumocytoma (PSP) is a rare benign neoplasm of the lung that predominantly affects middle-aged Asian women. Histologically, PSP is an epithelial tumor showing resemblance to pneumocytes (surface cells) and embryonic respiratory epithelium (round cells). The purpose of this report is to describe a case of PSH in a young Filipino man.

Methods: A 19-year-old Filipino man consulted at the outpatient department for re-evaluation and surgical management of a left upper lobe mass incidentally revealed during a pre-employment chest radiograph. He had no history of respiratory symptoms, pulmonary tuberculosis nor smoking. Thoracic computed tomography (CT) with angiography confirmed the presence of a solitary minimally-enhancing soft tissue mass in the left suprahilar area measuring 3.4 x 2.8 x 3.2 cm with no evidence of pulmonary vascular abnormality. A pre-operative CT-guided aspiration biopsy sample done at previous institution was compatible with a pneumocyte cell lesion. Baseline pulmonary function tests showed adequate lung volume reserve for surgery.

Results: Left posterolateral thoracotomy with wedge resection was performed, and a 2.9 cm well circumscribed lesion with cystic and solid areas was removed at the posterior segment of left upper lobe. Grossly the tumor was smooth, pink-tan, well-circumscribed, and ovoid shape. Cut sections showed grey-tan surfaces with foci of haemorrhage. Histopathologic examination revealed a biphasic tumor composed of surface and round cells arranged in solid, papillary and haemorrhagic patterns.

Immunohistochemistry results showed positive staining for cytokeratin AE1/AE3 in the surface cells, positive staining for TTF-1 and EMA in both surface and round cells, and negative staining for CD56 in both (see image). Final pathological findings confirmed diagnosis of pulmonary sclerosing pneumocytoma.

Conclusion: Definitive clinical diagnosis of PSP is challenging because of its histologic resemblance to lung adenocarcinoma and carcinoid tumor, hence a multidisciplinary approach is crucial for definitive management. Surgical excision is of curative intent and still recommended.

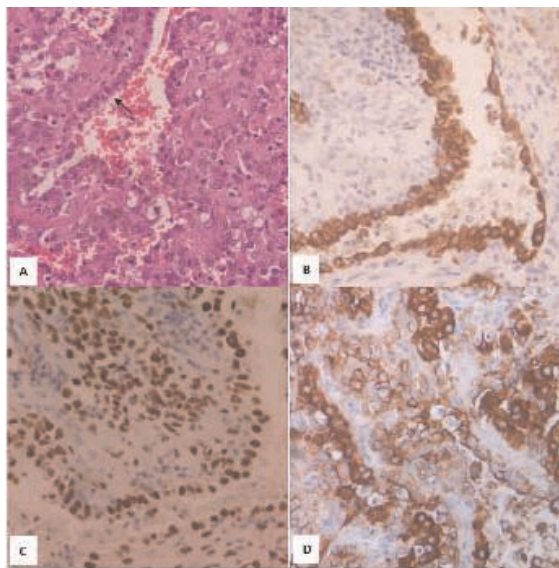


Figure 1. Sclerosing pneumocytoma. A. Tumor shows surface cells (arrow) lining a slit-like space, filled with blood, surrounded by round cells. B-D. Immunohistochemistry stains for pancytokeratin (B) shows cytoplasmic staining only in the surface cells, while TTF-1 (C) shows nuclear stain in both surface and round cells. Epithelial membrane antigen (D) shows cytoplasmic staining of both surface and round cells, with surface cells showing a stronger intensity.

AP230

LUNG CANCER WITH SMALL BOWEL METASTASIS AND PERFORATION WITH CHEMOTHERAPY-NAÏVE STATUS, A RARE CASE REPORT AND LITERATURE VIEW

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Background and Aims: Lung cancer is a leading cause of death by cancer worldwide. Most of the patients diagnosed as lung cancer was in advanced stage. However, small bowel metastasis was rare in patients with lung cancer.

Methods: We reported a 65 year-old man, a heavy smoker, presented with progressive shortness of breath and dry cough for 4 weeks.

Results: He had past medical history of hypertension and coronary artery disease status post two stents insertion in February. Plain radiograph of chest disclosed Right upper lung Cavitory mass. Computed tomography (CT) of chest revealed a thick-wall cavitory lesion at right upper lung area; one spiculated lesion at left upper lung area; necrotic mass-like lesion at right chest wall, supraclavicular and mediastinal region; and nodular lesion at right side adrenal gland. Lung cancer, squamous cell carcinoma was diagnosed by endobronchial biopsy. Palliative radiotherapy to right upper lung tumor was started first because severe right side bronchial stenosis by tumor invasion. Systemic chemotherapy

was scheduled after port-A insertion. However, severe abdominal pain with peritoneal sign developed before chemotherapy. Emergent CT of abdomen disclosed free air accumulation at peritoneal cavity, suspect hollow organ perforation. A tumor invasion related perforation was seen at 100 cm proximal to ileocecal valve by emergent abdominal laparotomy. Surgical intestinal tumor resection and end-to-end anastomosis was performed, but condition was down-hill with multiple organ failure after transferring to intensive care unit. The patient passed away 5 days after surgery.

Conclusion: Intestinal perforation without chemotherapy was a rare complication of lung cancer. It is difficult to predict if without evidence of gastrointestinal bleeding. Outcome was very poor even after surgical repair.

AP231

CHYLOTHORAX IN MEDIASTINAL TUMOR

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Background and Aims: Chylothorax is a rare condition that results from thoracic duct damage with chyle leakage from the lymphatic system into the pleural space, usually on the right side. Diagnosis involves cholesterol and triglyceride measurement in the pleural fluid.

Methods: A 17-year-old girl referred to our hospital with right pleural effusion in mediastinal tumor. The pleural effusion appearance is milky with pleural fluid triglyceride level was 1220 mg/dL, cholesterol level was 47 mg/dL, protein level 3.2 mg/dL, LDH serum 1680 and sudan III was positive. Superior cava vein syndrome occurred and pleural effusion became bilateral. Infiltrative lesion was found in right and left main bronchus.

Results: As approximately 2.4 l of chyle is transported through the lymphatic system every day, damage to, or rupture of the thoracic duct can give rise to a large and rapid accumulation of fluid in the pleural space. Mediastinal tumor may compress the lymphatic vessels preventing drainage of lymph from the lung periphery resulting in extravasation of chyle in to the pleural space. The exact diagnosis of chylothorax is based on the presence of chylomicrons in the pleural fluid. Cytological analysis of fluid stained with Sudan III will demonstrate chylomicrons. Sudan III was positive for this patient.

Conclusion: Chylothorax can be caused by traumatic or non-traumatic aetiologies. Thoracic duct obstruction due to malignancy is the commonest cause of non-traumatic chylothorax. The exact diagnosis of chylothorax is based on the presence of chylomicrons in the pleural fluid.

AP232

ADVANCED NON-SMALL CELL LUNG CANCER WITH TONSIL METASTASIS, A CASE REPORT

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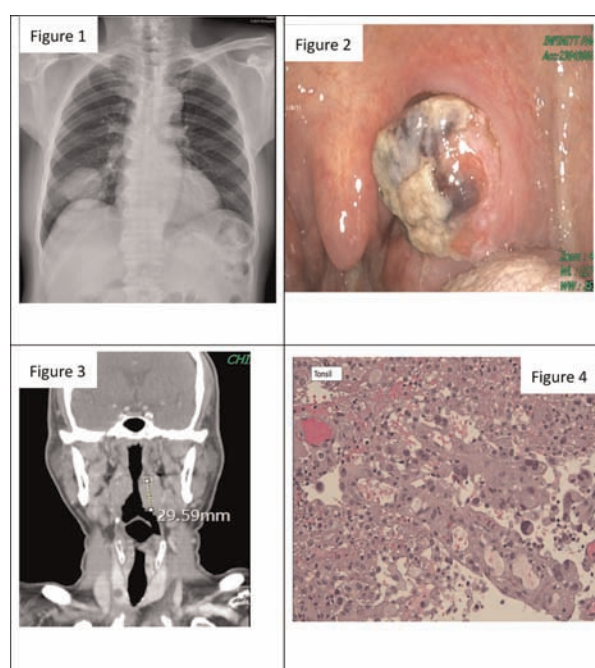
Background and Aims: Lung cancer is one of the most leading caused of cancer mortality in world wide. The cancer stage when diagnosis and some of the distant metastasis organ play the role for disease prognosis. Most common metastasis location except for the pleural and contralateral lung including brain, liver, adrenal gland, bone and extrathoracic lymph node.

Methods: We report a 75 never smoke male patient, presented at our chest outpatient department for intermittent haemoptysis without fever, chest pain, body weight loss or dyspnea symptoms. The Chest X-ray (Figure 1) of patient revealed a mass lesion which about 4 cm over right

lower lung field. Chest CT with contrast was arranged and the images showed a 4.2 cm huge mass with smooth margin with surrounding peripheral ground-grass opacity and some tiny nodules over bilateral lung fields.

Results: This patient was admitted for CT-guidance biopsy and pathology showed necrosis. RLL lobectomy with lymph node dissection and RUL wedge resection were done for the lung mass and another lung nodule. The pathology showed compatible with lung adenocarcinoma and RUL lung nodule was diagnoses as minimal invasive adenocarcinoma. Further complete staging as brain MRI, bone scan were negative but left side tonsil enlargement with ulcer formation was noted (Figures 2, 3). Further tonsil resection biopsy showed compatible with tonsil metastasis (Figure 4)

Conclusion: We reported this case due to rare metastasis location of left side tonsil. There still need further evidence for the correlation for tonsil metastasis and the disease prognosis. But rare metastasis should be keep in mind in the staging.



AP233

ADENYLATE CYCLASE-ASSOCIATED PROTEIN 1-TARGETED NANOPARTICLES AS A NOVEL STRATEGY FOR THE TREATMENT OF METASTATIC NON-SMALL CELL LUNG CANCER

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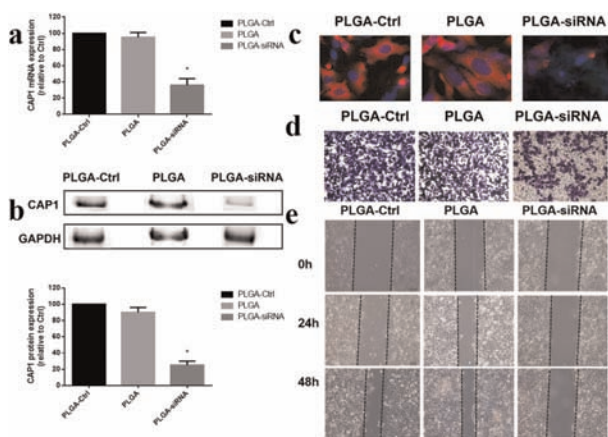
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Background and Aims: Non-small cell lung cancer (NSCLC) is the most common cause of cancer death in the world. Adenylate cyclase-associated protein 1 (CAP1) is a member of the cyclase-associated proteins contributing to tumor progression.

Methods: Our previous study has confirmed that CAP1 is associated with lung cancer and cancer cell metastasis. In the present research, PLGA/CAP1-siRNA nanoparticles were prepared and used to deliver CAP1-siRNA to A549 cells and down regulate CAP1 expression both in vitro and in vivo. The attractive performance of PLGA/CAP1-siRNA nanoparticles for delivering siRNA was confirmed by transwell assay, scratch assay and animal experiments.

Results: The results demonstrated that the multifunctional nanoparticles interfered with the expression of CAP1 and reduced NSCLC metastasis both in vitro and in vivo.

Conclusion: PLGA/CAP1-siRNA nanoparticles may become a new strategy of the treatment for metastatic NSCLC.



AP234

A 3-YEAR STUDY ON THE INCIDENCE AND PREDICTORS OF EARLY COMPLICATIONS RESULTING FROM CT-GUIDED TRANSTHORACIC BIOPSY AT THE LUNG CENTER OF THE PHILIPPINES

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Background and Aims: CT-Guided Transthoracic Biopsy remains one of the primary modalities in the diagnosis of intrathoracic lesions. A small percentage of complications would inevitably occur in the performance of such an invasive procedure. The occurrence of pneumothorax and haemoptysis were the endpoints of concern, since significant pneumothorax would necessitate evacuation, and even minimal post-procedural haemoptysis would prove distressing to patients. This study aims to show the complication rates of CT-guided biopsy at our institution, as well as the predictors of said complications.

Methods: 2133 patients who underwent CT-guided transthoracic biopsy were included. Review of records determined occurrence of complications noted immediately post-biopsy. Patient age, biopsy type, and length of biopsy needle tract through the lung were analyzed to determine causality.

Results: Overall complication rate was 9.6%. Subjects that underwent FNAB had 4.01% pneumothorax rate and 5.7% haemoptysis rate. Complication rates for core biopsy were 0% for Pneumothorax and 4.4% for haemoptysis. Chest tube placement was performed in 8.3% of pneumothorax. Only the distance traversed by the needle through the lung parenchyma showed a significant relationship with the occurrence of complications ($P < 0.001$). Longer distances showed progressively higher odds for developing complications.

Conclusion: CT-guided transthoracic biopsy is a safe diagnostic tool. Only the biopsy tract length showed correlation with complication incidence, shown by increasing odds ratios with longer tracts (Adjusted OR starting at 2.501 for 0.2–1.0 cm [$P = 0.013$] to 8.297 for >4 cm [$P = 0.000$], with greatest OR of 9.709 for lengths of 3.1–4.0 cm [$P = 0.000$]). The complication rates immediately post-procedure at our institution are comparable to data in published literature.

IMPACT OF ELDERLY ON ONE YEARS SURVIVAL RATES OF PATIENTS WITH NON SMALL CELL LUNG CANCER

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Background and Aims: Old age is one of lung cancer risk factors. Due to older age with lung cancer was suggested had lower survival rate than younger age, not all of them treated by standard chemotherapy and radiotherapy. Correlation between older age and survival rate of patient with lung cancer still debatable. This study was aimed to know one-year survival rate in Non-Small Cell Lung Carcinoma (NSCLC) older's patients (Ages >60 years).

Methods: Data were obtained retrospectively from medical records patient in pulmonary ward, Dr. Sardjito Hospital, from 2015 to 2016. All patients meeting with inclusion criteria such as patients with NSCLC and age >18 years old were involved in this study. Ninety four subjects were collected consecutively. These data were analyzed statistically using SPSS 16. The Kaplan-Meier method was used for estimation of survival distribution and differences in survival were assessed by the log-rank statistic.

Results: Of the 94 patients analyzed, 48 patients were ≥ 60 years old and 46 patients were <60 years old. The mean of patients age was 59.11 ± 1.23 years old, with the younger was 30 years old and the oldest was 89 years old. There were 63 (67.02%) males and 31 (32.98%) females. The majority of NSCLC type were Squamous Cell carcinoma 27 (77.14%) and Adenocarcinoma 44 (46.81%). The staging $\geq$ III were 61 (64.89%) patients. There were 30 (31.91%) smokers. and 32 (60.38%) patients had comorbidity. The 1-year survival rates in younger and elderly patients were 22.92% and 19.57%, respectively. The median survival time of elderly patient was not significantly different with younger patients (6.00 vs 6.00 bulan; $P = 0.718$).

Conclusion: Age was not the mayor prognostic factor impacting patient survival rate with NSCLC. Therefore, another factors should be considered, such as nutritional status and pulmonary function that require evaluation in elderly patients.

AP236

A CASE OF MALIGNANT PLEURAL MESOTHELIOMA THAT COMPLICATED WITH PERITONEAL DISSEMINATION DURING THE 10-YEAR SURVIVAL

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Background and Aims: Malignant pleural mesothelioma (MPM) that occurs in the visceral pleural is a rare and progressive cancer with poor patient prognosis.

Methods: An 80-year-old woman was admitted for dyspnea due to massive pleural effusion.

Results: Malignant cells were detected in the pleural effusion. Computed tomography and positron emission tomography findings did not reveal the intrapulmonary tumor, pleural thickening and the enlargement of lymph nodes. Immunohistochemical staining of collected cells in the pleural effusion showed MPM patterns. She was diagnosed with MPM of IMIG stage 1 and grade 1 performance status. Palliative care was selected because she had elderly and dementia. For improving dyspnea, the pleural effusion was extracted through a total of 82 thoracic puncture in last 10 years at the outpatient department and four times pleurodesis were also performed. However, large amounts of ascites were observed at age 87. The same malignant cells as in the pleural effusion were found in ascites, which was diagnosed as abdominal infiltration of MPM.

Abdominal puncture was performed 39 times in two years to excrete ascites. At age 89, she underwent an emergency operation due to umbilical hernia strangulation; abdominal disseminated lesions were found during the laparotomy, and pathological immunostaining of the excised specimens showed same patterns with the collected cells in the pleural effusion. She became bedridden postoperatively and died at age 90.

Conclusion: The 5-year survival rate of extra-pleural pneumonectomy was approximately 17%. The overall survival in CDDP-PEM chemotherapy for unresectable MPM cases was about 12 months. The 5-year survival rate of trimodality therapy with induction chemotherapy, extra-pleural pneumonectomy and adjuvant radiation for n0 cases of MPM was reported 55%. Ten-year survival case without surgical therapy or systemic chemotherapy has not yet been reported. For MPM cases with IMIG stages 1–2, repeated thoracic puncture might be one of the preferred and feasible treatment options.

AP237

DISCOVERY THE NOVEL COMPOUND FOR OVERCOMING EGFR-TKI RESISTANCE IN LUNG ADENOCARCINOMA

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Background and Aims: Abnormal epidermal growth factor receptor (EGFR) signalling is the major driver pathway in lung adenocarcinoma in Asia. Although first/second/third generation EGFR tyrosine kinase inhibitors (EGFR TKIs) have improved the prognoses in patients with activating EGFR-mutant lung adenocarcinoma, the acquired EGFR-TKI (Osimertinib) resistance was occurred due to the single point mutation in EGFR (C797S). However, there are no available targeting drugs to significantly suppress the EGFR with activating/T790M/C797S in cis (triple-mutant) mediated EGFR-TKI resistance.

Methods: The triple-mutant EGFR-expressing H1975 and BaF3 cells were incubated and treated with the Compound 1. After various treatments, cell proliferation or apoptotic proportion was evaluated by the Cell-Titer 96 Aqueous MTS assay or flow cytometry. The effects of Compound 1 on the EGFR activity and expression levels were evaluated by *in vitro* kinase assay and western blot, respectively. In preclinical studies, this Compound 1 was validated in the murine xenograft model by these ectopic EGFR-expressing cells.

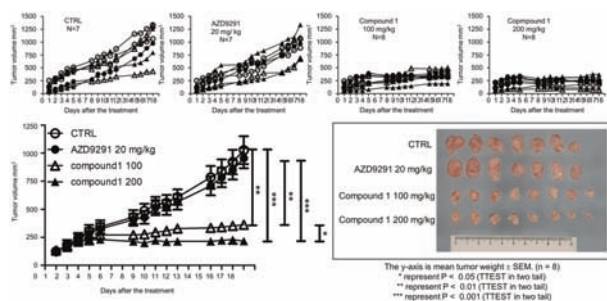


Figure 1. The anti-tumor growth effects of the small compound on triple mutant EGFR overexpression H1975 cells.

Results: In this study, we have identified the novel small molecule to overcome activating C797S/T790M mediated EGFR-TKI resistance after performed high throughput screening (HTS) assay. This compound 1 induced cell apoptosis and suppressed tumor growth in triple-mutant EGFR-expressing H1975 cell model, enabling the suppression rate were much higher than those in wild-type EGFR. Furthermore, the cytotoxicity of Compound 1 in BaF3 model was rescued by IL-3 addition. Overall,

these results implies that Compound 1 may selectively and specifically target triple-mutant EGFR while harbouring less activity toward wild-type EGFR and others.

Conclusion: This Compound 1 may overcome the EGFR third-generation TKI resistance and eventually translate into clinical application, enabling patients with lung adenocarcinoma to extend their survival rates.

AP238

COMPARABILITY OF AUTOMATED IMAGE CYTOMETRY RESULTS OF BRONCHIAL WASHINGS WITH MANUAL CYTOLOGY AND HISTOPATHOLOGY IN DIAGNOSIS OF LUNG CANCER AT LUNG CENTER OF THE PHILIPPINES

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Background and Aims: Manual Cytology is an integral diagnostic tool in evaluation of lung cancer but has several methodological limitations. Automated image cytometry is a method of quantitative analysis of nuclear structure and DNA content of exfoliative cells. Automation in cytologic assessment may reinforce cytological analysis diagnostic pathway in lung cancer diagnosis. Our study aimed to compare diagnostic quality of Automated Quantitative Image Cytometry (ClearCyte™) with manual cytology of bronchial washings and histopathology in the diagnosis of lung cancer for patients suspected with lung malignancy seen at the Lung Center of the Philippines.

Methods: A total of 112 patients suspected for lung cancer seen in Lung Center of the Philippines underwent fibre optic bronchoscopy and bronchial washings were collected. Specimen per patient were divided into 2 portions sent for manual cytology and ClearCyte™ automated quantitative image cytometry for analysis. Biopsy was done during bronchoscopy or as additional diagnostic procedure.

Table 1. Characteristics of subjects evaluated for lung cancer

	n = 112
Age in years	59.7 ± 12.1
Gender	
Male	78 (69.6%)
Female	34 (30.4%)
Radiologic Feature	
Pulmonary Mass	100 (89.3%)
Pulmonary Mass with pleural effusion	7 (6.2%)
Pleural Effusion	5 (4.5%)
Radiologic Localization of Pulmonary Lesion	
Central	37 (33.0%)
Peripheral	70 (62.5%)
Not Specified	5 (4.5%)

Table 2. Histopathology results of subjects

	(+) lung cancer n=71	(-) lung cancer n=22	No biopsy n=19
Age in years	62.8 ± 8.2	57 ± 14.2	50 ± 16
Gender			
Male	52 (73.2%)	15 (68.2%)	11 (58.0%)
Female	19 (26.7%)	7 (31.8%)	8 (42.1%)
Localization of Pulmonary Lesion			
Central	22 (31.0%)	7 (32.0%)	8 (42.1%)
Peripheral	46 (65.0%)	15 (68.0%)	9 (47.3%)
Not Specified	3(4.0%)	--	2 (10.5%)

Table 7. Comparison of lung cancer Diagnostic Indices of ClearCyte™ Quantitative Cytology, Manual Cytology, and Manual Cytology (Cell Block) in bronchial washing according to histopathology Results

	ClearCyte™ automated quantitative image cytometry	Manual Cytology	Manual Cytology (Cell Block)
	(%)	(%)	(%)
Sensitivity	10.6383 (3.9834, 23.8934)	38.4615 (15.134, 67.7227)	25 (4.4544, 64.4244)
Specificity	100 (75.9265, 100)	100 (92.8397, 100)	100 (30.9989, 100)
PPV	100 (46.2945, 100)	100 (46.2945, 100)	100 (19.7868, 100)
NPV	27.5862 (17.0465, 41.1111)	88.7324 (5.3357, 21.5331)	33.3333 (9.0418, 69.0823)
Accuracy Rate	10.6383 (3.9834, 23.8934)	38.4615 (15.134, 67.7227)	25 (4.4544, 64.4244)

Abbreviation: PPV: Positive Predictive Value, NPV: Negative Predictive Value

Results: Out of the 112 eligible patients suspected with lung cancer, 83% was confirmed with histopathology. ClearCyte™ automated quantitative image cytometry were positive for atypical cells in 5 out of the 112 specimens, negative for 71, and no detectable analyzable epithelial cells in 36 cases. ClearCyte™ automated quantitative image cytometry showed 10.6% sensitivity, 100% specificity compared to 36% sensitivity, 86% specificity of manual cytology and 93% sensitivity, 50.0% specificity of manual cytology (cell block). ClearCyte™ automated quantitative image cytometry showed 100% specificity for diagnosis of NSCLC, adenocarcinoma, and SCLC.

Conclusion: ClearCyte™ automated quantitative image cytometry of bronchial washing showed 10.64% sensitivity, lower for both manual cytology and manual cytology (cell block), but higher specificity of 100% compared to both. Compared to manual cytology of bronchial washing, ClearCyte™ has 100% specificity for NSCLC and adenocarcinoma, and SCLC.

AP239

MULTIPLE PRIMARY LUNG CANCER OR RELAPSE? A REPORT OF TWO CASES

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Background and Aims: It is important to assess the recurrence of lung cancer whether a primary lung cancer (MPLC) or relapse due to intrapulmonary metastasis. This will affect the staging of lung cancer and also affect the therapy.

Methods: Case report.

Results: Here, we describe the case of two patients who diagnosed as NSCLC and received chemotherapy. Mrs. Tj, 57 years, was referred to Soetomo General Hospital for lung mass sinistra evaluation. After investigation, patients diagnosed was lung adenocarcinoma stage IV EGFR (+) in exon 19. Previously in 2012, patient underwent superior lobectomy in left lung with histopathology results is adenocarcinoma stage IIA EGFR mutation (+). Mrs Tj got gefitinib for 9 months and declared complete response. Second patient, Mrs Nyk, 60 years, in 2016 came to Soetomo General Hospital with chief complaint is cough with phlegm, sometimes accompanied by a blood cough. Then the patient was diagnosed with lung

adenocarcinoma sinistra with EGFR mutation (-). in 2010, patient underwent platinum-based chemotherapy because she diagnosed with stage IV lung adenocarcinoma (D) and got complete response in 2011.

Conclusion: In cases of MPLC, it is often difficult to differentiate between multiple primary lung cancer, a single lung cancer with intrapulmonary metastasis, or pulmonary metastasis from primary cancer in other organs, especially when multiple tumours are found in the same lobe. The incidence of multiple synchronous primary lung cancer lies may be more than reported. The key to early diagnosis of multiple primary lung cancer lies in clinical suspicion, detailed examination of the respiratory tract and regular follow-up of those who have undergone initial resection of primary lung cancer.

AP240

THE RISK OF MECHANICAL VENTILATION IN PATIENTS WITH LUNG CANCER AT END-OF LIFE IN TAIWAN

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Background and Aims: Background: The respiratory care and management for patients with lung cancer at the end-of-life (EOL) are controversial issues. Aim: To investigate factors associated with different respiratory therapies for patients with lung cancer at the EOL

Methods: Method: We retrospectively reviewed the lung cancer patients who died in our hospital (between May 2014 and Dec 2017). The clinical data, records of treatment and decision making, the respiratory therapies of last admission were analyzed. We compared the dying patients who received mechanical ventilation (MV) and those received non-invasive ventilation or O₂ therapy.

Results: A total of 117 patients with the diagnosis of lung cancer died in our hospital were analyzed. Of them, 26 (22.2%) patients received MV and 91 (77.8%) patients received non-invasive respiratory care (7 received NIV and 84 received O₂ therapy). Up to 45.2 % patients received anticancer therapies before death. The duration of hospital stay was relatively longer in patients received MV (26.6 vs 22.4, $P = 0.384$). Patients with smoking history, better performance status (ECOG:0–1), malignant pleural effusion and multiple metastatic sites had higher risk of intubation at EOL. In contrast, patients with hospice care before last admission had lower risk of intubation (47.3% vs 11.5%, $P = 0.001$). Multi-variant analysis showed that patients with poor performance status and prior hospice care were associated with lower risk of intubation before death. (OR:0.104, $P = 0.009$ and OR:0.113, $P = 0.013$, respectively).

Conclusion: Around one-fifth of lung cancer patients died on mechanical ventilation. Prior hospice care and poor performance status were associated with lower risk of MV at EOL for patients with lung cancer.

AP241

NIVOLUMAB-INDUCED SEVERE ACUTE KIDNEY INJURY WITH A LONG LATENT PHASE IN A PATIENT WITH NON-SMALL CELL LUNG CANCER: A CASE REPORT

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Background and Aims: Immune checkpoint inhibitors (ICIs) have become the mainstream treatment of lung cancer, and the anti-

programmed cell death-1 (PD-1) antibody, nivolumab, has been widely used as an ICI. ICIs have a unique adverse event known as immune-related adverse event (irAE) which manifest most frequently as a skin disorder, and very rarely as a renal disorder.

Methods: We experienced a case report in which nivolumab induced severe acute kidney injury (AKI) which required haemodialysis.

Results: A 71-year old man was admitted to our hospital for the treatment of lung adenocarcinoma with no driver mutation and received immune checkpoint inhibitor; nivolumab. The best clinical response was partial response with nivolumab monotherapy, however, AKI which was likely to be associated with irAE, developed after 26 cycles of it; Serum creatinine level was elevated to 4.61 mg/dL. Administration of corticosteroid recovered the kidney function and nivolumab monotherapy was rechallenged, leading to the recurrence of severe AKI (serum creatinine level: 8.05 mg/dL) which required haemodialysis. Renal biopsy was performed and it showed acute tubulointerstitial nephritis with infiltrating neutrophils and lymphocytes.

Conclusion: Though the incidence of AKI induced by ICIs is less than that of other organ dysfunction, patients may develop severe AKI requiring haemodialysis. ICIs induced-AKI is characterized by late onset after administration, and in our case, it was the longest duration among the reported cases. It is speculated that ICIs re-program the immune system, leading to the loss of tolerance to endogenous and exogenous antigens, which is different from the mechanism underlying AKI induced by other medications. Therefore, re-challenging ICIs after recovery of the renal function should be tried. Nevertheless, prolonged follow up is needed to detect the late recurrence of severe AKI as reported in our case.

AP242

RISK FACTORS OF LUNG CANCER IN MALE NEVER-SMOKERS IN PERSAHABATAN NATIONAL HOSPITAL

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Background and Aims: Lung cancer is one of world's deadliest cancer, with 1.8 million new cases and 1.59 million deaths caused by lung cancer in 2012. Lung cancer is also known to be more prevalent in males than in females. Although active smoking is already known to have causative relationship with lung cancer, about 25% of lung cancer cases worldwide are not associated with active smoking. In Southeast Asia, approximately 50% of lung cancer cases are thought to have nothing to do with active smoking.

Methods: This study is a case-control study with 45 subjects in total: 27 with lung cancer and 18 with no lung cancer who enrolled to Persahabatan National Hospital in July 2016 – January 2017. The data regarding demographics, smoking status, exposure to environmental tobacco smoke, family history of cancer, history of tuberculosis, and exposure to indoor air pollution of each patient were obtained. Descriptive statistics, Chi square hypothesis test, and logistic regression hypothesis test were used for analysis.

Results: Results from bivariate analysis showed that environmental tobacco smoke (ETS) (OR = 6.914; CI 1.78–26.853) and family history of cancer (OR = 8.5; CI 0.971–74.424) were associated with increased risk of lung cancer in male never-smokers, while other risk factors were not found to have been associated with lung cancer in male never-smokers. Multivariate analysis showed both ETS and family history of lung cancer were associated with risk of lung cancer in male never-smokers, with ETS being the most associated factor having individuals with exposure to ETS to have 8,479 more likely odds of developing lung cancer.

Conclusion: There is a significant association between exposure to environmental tobacco smoke (ETS) and family history of cancer with increased risk of lung cancer in male never-smokers, with ETS being the most associated factor with the increased odds of developing lung cancer in male never-smokers.

AP243

MOLECULAR BIOLOGICAL ANALYSIS IN A PATIENT WITH MULTIPLE LUNG ADENOCARCINOMA

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Background and Aims: In general, the utility of molecular biological analysis in lung adenocarcinoma has been demonstrated. Here we report a rare case presenting as multiple lung adenocarcinoma with four different EGFR gene mutations detected in three lung tumours.

Methods: The patient was a 64-year-old woman who was found to have right lung segment S4 ground-glass nodule (GGN) on chest computed tomography (CT) following opacification detected on routine chest X-ray. Follow-up CT revealed a 42-mm GGN nodule with a 26-mm nodule (S6) and a 20-mm GGN (S10).

Results: Histopathology of resected specimens from the right middle and lower lobes revealed all three nodules were adenocarcinoma. Four EGFR mutations were detected; no three tumours had the same mutations.

Conclusion: Molecular biological analysis is a promising tool for the diagnosis of primary tumours in patients with multiple lung carcinoma of the same histotype, enabling appropriate treatment.

Paediatric Lung Disease 1

AP244

THERAPEUTIC EFFECT OF LEUKOTRIENE RECEPTOR ANTAGONIST MONTELUKAST IN TREATMENT OF RESPIRATORY TRACT MYCOPLASMAL INFECTIONS IN CHILDREN

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Background and Aims: *Mycoplasma pneumoniae* is the main pathogen in upper respiratory tract infection among children, and the morbidity is also high. In addition to causing respiratory mucosa, it can act as an allergen to cause airway hyperresponsiveness, result in long-range cough, even trigger or develop asthma. Leukotriene receptor antagonist montelukast can block *Mycoplasma pneumoniae* that stimulates the inflammatory response of the respiratory tract as an allergen after infection, and lower airway hyperresponsiveness.

Methods: Totally 100 children infected with *Mycoplasma pneumoniae* from June 2015 to June 2016 in paediatrics department of our hospital were selected to randomly assign into the observation group and the control group. Both groups took conventional anti-mycoplasma therapy, but the observation group simultaneously took montelukast for 4 days and 7 days, then their cough conditions were observed and compared.

Results: *Mycoplasma pneumoniae* infection after application of conventional anti-mycoplasma therapy (azithromycin) and symptomatic treatment, supplemented by montelukast special treatment, the symptom remission of cough in the observation group was significantly better than that of the control group.

Conclusion: Leukotriene receptor antagonist can block mycoplasma pneumoniae that stimulates the inflammatory response of the respiratory tract as an allergen after infection, lower airway hyperresponsiveness, reduce mucus secretion, ease bronchial spasm, and shorten the duration of cough.

AP245

This abstract has been withdrawn.

AP246

AN UNEXPECTED FINDING OF PERSISTENT RIGHT LUNG COLLAPSE; CHILDHOOD ENDOBRONCHIAL TUMOUR:

A CASE REPORT

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Background and Aims: Introduction- Childhood endobronchial tumour is a rare condition in which patient usually presents with common respiratory symptoms like chronic cough, recurrent wheeze or lung collapse.

Methods: Case- A 6-year-old girl was referred to our unit for persistent right lung collapse. She presented with history of cough and exertion dyspnea for 2 months. She was treated as necrotizing pneumonia and after 3 weeks of antibiotics; she had minimal clinical improvement and chest X-ray showed persistent right lung collapse. Examination showed she was tachypnoeic with reduced chest expansion and breath sounds on the right lung. Otherwise no crepitation or rhonchi was heard.

Investigations- She was investigated extensively, including pulmonary tuberculosis and it was negative. Ultrasound thorax and CECT thorax showed collapsed consolidation consistent with necrotizing pneumonia and nodular like echogenic lesion in a consolidated lung parenchyma. Bronchoscopy revealed intraluminal vascularized mass at right main bronchus causing almost complete obstruction.

Results: Managements -Excision biopsy was done with intraoperative finding of large vascularized mass from right main bronchus extending to the right upper lobe with multiple irregular nodules. Histopathology reported as Large Cell Neuroendocrine Carcinoma. In view of no standard guideline of chemotherapy in this type of carcinoma, she was treated as rhabdomyosarcoma-like tumour with vincristine, ifosfomide, doxorubicin and actinomycin. She underwent right thoracotomy and gross tumour excision after 2 cycles of chemotherapy. The tumour was excised as much as possible however residual tumour was still seen encircling the trachea, hoping that it will shrink further with subsequent cycle of chemotherapy.

Conclusion: Large Cell Neuroendocrine Carcinoma is a rare primary endobronchial tumour and no standard therapy yet known to treat the condition.

AP247

MASSIVE HEMOPTYSIS IN CHILDREN DUE TO INTRALOBAR PULMONARY SEQUESTRATION (CASE REPORT)

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Background and Aims: Massive haemoptysis is defined as blood loss more than 200 mL per day, rare but potentially life threatening in

children. Acute lower respiratory infection and foreign body aspiration are the most common cause of haemoptysis in children. Pulmonary sequestration (PS) is a rare congenital bronchopulmonary malformation accounting for 0.15%– 6.4% of all congenital pulmonary malformations that can be classified into intralobar sequestration (ILS) and extralobar sequestration (ELS). Its receive blood supply from systemic circulation arteries (mainly thoracic aorta and aorta abdominalis). ILS is the most common type (75–85%). Main manifestations of PS are recurrent respiratory tract infection. Haemoptysis is not a common symptom in PS.

Methods: Eight years old male child came to emergency department with massive haemoptysis (>400 mL in 24 h), with chest X-ray showing an opacity in the right lower lobe. This patient has a history of haemoptysis 10 months before and treated with antituberculosis drug but no improvement. We performed a flexible bronchoscopy to identify the source of bleeding.

Results: We found an active bleeding from the right lower lobe. We also found a multiloculated infiltration mass like polyp in right lower lobe and left lower lobe. CT angiography was done which demonstrated an intralobar pulmonary sequestration in the right and left lower lobes that provide arterial blood supply from thoracic aorta, vertebra artery and pulmonary artery.

Conclusion: We demonstrated a case of the lung sequestration in male children. Massive haemoptysis is not common symptom in pulmonary sequestration. Congenital pulmonary sequestration is a rare lung malformation. In cases of recurrent pulmonary infections of identical localization or recurrent haemoptysis, lung sequestration should be considered in children so that a diagnosis by imaging methods can be confirmed rapidly. The fact that using flexible bronchoscopy can find the source of bleeding and the abnormality of the airway.

AP248

PULMONARY INTRALOBAR SEQUESTRATION WITH CONGENITAL PULMONARY AIRWAY MALFORMATION TYPE II (CPAM TYPE II)

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Background and Aims: Pulmonary sequestration is an uncommon congenital abnormality in which nonfunctioning lung tissue is supplied by an anomalous systemic artery. Both the extralobar and intralobar forms probably develop from an accessory lung bud from the primitive foregut. Their etiology is far from understood, with various proposed theories. This case report aims to discuss a case of a 1-month old male who presented with persistent respiratory distress since birth.

Methods: The patient was born to a 36 y/o G3P2 (3012) mother, full term, via repeat CS. At birth, the patient was noted to be tachypneic. Clear breath sounds is appreciated on the left with decreased breath sounds on the right. CT scan showed intralobar sequestration of the right lower lobe with adjacent cysts to consider CPAM type 2. Right lower lobe lobectomy was done which showed large arterial branch from the aorta connected to the right lower lobe, with right lower lobe consolidation and cystic areas. Final histopathology result showed CPAM type II.

Results: Pulmonary sequestration consists of 2 types. Intralobar sequestration is usually found in the posterior basal segment of the left lower lobe encircled by visceral pleura without pleural separation from the rest of the lobe. Symptoms in neonates and infants are uncommon. It affects males four times more frequently than females. In both types, the pulmonary tissue is largely cystic and contains disorganized, airless alveoli, bronchi, cartilage, respiratory epithelium, and a systemic artery. It is often secondarily infected, bronchiectatic, or atelectatic, and may show histology of a CCAM, particularly type 2 CCAM in extralobar variants.

Conclusion: Pulmonary sequestration is a rare disease with multiple theoretical aetiologies, often misdiagnosed due to its variable and non-specific presentation. CT scan/angiography and other imaging modalities which can accurately identify the arterial supply and venous drainage of the sequestered segment, are essential for diagnosis and preoperative planning.

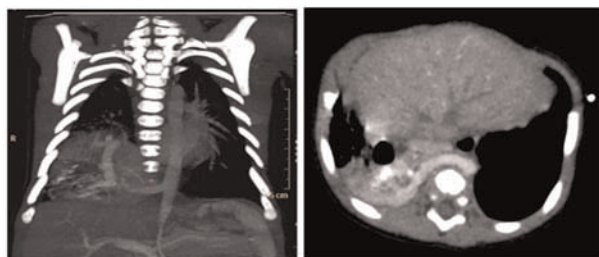


Figure 2

Figure 3

Figure 2 and 3: CT scan of the chest revealing the arterial supply from the distal branch of descending aorta which supplies the posterior segment of the right lower lobe without communication to the tracheobronchial tree.

Pulmonary Circulation 1

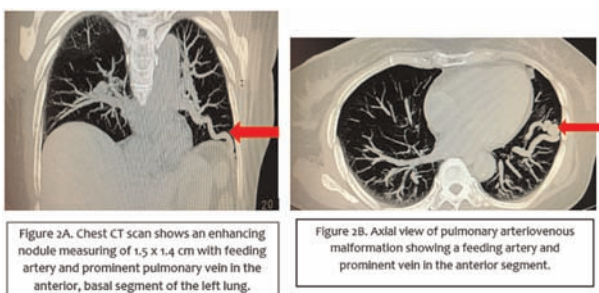
AP249

PULMONARY ARTERIOVENOUS MALFORMATION PRESENTING AS RECURRENT ISCHEMIC STROKE: A CASE REPORT

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Background and Aims: Arteriovenous malformations (AVMs) are lesions in the vasculature that allow blood to flow directly from arteries to veins thereby bypassing the capillaries.¹ Pulmonary AVM (PAVM) is a connection between a pulmonary artery and a vein and usually congenital in origin. The diagnosis of PAVMs is difficult due to its varied presentations. PAVMs most commonly present with haemoptysis, dyspnea or hemothorax, transient ischemic attack or cerebrovascular disorder (CVD).



Methods: A case of a 62-year-old Filipino female, with recurrent episodes of left sided weakness and slurring of speech was initially evaluated as recurrent stroke since 2003. Computed tomography (CT) scan of the head was unremarkable. A Chest radiograph was done which showed an incidental finding of pulmonary nodule on the left lower lobe. A probable pulmonary malignancy with brain metastasis was entertained. A Chest CT scan with contrast was performed in order to characterize the pulmonary nodule which revealed a PAVM.

Results: After thorough work up, a diagnosis of PAVM presenting as recurrent ischemic stroke was established. In scientific literatures, PAVM presenting as CVD account for 6.3–36.5%.¹² Patient was referred to a thoracovascular surgeon and successful resection of the PAVM was done.

Conclusion: The diagnosis of PAVMs posed a great challenge especially in patients presenting as recurrent stroke. Thus in patient with this kind of presentation, a differential diagnosis of PAVM as etiology should be considered.

AP250

RISK OF SYMPTOMATIC VENOUS THROMBOEMBOLISM IN PATIENTS FOLLOWING APPENDECTOMY: A NATIONWIDE COHORT STUDY

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Background and Aims: Although an appendectomy is the most common abdominal emergency surgery, the surgeons do not regard an appendectomy as a major surgery, which needs preventive strategies for venous thromboembolism (VTE) in Taiwan. We conducted a nationwide cohort study to investigate the incidence and risk of symptomatic VTE in patients following appendectomy in Taiwan.

Methods: We studied the entire hospitalized population in Taiwan ($N = 23.74$ million) from 2000 to 2012, with a follow-up period extending to the end of 2013. We identified patients receiving appendectomy by using the Taiwan National Health Insurance Research Database as the appendectomy cohort, and selected a non-appendectomy cohort that was 1:4 frequency-matched by age (5-year interval), sex, and index year from the general population. We used Cox models to estimate hazard ratios (HR) of symptomatic VTE and 95% confidence interval (CI) in the appendectomy cohort compared with the non-appendectomy cohort.

Results: The appendectomy cohort showed a higher incidence of symptomatic VTE than did the non-appendectomy cohort (5.90 vs 3.29 per 10,000 person-year). After adjustment for covariates, a 1.68-fold adjusted HR of symptomatic VTE in the appendectomy cohort compared with the non-appendectomy cohort (95% CI = 1.56–1.81). Compared with non-appendectomy, open appendectomy showed a 1.73-fold increased adjusted HR of symptomatic VTE (95% CI = 1.61–1.87). Laparoscopic appendectomy did not show significant association with symptomatic VTE.

Conclusion: Open appendectomy carried an increased risk of symptomatic VTE.

AP251

HAEMOPTYSIS DUE TO A RARE CAUSE IN THREE PATIENTS FROM CENTRAL SRI LANKA

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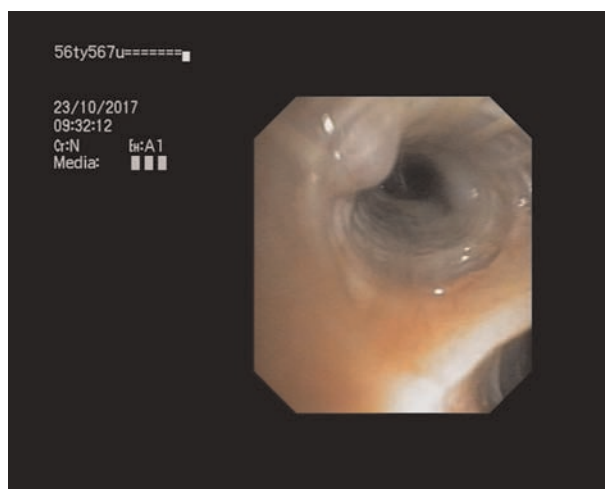
Background and Aims: Haemoptysis is a common symptom of many different aetiologies. Arteriovenous malformations (AVM) are rare, yet an important cause of haemoptysis. However, AVM can be unrecognized easily in the absence of targeted investigations.

Methods: We describe 03 patients presenting with haemoptysis, diagnosed as pulmonary AVMs.

Results: All were males with age 53, 59 and 65 years. All patients presented with haemoptysis, <100 mL/day in one and 100–250 mL/day in two patients. All had history of recurrent haemoptysis, for 06 months to 07 years. None had dyspnoea, chest pain or family history of vascular

anomalies. 02 were ex-smokers. One had grade I clubbing. None had cyanosis. Cardiovascular, respiratory and abdominal examinations were normal in all three. Chest X-ray showed mild bronchiectasis in lower lobes in one patient, but normal in others. Mucosal nodules suggestive of AVMs were noted during bronchoscopy (FOB) in 02 patients, located at apicoposterior segment of left upper lobe (figure) and origin of right upper lobe. These were not biopsied due to bleeding risk. FOB was normal in the other, in which AVM was visualized in computer tomographic pulmonary angiography (CTPA). Thoracic surgical and interventional radiological opinions were taken. However, they were managed conservatively and currently being followed up closely. None had further episodes of haemoptysis up to the time of reporting.

Conclusion: AVMs should be suspected during investigation of haemoptysis, even if characteristic clinical features are absent. AVMs may be seen in bronchoscopy or CTPA even when chest X-ray is normal. This illustrates the need for comprehensive investigations for evaluation of haemoptysis.



AP252

AIR-CRESCENT IS NOT ALWAYS INFECTIOUS EVENT

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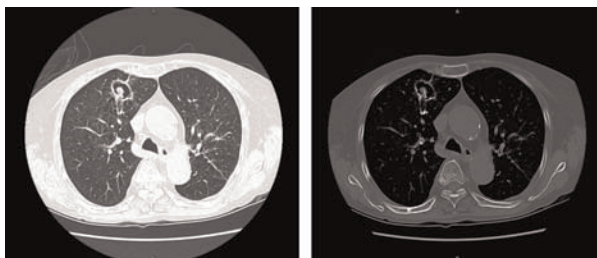
Background and Aims: Air-crescent sign is commonly observed in lung infection such as invasive aspergillosis and tumor thromboembolization. However, due to medical progression, new materials have been applied to our patient. Vertebral body instability due to osteoporosis has been a major issue. Percutaneous vertebroplasty is newly developed method to treat vertebral fracture. However, bone cement embolism has been widely reported ranging from 3.5–25%. Most cases of bone cement embolism are self-limited. Here, we presented an unusual case of pulmonary gangrene after bone cement injection.

Methods: A 75-year-old female presented to our clinic due to dyspnea on exertion with the diagnosis of asthma. Interestingly, the CXR revealed white linear structure in both lung field. Tracing back her history, she received percutaneous vertebroplasty years ago for her backbone fracture. Her wheezing and dyspnea bothered her so much, and computed tomography (CT) was arranged.

Results: A 75-year-old female presented to our clinic due to dyspnea on exertion with the diagnosis of asthma. Interestingly, the CXR revealed white linear structure in both lung field. Tracing back her history, she received percutaneous vertebroplasty years ago for her backbone

fracture. Her wheezing and dyspnea bothered her so much, and computed tomography (CT) was arranged.

Conclusion: Air-crescent sign has been linked to lung infections such as bacterial pneumonia, abscess leading gangrene change. Also, invasive aspergillosis is also another major cause. Few reports described vascular occlusion due to tumor thromboembolization leading to pulmonary gangrene. We reported an unusual form of bone cement embolization leading to pulmonary gangrene presenting as air-crescent.



AP253

PATHWAYS HSA_CIRC_0026480-MIR-27A-3P-ATXN1 AND HSA_CIRC_0046159-MIR-1226-3P-ATP2A2 ARE INVOLVED IN THE DEVELOPMENT OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Background and Aims: We aimed to find a possible molecular mechanism of chronic thromboembolic pulmonary hypertension (CTEPH) by integration analysis of microRNAs (miRNAs) and circular RNAs (circRNAs).

Methods: We performed differential expression analyses on an Affymetrix miRNA chip (CTEPH: 160039K-1, 160039K-2, 160039K-3, and 160039L-1; control: 160039J-6, 160039J-7, 160039J-8, 160039J-9, and 160039J-10) and an Agilent circRNA chip (CTEPH: 160039E&H-1, 160039E-2, 160039E&H-3, 160039G-1, and 160039E&H-4; control: 160039F-1, 160039F-2, 160039F-3, 160039F-4, and 160039G-2). Then, a series of bioinformatic analyses were conducted, including prediction of target genes of differentially expressed miRNAs, functional enrichment analysis of miRNAs and circRNAs, prediction of miRNA partners of differentially expressed circRNA, coexpression analysis of differentially expressed circRNA and miRNA, competing endogenous RNA (ceRNA) analysis, and network construction. Finally, circRNAs were detected by RT-PCR.

Results: Hsa_circ_0026480 and hsa_circ_0046159 interacted with miR-27a-3p and miR-1226-3p, respectively, and had a higher degree value in the miRNA-circRNA regulatory network. ATXN1, having a ceRNA relation with hsa_circ_0026480, was one of the target genes of miR-27a-3p, and ATP2A2, having a ceRNA relation with hsa_circ_0046159, was one of the target genes of miR-1226-3p. Besides, a verification experiment showed that the expression of hsa-circ-0026480 in group CTEPH was lower than that in the control group, and expression of hsa-circ-0046159 in group CTEPH was significantly higher than that in the control group.

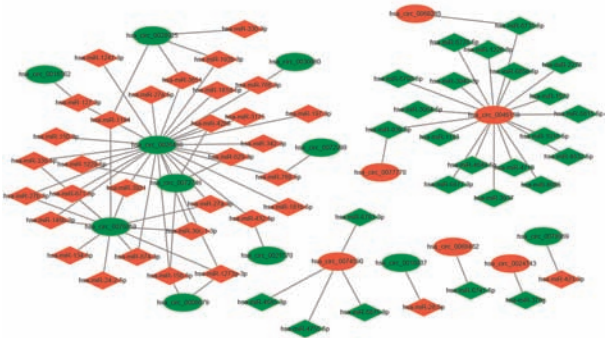
Conclusion: Hsa_circ_0026480 promotes CTEPH development and functions as a ceRNA to regulate ATXN1 expression by sponging miR-27a-3p in CTEPH, while hsa_circ_0046159 promotes CTEPH

development and functions as a ceRNA to regulate ATP2A2 expression by sponging miR-1226-3p in CTEPH.

Table 1 The statistical results of ceRNA

circRNA	mRNA	degree
hsa_circ_0026480	ATXN1	17
	TFCP2L1	17
	ONECUT2	17
	HIPK2	16
	PGPEP1	16
hsa_circ_0046159	ATP2A2	7
	ZNF609	6
	C1orf21	6
	ZHX3	5
	BSN	5

Degree: the number of miRNA regulated by circRNA and mRNA.



Respiratory Infections (Non-Tuberculous) 1

AP254

THE PHYSICIAN'S PERSPECTIVES ON THE DEFINITION, CLINICAL PRACTICES AND CLINICALLY IMPORTANT OUTCOMES IN THE MANAGEMENT OF ACUTE BRONCHIOLITIS IN THE TERTIARY HOSPITALS OF CEBU CITY, PHILIPPINES

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¹Chong Hua Hospital, Philippines

Background and Aims: Acute bronchiolitis (AB) is the most common lower respiratory tract infection in infants. It is a clinically diagnosed condition characterized by a wheezing illness associated with an upper respiratory tract infection. However, there is a wide practice variation among clinicians and there is inconclusive evidence for many therapeutic approaches. This study was designed to determine the physician's perspectives on the definition, clinical practices and the clinically important outcomes in the management of AB in the tertiary hospitals of Cebu City, Philippines.

Methods: Design: A cross-sectional survey
Setting: The study was conducted in the tertiary hospitals of Cebu City, Philippines

Participants: The study included all board-certified paediatricians who are registered in the Philippine Paediatric Society–Central Visayas (PPS-CV) and practicing in Cebu City, Philippines.

Methodology: A pre-tested 10-item questionnaire was used.

Statistical Analysis: Qualitative data were expressed as percentage.

Figure 1. The perspectives of pediatricians on what age group (A) and how many episodes of wheeze before bronchiolitis is considered (B)

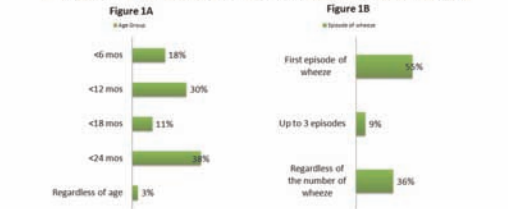


Figure 2. Perspectives of Pediatricians on key history and clinical findings in AB

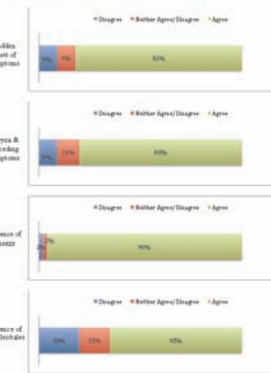


Table 1: Clinical practices of physician respondents in the management of AB

Clinical practices	Pediatricians n=66 (100)
Diagnostic test	
Chest radiograph – n (%)	41 (65)
Treatment – n (%)	
Oxygen	62 (94)
Hypertonic saline	19 (29)
Chest physiotherapy	13 (20)
Epinephrine nebulization	26 (39)
Salbutamol nebulization	51 (77)
Ipratropium nebulization	13 (20)
Montelukast	3 (5)
Antibiotics	13 (20)
Corticosteroids	29 (44)

Table 2: Physicians perspectives on the definition, diagnosis and management of AB compared to AAP guidelines

Variables	Physicians' perspective	AAP guidelines
Definition		
Age Group	<24 months in 38%	<24 months
Episodes of wheeze	1 st episode of wheeze	Not specified
Presence of coryza and preceding symptoms	80% agreed	Present
Presence of crackles	65% agreed	Present
Clinical Practices ^a		
Diagnostic Chest x-ray	65% agreed	Not recommended
Treatment with		
Oxygen	94% agreed	Recommended in some ^b
Hypertonic saline	29% agreed	Recommended in some ^b
Chest physiotherapy	20% agreed	Not recommended
Epinephrine	39% agreed	Not recommended
Salbutamol	77% agreed	Not recommended
Ipratropium	20% agreed	Not recommended
Montelukast	5% agreed	Not recommended
Antibiotics	20% agreed	Not recommended
Corticosteroids	44% agreed	Not recommended

^a The parameters where physician perceived to be necessary in the diagnosis and treatment of acute bronchiolitis.
^b Clinicians may choose not to administer supplemental oxygen if the oxygen saturation exceeds 90% in infants and children with a diagnosis of bronchiolitis.
^c Clinicians may administer nebulized hypertonic saline to infants and children hospitalized for bronchiolitis.

Results: A total of 66 participating paediatricians were recruited to this study. Most of our respondents (38%) defined AB as an illness involving children less than less than 24 months. The majority of the paediatricians agreed on the presence of preceding symptoms in AB (80%), and on the presence of wheeze (96%) and crackles (65%) as a pertinent physical examination finding. The majority of our paediatricians (65%) requests for a chest X-ray in suspected AB patients. In treating AB, majority would gave oxygen therapy (94%), salbutamol nebulization (77%) and corticosteroid (44%). However, about 20% will still give antibiotics.

Conclusion: The study showed that most paediatricians defined AB as a viral illness preceded by coryza followed by a sudden onset of respiratory symptoms in an infant and young children less than 2 years old. Some paediatricians would still do a chest radiograph in the diagnosis of AB. Some paediatricians gave salbutamol nebulization, corticosteroids and even antibiotics in the management of AB despite the AAP recommendations. The recognized treatment outcome parameters by most paediatricians were the improvement of respiratory distress and reduction of the risk for hospitalization.

AP255

DIAGNOSTIC PREDICTIVE FACTOR OF ADENOVIRAL PNEUMONIA IN PATIENTS ADMITTED FOR COMMUNITY-ACQUIRED PNEUMONIA IN SOUTH KOREA MILITARY TRAINEES

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Background and Aims: In immunocompetent patients, adenovirus causes mostly self-limiting upper respiratory infections which may progress to fatal respiratory failure. There are reports of cases of pneumonia diagnosed in young men in the military in Korea and in other countries. However, there is limited data on which early clinical features may be predictive of adenoviral pneumonia compared to other etiologic agents of pneumonia.

Methods: Medical records of patients who were admitted to Armed Forces Chuncheon Hospital for treatment of community acquired pneumonia (CAP) between January of 2014 to December of 2016 and in whom initial antibiotics treatment were deemed ineffective were retrospectively analyzed. The patients were divided into two groups according to the results of polymerase chain reaction (PCR) test for adenovirus from respiratory specimen; adenovirus-positive (Adv +) group and adenovirus-negative (Adv -) group. Patient demographics, laboratory findings, and radiologic findings on admission were compared to look for predictive factors for adenoviral pneumonia.

Results: Out of 147 patients diagnosed with CAP during the study period, 65 were classified into Adv + group while 82 were Adv - group. Proportion of patients with history of Smoking, lymphocytopenia, monocytopenia, pleural effusion, and severe ineffective response to antipyretic treatment were significantly higher in Adv + group. On univariate and multivariable analysis, severe ineffective response to antipyretic treatment (Adjusted OR: 7.42, 95% CI: 2.88–14.01; $P = 0.032$) were significantly higher in adenoviral pneumonia group.

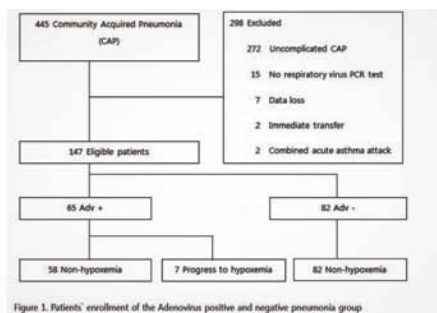


Figure 1. Patients' enrollment of the Adenovirus positive and negative pneumonia group.

Table 4. Univariate and multivariable analysis with logistic regression test for predictive factors of adenoviral pneumonia

Variables	Univariate analysis			Multivariable analysis		
	Odds Ratio (OR)	95% Confidence Interval (CI)	p value	Adjusted OR	95% CI	p value
Smoking	5.88	0.17-9.61	0.133			
Initial laboratory findings						
Leukopenia	0.67	0.28-1.34	0.215			
Thrombocytopenia	2.55	0.85-4.85	0.125			
Lymphocytopenia	2.96	0.57-8.63	0.067			
Monocytopenia	5.40	1.47-10.78	0.009			
Pleural effusion	8.69	4.12-29.34	0.106			
IRAT						
Mild	8.25	1.39-29.63	0.096			
Severe	23.45	6.88-74.01	<0.001	7.42	2.88-14.01	0.032

IRAT, Ineffective response to antipyretic therapy

Conclusion: In military recruits with CAP, patients who had inappropriate response to antibiotic therapy during 72 h and ineffective response to antipyretic agents at first 24 h, especially severe ineffective response to antipyretic treatment should suspected adenoviral pneumonia.

AP256

CT-GUIDED DRAINAGE FOR LUNG ABSCESS

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Background and Aims: Lung abscess is known to be the infection that is occurring to whom repeats aspiration, and the common pathogen of lung abscess is anaerobes.

It often takes more time for the treatment of lung abscess than pneumoniae, and the mortality is higher than pneumoniae.

Methods: Retrospective review of patients who underwent CT-guided lung abscess drainage at our hospital from April 2015 to March 2018 was performed. In total 3 cases were identified; two females and one male.

Results: Case 1: 79F. She was treated by TAZ/PIPC. She had diabetes. CT-guided drainage was performed on the day 3 after admission. *Fusobacterium nucleatum* was detected by the pus.

She was discharged 30 days after admission.

Case 2: 57F. CT-guided drainage was performed on the day of admission. She was treated by TAZ/PIPC. *S. intermedius* and *Fusobacterium mortiferum/varium* were detected by the pus. She was discharged 20 days after admission.

Case 3: 81M. He was treated by TAZ/PIPC. CT-guided drainage was performed on the day 3 after admission. Anaerobic gram-negative rod was detected (not identified). Lung abscess was improved, but grew weak from disuse atrophy and led to death.

Conclusion: CT-guided drainage for lung abscess has no fetal complication, and is useful for detection of pathogen. Moreover it may improve the duration of term for treatment and therapeutic success for lung abscess.

Though it depends on the location of lung abscess, CT-guided drainage for lung abscess is considered to be as a part for the treatment.

AP257

PROGRESSIVE DISSEMINATED HISTOPLASMOSIS DERIVED FROM ACUTE PULMONARY HISTOPLASMOSIS IN A 61-YEAR-OLD MALE IN NORTH-WESTERN CHINA: A CASE REPORT AND REVIEW OF LITERATURE

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Background and Aims: Progressive disseminated histoplasmosis (PDH) is an endemic communicable disease, which is not easy to be diagnosed because it may have similar radiographic findings with other pulmonary disease such as pneumonia and tuberculosis. In the North-western China, it is not known as an endemic area for histoplasma.

Methods: We reported a case of PDH derived from acute pulmonary histoplasmosis (APH) in the North-western China.

Results: A 61-year-old male was admitted to the hospital for evaluation of multiple pulmonary patchy lesions in the computed tomography (CT) scan of the chest. He was first identified as pneumonia, but treatment with antibiotic was invalid. Finally he was diagnosed as PDH by a bone marrow biopsy with haematoxylin and eosin stain. The patient was recovered completely following liposomal amphotericin B and voriconazole treatment.

Conclusion: This is the rare case of PDH, not associated with either immunocompromise or endemicity in north-western China. Recognition of PDH is possible if it is considered in the differential diagnosis of pyrexia of undetermined origin.

AP258

CLINICAL SIGNIFICANCE OF SERUM PRESEPSIN LEVEL IN HOSPITALIZED PNEUMONIA

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Background and Aims: Presepsin, the soluble CD14 subtype, is known as a diagnostic biomarker for sepsis. However, the evaluation concerning serum presepsin level in pneumonic patients has not been done enough. We investigated the clinical significance of serum presepsin level in hospitalized patients due to pneumonia.

Methods: This retrospective study was performed in hospitalized patients due to pneumonia from May 2016 to November 2017. Those who had the measurement of serum presepsin level on admission were enrolled. Patient characteristics, vital signs, blood examinations, microbiological tests, and chest radiographic findings were retrieved from electronic medical record. Pneumonia Severity Index (PSI) and A-DROP score, pneumonia severity assessment scale proposed by the Japanese Respiratory Society, were calculated. Prognostic value in 30-day mortality was assessed by a receiver operating characteristic (ROC) analysis for each parameter. Correlations between serum presepsin level and other parameters were assessed using Spearman's test.

Results: The total number of enrolled patients was 172. One hundred seven patients (62.2%) were from community, while 65 patients (37.8%) were from nursing homes. Seventeen patients (9.9%) died within 30 days of admission. The deceased patients significantly had higher value of serum presepsin level on admission than the survivors had (539 vs 334 pg/mL, $P = 0.001$). The areas under ROC curve of predicting 30-day mortality were 0.742 for serum presepsin level, 0.606 for serum C-reactive protein level, 0.755 for A-DROP score, and 0.774 for PSI respectively. Serum presepsin level had stronger correlation with serum creatinin level ($r = 0.524$, $P < 0.001$) than with A-DROP score ($r = 0.395$, $P < 0.001$) and PSI ($r = 0.384$, $P < 0.001$).

Conclusion: Serum presepsin level on admission could be a useful prognostic biomarker in hospitalized patients due to pneumonia. However, serum presepsin level should be assessed carefully because it has a considerable correlation with renal function.

FOB revealed endobronchial tree of both lungs were studded with diffuse whitish patches, starting from subglottic region up to lobar bronchus, mostly over trachea. Mucus membrane was fragile and bleeds easily. He was nondiabetic, did not take corticosteroid. There was no joint pain or abdominal complaints. HIV serology was negative. BAL was negative for AFB, GeneXpert, fungal hyphae. No granuloma or malignant cells were detected in biopsy specimen. BAL culture yielded growth of pseudomonas with resistant to co-amoxycylav but sensitive to meropenem. A diagnosis of inflammatory tracheobronchitis caused by *P. aeruginosa* was made. Treatment was started accordingly.

Results: His condition was gradually improving with subsidence of fever, cough and haemoptysis. A follow-up FOB was done 27 days later, showing significant reduction of mucosal inflammation. He was discharged with advice of follow-up.

Conclusion: Inflammatory tracheobronchitis is a relatively rare, but potentially life-threatening disease. *Aspergillus* is most common culprit, whereas only few case reports were found due to *P. aeruginosa*. Bronchoscopy is essential for accurate diagnosis, and it may resolve completely with appropriate antibiotic therapy.



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INFLAMMATORY TRACHEOBRONCHITIS: A RARE PRESENTATION OF PSEUDOMONAS AERUGINOSA INFECTION

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Background and Aims: Inflammatory tracheobronchitis is an uncommon manifestation of *P. aeruginosa* infection and almost fatal. Although mostly infects immunocompromised ones, immunocompetent individuals may manifest the disease and if diagnosed early, can be life-saving.

Methods: A 24-year-old man presented with cough, occasional sputum and halitosis for 3 months and haemoptysis for 10 days. On examination, he looked ill, having foul-smell in breath. Temperature 100°F, clubbing absent, oral cavity and chest findings were normal. Total count 9600/cmm, with 65% neutrophil, ESR 25 mm. Chest X-ray was unremarkable, sputum AFB, GeneXpert was negative, culture yielded no growth. Oral co-amoxycylav and clindamycin was started. He returned after 7 days as he was feeling unwell. CT chest revealed inflammatory changes in medial segment of right middle lobe. A diagnostic fiberoptic bronchoscopy (FOB) was planned.

TRANSBRONCHIAL INSTILLATION OF LIPOSOMAL AMPHOTERICIN B: TOPICAL THERAPY FOR CHRONIC PROGRESSIVE PULMONARY ASPERGILLOSIS

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Background and Aims: Patients with chronic progressive pulmonary aspergillosis (CPPA) are usually intolerant to surgery due to the poor condition of their lungs. Inoperable patients are likely to receive systemic antifungal therapy; however, adverse effects and drug interactions make long-term pharmacotherapy challenging. Topical instillation of liposomal amphotericin B (L-AMB) may be an effective treatment because liposomal formulations demonstrate lower distribution and toxicity to normal animal tissues but higher to fungal cytomembranes.

Methods: We retrospectively reviewed three patients (1 female and 2 males) who received transbronchial instillation of L-AMB into CPPA lesions between January 2016 and March 2018 at our hospital. L-AMB solution (1 mg/mL) was injected through a bronchoscope, with or without a spraying tube. We used 10–20 mL solution for each procedure and performed the instillation 2–5 times a week.

Results: All patients displayed poor tolerance to antifungals because of the adverse effects. Their conditions were worsened by recurrent

haemoptysis and/or bacterial pneumonia. Case 1: a 71-year-old male with multiple cavitary lesions and emphysema. He received three courses of therapy: one for 5 months, one for a month, and one for a month and half. Pericavitary infiltrates and wall thickening were improved on chest imaging, and his weight and serum albumin levels increased. Case 2: an 82-year-old male with cavities and nodules preceded by severe panlobular emphysema. He received two 1-month treatments and exhibited no significant improvement on radiography. Case 3: a 68-year-old female with cavities and bronchiectasis with consolidation opacities. Instillation was ceased within 2 weeks because of mild bronchial bleeding.

Conclusion: Transbronchial instillation of L-AMB may improve symptoms and systematic inflammation in some patients with CPPA. It is a possible alternative for surgery or systematic antifungal therapy even for patients with a poor physical status.

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TANREQING INJECTION FOR BRONCHIECTASIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Tanreqing Injection (TI) has been widely used to treat bronchiectasis. This review aims to evaluate the efficacy of TI for bronchiectasis.

Methods: PubMed, Embase, The Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Chongqing VIP (VIP) and Wanfang Data were searched. The randomized controlled trials (RCTs) evaluating the effect of TI on bronchiectasis patients were included. Outcome measures included pulmonary function, inflammatory markers, arterial blood gas, clinical effective rate and adverse reactions. Study selection, data extraction and risk of bias assessment were independently undertaken, respectively. Statistical analysis was conducted by RevMan software (version 5.3).

Results: Eleven studies (825 participants) were included. Compared to the control group, effective rate was higher [RR = 1.16, 95%CI (1.08,1.24); Z = 4.17, $P < 0.0001$], and pulmonary function improved more in the treatment group, with forced vital capacity (FVC) [MD = 0.45, 95% CI (0.34, 0.56); Z = 8.01, $P < 0.00001$], forced expiratory volume in one second (FEV₁) [MD = 0.39, 95% CI (0.24,0.54); Z = 5.06, $P < 0.00001$], FEV₁% predicted [MD = 6.35, 95%CI (3.80, 8.90); Z = 4.87, $P < 0.00001$] and peak expiratory flow (PEF) [MD = 0.73, 95% CI (0.38, 1.09); Z = 4.05, $P < 0.0001$], respectively. In addition, arterial partial pressure of oxygen (PaO₂) [MD = 4.25, 95%CI (0.26, 8.24); Z = 2.09, $P = 0.04$], neutrophils ratio [MD = -11.69, 95%CI (-20.56, -2.83); Z = 2.59, $P = 0.010$] and procalcitonin [MD = -0.13, 95% CI (-0.15, -0.11); Z = 13.38, $P < 0.00001$] improved more in the treatment group. There was no significant difference between the two groups in reducing arterial partial pressure of carbon dioxide (PaCO₂) [MD = -3.29, 95%CI (-9.75, 3.17); Z = 1.00, $P = 0.32$] and white blood cell count [MD = -1.72, 95%CI (-4.26, 0.82); Z = 1.33, $P = 0.18$]. There was no serious adverse reaction.

Conclusion: On the basis of western medicine, TI might enhance clinical efficacy, improve pulmonary function, increase PaO₂, reduce neutrophils ratio and procalcitonin of bronchiectasis patients, and have no serious adverse reaction. However, the efficacy and safety of TI for bronchiectasis remain to be further verified by high quality multi-center RCTs.

RETROSPECTIVE ANALYSIS OF SURGERY FOR THE MANAGEMENT OF PARAPNEUMONIC PLEURAL EFFUSION AND ACUTE EMPYEMA

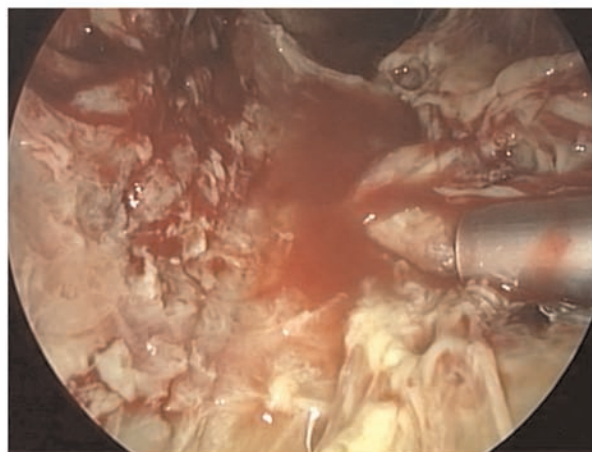
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Background and Aims: In patients with parapneumonic pleural effusion and acute empyema, effusion enhances gelling and multilayering. Pleural drainage becomes difficult to manage, and surgical intervention is necessary. Thoracoscopic surgery (TS) is now widely performed due to its low invasiveness. However the number of high risk cases with poor PS and complications are increasing in Japan recently. Aim of this study was to review the clinical and surgical outcome of patients who underwent surgery.

Patient characteristics

Variable	
Age (median)	61 (2-84)
Sex (M : F)	18 : 7
Performance status (0-2 : 3-4)	22 : 3
Body mass index (kg/m ²)	23.1 ± 5.9
PS (0-2 : 3-4)	17 : 3
Comorbidity	10 (50%)
	Heart disease 4
	psychiatric disorder 3
Pleural effusion culture	Negative 17 Positive 3 (<i>Streptococcus</i> sp 2, MRSA 1)
Serum albumin (g/dL)	2.1 ± 0.3
leukocyte count (/μL)	18,880 ± 7,800
C-reactive protein (mg/dl)	23.1 ± 11
Light's classification	Class5 5 Class7 20



Methods: This retrospective study included who underwent surgery for parapneumonic effusion or acute empyema in our department from January 2006 to April 2018 at our institute. Pre-, intra-, and postoperative characteristics were observed.

Results: 1. Preoperative characteristics: Total of 25 patients (male: 22, female: 3) with median age of 64 years (range: 2 to 84). preoperative clinical characteristics in detail were shown in Table. The average period from symptom onset to surgery and from hospital admission to surgery was 6.8 ± 10.5 (1-16) days.

2. Intraoperative characteristics: The operation was accomplished by TS in 23 (92%), and conversion to thoracotomy was in 2 (2%). Cause of

open conversion was dense adhesion. Average operation time was 130 ± 60 min. The amount of bleeding was 170 ± 320 mL. The mean duration of chest drainage was 6 ± 3 days and post-operative hospitalisation was 13 ± 7 days. Mean period of postoperative antibiotic use was 10 ± 4 days.

3 Postoperative characteristics: There were no postoperative complication, but 2 cases (8%) of recurrence were observed. One case needed fenestration, the other case suffered from bronchopleural fistula (BPF) and was received BPF closure using pedicled diaphragm muscle flap.

Conclusion: This study demonstrated improved outcomes by decortication by TS, even in patients poor PS and complicated patients. Also, the postoperative drainage period and number of hospital days, tended to be relatively short compared with previous reports.

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PULMONARY INFECTIONS IN POST-LUNG TRANSPLANTATION PATIENTS: CASE SERIES OF A TERTIARY MEDICAL CENTER IN TAIWAN

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Background and Aims: Infectious complication is a serious cause of morbidity and mortality in lung transplantation patients. In this study, we analyzed the pulmonary infection condition and microbiology data in post-lung transplantation patients.

Methods: We collected all of the lung transplantation patients in Chang Gung Memorial Hospital, Linkou branch since Dec. 2016 to Dec. 2017. All of the patients used prophylaxis antibiotics after the operation including a glycopeptide, a carbapenem, cotrimoxazole, valganciclovir and anidulafungin. The donor lung tissue swab cultures were sent routinely during the transplantation. The sputum cultures were collected according to the clinical suspicious, and the bronchoscopy with bronchoalveolar lavage (BAL) would be arranged routinely.

Results: Total 8 patients had done the bilateral lung transplantation in this period. All of the donor lungs tissue swab cultures were positive that the *Klebsiella pneumoniae* was the most common bacterial pathogen. However, only 1 patient had the same microbiology result from donor lung tissue swab culture and BAL after the transplantation (both revealed *Stenotrophomonas*). No patient had positive result of aspergillus, cytomegalovirus, *Pneumocystis jirovecii* pneumonia or tuberculosis within 1 month post-transplantation. The aspergillus tracheobronchitis was noted in a patient 35 days after transplantation which was confirmed by biopsy pathology. There were 4 patients had positive BAL bacterial culture within 1 week post-operation, and 3 of them were mortality within 6 months post-operation due to different etiology. All other patients who had no positive BAL culture data within 1 week post-operation were survival till now ($P = 0.028$).

Conclusion: The prophylaxis antibiotics regimens we used were effective in preventing post-lung transplantation infection from the donor lung or other opportunistic infection. The early positive BAL culture (post-lung transplantation within 7 days) may be a predictor for early mortality in lung transplantation patients.

MULTICENTER SURVEY OF POST-INFLUENZA RESPIRATORY COMPLICATIONS IN THE SEASON BETWEEN 2017 AND 2018 IN TOKYO CENTRAL AREA

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Background and Aims: In the season between 2017 and 2018 in Japan, there was the biggest influenza epidemic in the past 10 years. Usually in Japan, influenza A becomes prevalent in early winter and epidemic of influenza B is delayed. However, influenza A and influenza B were prevalent almost simultaneously in this season, and there were a large number of patients who underwent inpatient treatment due to post-influenza respiratory complications. Here we report the clinical features of post-influenza respiratory complications that required hospitalization treatment.

Methods: This study was a multicenter retrospective observational study. Patients who were diagnosed as post-influenza respiratory complications and required hospitalization treatment during the period from October 2017 to March 2018 in four core hospitals in Tokyo central area were included to the study.

Results: Seventy patients were enrolled from four hospitals. Median age was 81 years (range 46–97). There were 38 (54%) males. In comorbidity, 28 (40%) had heart disease, and 23 (33%) had dementia or cerebrovascular disease. Influenza A was 38 cases (52%). Eight cases (11%) died. There was no significant difference in patient background between the deceased and survivors. In post-influenza respiratory complications, 79% of surviving groups had secondary or coexisting bacterial pneumonia, and ARDS was diagnosed in 3 cases (5%). On the other hand, 5 cases (62%) had secondary or coexisting bacterial pneumonia and 3 cases (38%) had ARDS in the deceased group. Sputum culture revealed that *S. aureus* was the most frequent and found in 11 cases (16%), and all cases survived. Gram-negative bacilli were found in 14 cases (20%), and 4 of them (29%) died.

Conclusion: The post-influenza respiratory complications that require hospitalization are frequent among elderly people with underlying diseases, and the mortality rate was as high as 11%. Attention should be paid because of the high mortality rate when gram negative bacilli infection is combined.

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FREQUENT EMPIRIC BROAD-SPECTRUM ANTIMICROBIAL USE AMONG HOSPITALIZED PATIENTS WITH LOWER RESPIRATORY TRACT INFECTION IN SOUTHERN SRI LANKA

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Background and Aims: Lower respiratory tract infections (LRTIs) account for 4 million deaths annually and together are the leading cause of mortality in children ≤ 5 years. Understanding prescribing patterns of antimicrobials for LRTIs is important in optimizing antimicrobial use, especially given increasing antimicrobial resistance globally. We investigated

the prevalence, classes, and diagnostic rationale for antimicrobial usage for LRTIs in southern Sri Lanka.

Methods: A point-prevalence study of patients hospitalized at one tertiary, one secondary, and three primary-level public hospitals in Southern Province, Sri Lanka, was conducted from June-August 2017. Medical charts were surveyed in medical, surgical, and paediatric wards and intensive care units (ICUs) for systemic antimicrobial use in 1-day point-prevalence studies. Potentially inappropriate antimicrobial combinations were defined as ≥ 2 beta-lactam antibiotics or ≥ 2 antibiotics covering anaerobes, *Pseudomonas aeruginosa*, or methicillin-resistant *Staphylococcus aureus*.

Results: Of 1,709 surveyed patients, 935 (54.7%) received antimicrobials; among these patients, LRTI was the leading indication for antimicrobial use (20.7%). Patients with chronic pulmonary disease were significantly more likely to receive antimicrobials ($P < 0.001$) than other patients. Approximately one-fifth (17.9%) of surveyed LRTI cases required ICU-level care. Amoxicillin & clavulanic acid (39.8%), clarithromycin (39.3%), and third-generation cephalosporins (32.5%) were the most frequent antimicrobials used to treat LRTIs. Of all LRTI patients treated with antimicrobials, 5.2% had pertinent culture data of which only one culture result was positive. Potentially inappropriate antimicrobial combinations were observed in 17.1% of total patients, 41.0% of ICU patients, and 6.2% of LRTI patients.

Conclusion: In this first point-prevalence study of antimicrobial use in public hospitals in southern Sri Lanka, LRTI was the leading indication for antimicrobial use in all wards/units. Culture confirmation was low among LRTI patients, but broad-spectrum antimicrobial use was common. These findings highlight important targets for antimicrobial stewardship efforts.

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ROLE OF BRONCHOSCOPY FOR PATHOGEN DIFFERENTIATION IN PATIENTS WITH EMPYEMA

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Background and Aims: Empyema is defined as bacterial invasion of the pleural cavity, which is a serious illness associated with considerable morbidity and mortality. Many guidelines recommend appropriate antibiotic treatment in accordance with pathogen. Unfortunately, about 30–40% of cases are only culture positive. The choice of antibiotic in the remaining case should be decided as the physician's clinical experience. The role of bronchoscopy in empyema is not clearly. Previous studies have focused on the distinction of structural abnormality through bronchoscopy. Bronchoscopy will provide more diagnostic information than routine microbiological cultures. However, there was no study about the yield of cultures through bronchoscopy in empyema. Therefore, the aim of our study was to assess the pathogen differentiation of bronchoscopy at empyema.

Methods: We retrospectively analyzed consecutive 153 patients with empyema who were admitted to the tertiary care hospital, South Korea between January 1, 2013 and April 30, 2018.

Results: The cultures of pleural effusion were identified pathogen in 34.6%. The most common pathogen was *Streptococcus milleri* group (8.5%), followed by anaerobic microbes (7.8%) and Enterobacteriaceae (5.2%). The cultures of sputum were identified pathogen in 14.4%. The most common pathogen was Enterobacteriaceae (5.2%), followed by *Pseudomonas aeruginosa* (2.6%) and *Staphylococcus aureus* (2.0%). Among all patients, bronchoscopy was performed in 60 patients. The bacterial isolated rate from bronchial washing was 30%. The most common pathogen was *Staphylococcus aureus* (10%), followed by

Enterobacteriaceae (8.3%) and other streptococci (5%). The percentage of isolates with pleural effusion, sputum and bronchial washing was 45.8%, which was higher than that of pleural effusion alone (34.6%) or both pleural effusion and Sputum (41.8%).

Conclusion: Bronchoscopy may be helpful in the selection of appropriate antibiotics for empyema patients.

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RISK FACTORS OF DISCONTINUATION OF MULTIPLE DRUGS TREATMENT OF MAC LUNG DISEASE

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Background and Aims: Drugs therapy for MAC lung disease involves multiple antibiotics containing macrolide. The goal of therapy is 12 months of negative sputum cultures while on therapy. It is very long, therefore, the risk of adverse drug reaction is high and treatment with multiple drugs is often discontinued. The aim of this study was to clarify the risk factors of discontinuation of multiple drugs in the treatment of MAC lung disease.

Methods: A retrospective was conducted in Shinshu University Hospital. We reviewed the medical records of patients with MAC lung disease who treated with multiple drugs between 2000 and 2016.

Results: Twenty-nine patients received complete treatment (completion group) and 29 patients had discontinuation of multiple drugs in treatment(discontinuation group). The number of discontinuation by adverse drug reaction was 21 patients (36.2%). BMI was significantly lower in the discontinuation group (17.7 kg/m²) than in the completion group (19.9 kg/m²). The reasons of discontinuation were as follows: adverse drug reaction (21 patients), complication disease (7 patients), acquisition of macrolide resistant (1 patient). The details of adverse drug reactions were as follows: allergy (8 patients), visual impairment (8 patients), general fatigue (3 patients), hepatitis (1 patient), and thrombocytopenia (1 patient). Median time of discontinuation of multiple drugs treatment due to allergy and visual impairment were 14.5 days and 43.4 days, respectively.

Conclusion: In this study, the discontinuation rate of multiple drugs in treatment due to adverse drug reaction was similar to that in the previous report. In the discontinuation group, BMI was significantly reduced. It is considered that the increase of relative dose increased the risk of developing adverse drug reaction. We should pay attention especially to adverse drug reaction in low BMI patients with MAC lung disease.

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UTILIZATION OF PROCALCITONIN AS A DIAGNOSTIC BIOMARKER OF PEDIATRIC VENTILATOR-ASSOCIATED PNEUMONIA IN PATIENTS WITH CONGENITAL HEART DISEASE FOLLOWING CARDIAC SURGERY

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Background and Aims: Ventilator-associated pneumonia (VAP) is a common nosocomial infection following cardiac surgery and is associated with increase morbidity and mortality rate. Procalcitonin (PCT) is a promising biologic marker that will provide an early clue and accurate diagnosis in treatment of VAP. The aim of this study was to determine the utility of procalcitonin as an early biomarker of paediatric VAP in patients with congenital heart disease following cardiac surgery.

Variables	Non-VAP patients (n=35)	VAP patients (n=23)	p
Average age (years)	1 (0.25-1)	0.33 (0.08-3)	(0.14) NS
Male/Female	19/16	18/5	(0.06) NS
Average weight (kg)	6.8 (3.5-13)	4 (3.2-12.1)	(0.22) NS
Comorbidities (n)	3 (8.5%)	4 (17.4%)	(1.00) NS
a. Pulmonary Hypertension	1	2	
b. Down Syndrome	1	1	
c. Bronchial Asthma	1	0	
d. L. occipital lobe infarction	0	1	
Cardiac lesion (n)			
a. VSD	6	4	
b. d-TGA	3	5	
c. TOF	8	3	
d. TVA	3	2	
e. PVA	3	2	
f. Others	10	7	
Surgical Procedure (n)			
a. VSD closure	6	5	
b. TOF correction	7	2	
c. Atrial Switch Operation	3	3	
d. Blalock Taussig Shunt	8	4	
e. Pulmonary artery banding	3	3	
f. Others	8	6	
LVEF (%)	70 ± 15	70 ± 10	(0.44) NS
CBP time (minutes)	132 (84-186.5)	112 (82-268)	(0.74) NS
Length of MV (days)	5 (3-8)	8 (3-21)	(0.10) NS
Length of ICU stay (days)	9 (4-20)	21 (8-26)	(0.02) S
Procalcitonin level (ng/mL)	0.57 (0.38-1.2)	2.79 (1.68-9.9)	(0.001) S
Post-operative complication (n)	6 (17%)	12 (52%)	(0.005) S
a. Pulmonary edema	3	4	
b. Chylothorax	0	2	
c. Diaphragmatic paralysis	1	1	
d. Pneumothorax	1	1	
e. Acute Kidney Injury	0	2	
f. Bleeding on surgical site	1	0	
g. Sepsis	0	2	
Mortality	1	7	(0.005) S

VSD- Ventricular septal defect, dTGA- Dextroposition of the great arteries, TOF- Tetralogy of Fallot, TVA- Tricuspid Valve Atresia, PVA- Pulmonary valve atresia, LVEF- left ventricular ejection fraction

	Optimal cut-off	AUC	Sensitivity%	Specificity %	Accuracy	LR (+)	LR (-)
PCT level ng/mL	1.77	0.84	73.91%	85.71%	81.03%	5.17	0.30

Methods: This is a prospective cohort study conducted in the critical care unit of a subspecialty hospital between August 2017 to January 2018 involving mechanically ventilated patients suspected with VAP. The PCT level was obtained from the qualified subjects on the day of VAP suspicion. All tests were done using enzyme-linked fluorescent assay technique. Receiver operating characteristics analysis was used to determine the diagnostic parameters of PCT. The population was divided into VAP and no-VAP group.

Results: A total of 58 patients were enrolled in this study. No significant difference was observed in preoperative characteristics between the VAP and non-VAP group. The occurrence of postoperative complications ($P = 0.005$), duration of ICU days ($P = 0.02$), and mortality ($P = 0.005$) were statistically significant in VAP group when compared with the non-VAP group. The optimum diagnostic PCT cut-off value for VAP on the day of suspicion was 1.77 ng/mL, with a sensitivity of 74% and specificity of 86%. The areas under the ROC curve was 0.84

Conclusion: The result suggested that PCT may be utilized as a diagnostic biomarker for pediatric VAP following cardiac surgery.

SINGLE-TROCAR VIDEO-ASSISTED FLEXIBLE THORACOSCOPIC DEBRIDEMENT UNDER LOCAL ANAESTHESIA FOR MULTILOCULATED PARAPNEUMONIC EMPYEMA

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Background and Aims: Surgical procedures are recommended for parapneumonic empyema (PE) in the advanced stages. The role of video-assisted flexible thoracoscopic (VAFTS) debridement via a single trocar under local anaesthesia for multiloculated PE has not been established, although some studies have reported on VAFTS debridement cases. We explored the effectiveness and safety of VAFTS debridement under local anaesthesia for multiloculated PE and the preoperative clinical features that affect the success of the procedure.

Methods: We retrospectively reviewed the medical records of patients who underwent VAFTS debridement under local anaesthesia for multiloculated PE from January 2007 to December 2017. The baseline patient data, including haematology, radiologic findings, and bacterial examinations, were collected. The primary outcome was hospital mortality without additional operation under general anaesthesia. The potential predictors were analyzed for possible association with the outcomes.

Results: A total of 69 patients with multiloculated PE were treated by VAFTS debridement. Based on the Light classification, infection was staged as class 5 in 45 patients and as class 7 in 24 patients. The average onset of symptoms was 13.3 ± 13.8 days before the procedure. VAFTS debridement was successful in 59 patients (85.5%); 7 patients required subsequent operation under general anaesthesia and 3 patients died due to sepsis. Complications occurred in 3 patients (4.3%). A microbiological diagnosis could be made in 26 patients (44.1%). Multivariate logistic regression analysis revealed that leukocytosis of $>15,000/\mu\text{L}$ ($P = 0.016$) and duration from the onset of symptoms to the procedure ($P = 0.010$) were independently associated with the success of this procedure.

Conclusion: Single-trocar VAFTS debridement can be an acceptable first choice of treatment in patients with multiloculated PE. Importantly, this procedure should be performed as early as possible for a successful outcome and to obtain useful information on the nature of the pleural effusion and the status of the pleural cavity.

URINARY ANTIGEN TESTING IN COMMUNITY-ACQUIRED PNEUMONIA: CLINICAL UTILITY, COST EFFECTIVENESS AND THE IMPACT ON ANTIBIOTIC TREATMENT

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Background and Aims: Pneumonia is a significant contributor to morbidity and mortality. Current Australian treatment guidelines on community-acquired pneumonia recommend performing blood cultures on all hospitalised patients and urinary antigen testing in severe disease, based on the SMART-COP or CORB severity scores. However, diagnostic yield for aetiology remains low.

The availability of urinary antigen testing for *S. pneumoniae* and *Legionella pneumophila* has enabled rapid aetiological diagnosis and directed antibiotic therapy. There is conflicting data on the clinical utility of pneumococcal and legionella urinary antigen testing and its impact on antibiotic prescribing in community-acquired pneumonia.

The aim of this study was to evaluate the clinical utility of pneumococcal and legionella urinary antigen testing and its cost effectiveness within Western Health, a tertiary public hospital servicing the west of Melbourne.

Methods: A retrospective audit of medical records was performed. All adult patients discharged from Western Health between 1st May and 31st October 2017 with a diagnosis of community-acquired pneumonia were included. Medical records were reviewed to evaluate the proportion of cases where antibiotic treatment was de-escalated in the setting of a positive urinary antigen result. Observance of local guidelines for diagnostic testing and evaluation of cost-benefit analysis of urinary antigens were also assessed.

Results: Preliminary results demonstrate a low prevalence of positive urinary antigen in our study population. Positive urinary antigen tests resulted in de-escalation from empirical to targeted antibiotics in only a small proportion of cases.

Conclusion: The diagnostic and clinical utility of pneumococcal and legionella urinary antigens is low in community-acquired pneumonia. Due to the low prevalence of positive urinary antigen results, routine testing in hospitalised patients is not cost-effective.

AP271

EFFICACY OF CORTICOSTEROID ADMINISTRATION IN SEVERE COMMUNITY-ONSET PNEUMONIA PATIENTS: USING THE JAPANESE DIAGNOSTIC PROCEDURE COMBINATION DATABASE

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Background and Aims: The Diagnostic Procedure Combination (DPC), which is a huge inpatient database and links with a lump-sum payment system that has introduced by the Japanese government in 2002, has been actively used for evaluating pneumonia patients. According to the 2017 Japanese guidelines, it is weakly recommended to add low-dose corticosteroid to antibiotic therapy for severe pneumonia patients. However, the efficacy of corticosteroid add-on therapy for severe community-onset pneumonia patients remains unclear. We therefore evaluated the efficacy of corticosteroid add-on treatment for severe pneumonia using the DPC database.

Methods: Adult patients with severe community-onset pneumonia patients (more than 3 points in the A-DROP system) treated in hospital between January and December 2012 were identified in the DPC database. The background factors were adjusted using the inverse probability of treatment weighting (IPTW) method, and the patients that high-dose corticosteroids (methylprednisolone ≥ 500 mg/day) were administered were excluded. The patients were divided into two groups based on the presence or absence of low-dose corticosteroid treatment in addition to antibiotic therapy. The 30-day survival rate was evaluated using the Kaplan-Meier method.

Results: The average ages and male ratios of the corticosteroid add-on (A) group (1,338 patients) and corticosteroid non-add-on (B) group (11,939 patients) were 81.6 and 83.4 years old, 67.2% and 61.0%, respectively. We found no significant differences of the 30-day survival rate between A and B group (weighted hazard ratio: 1.08; 95% confidence interval: 0.91–1.29; $P = 0.38$).

Conclusion: Low-dose corticosteroid add-on therapy in addition to antibiotic medication for severe community-onset pneumonia patients may not be related to an improvement of the prognosis.

RISK FACTORS AND IMPLICATIONS FOR READMISSION OF PATIENTS FOLLOWING HOSPITALIZATION FOR COMMUNITY-ACQUIRED PNEUMONIA IN SOUTH KOREA

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Background and Aims: Identification of the reasons and risk factors associated with readmission is important concerning discharge planning. The purpose of this study was to clarify the rates, reasons and risk factors associated with 30 day readmission following hospitalization for community-acquired pneumonia (CAP).

Methods: We performed a retrospective observational study of 1,021 patients with CAP who were hospitalized at Yeungnam University Hospital between March 2012 and February 2014. The primary end point was all-cause readmissions to the hospital within the 30 days following discharge after initial hospitalization. Hospital readmission was classified as (1) pneumonia-related readmission or (2) pneumonia-unrelated readmission.

Results: During the study period, 1,021 patients were eligible for the study. 121 patients died during the initial hospitalization, 35 patients discharged against medical advice and refused outpatient follow up, and 3 patients transferred to another acute care facility. Of the 862 patients who survived to hospital discharge, 72 (8.4%) were rehospitalized within 30 days following discharge. Pneumonia-related causes accounted for 37.5% (27 patients) and pneumonia-unrelated causes accounted for 62.5% (45 patients) of the total reasons for 30 day readmission. In the multivariable analysis, pneumonia related hospital readmission was associated with para/hemiplegia, malignancy, pneumonia severity index (PSI) class ≥ 4 and clinical instability ≥ 1 at hospital discharge. Underlying comorbidities such as chronic lung disease, chronic kidney disease, hospitalization for ≥ 2 days during the preceding 90 days, treatment failure and decompensation of comorbidities were associated with pneumonia-unrelated hospital readmission within 30 days.

Conclusion: Rehospitalizations within 30 days following discharge were frequent among patients with CAP. Different risk factors are associated with hospital readmission related to pneumonia or to pneumonia-unrelated causes. Identification of the risk factors associated with hospital readmission in two different groups might have implications for discharge planning and follow up of patients with CAP.

AP273

RARE PRESENTATION OF HYDATID CYST

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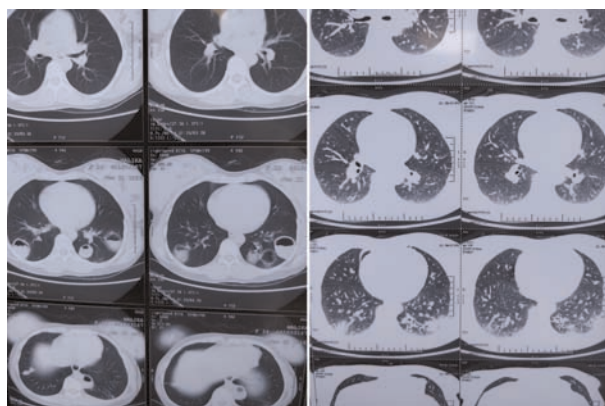
Background and Aims: Echinococcosis or hydatid disease is caused by larvae of the tapeworm *Echinococcus*. Four species are recognised and the vast majority of infestation in humans are caused by *E. granulosus*. It causes cystic echinococcosis, which has a worldwide distribution most commonly in Asia. Humans are exposed less frequently to *E. multilocularis*, which causes alveolar echinococcosis. *E. vogeli* and *E. oligarthrus* are rare species and cause polycystic echinococcosis.

Methods: case report- A 26 year old female from Afghanistan has presented with complains of cough with white sputum, low grade fever. Left side chest pain since around 2 months. No history of TB in past, history of exposure to sheep present. Blood report shows normal TLC with raised 30 % eosinophil count, chest X-ray shows b/l opacity well rounded involving lower lobes. Diagnosis was not made so advised HRCT chest, which shows multiple well rounded thin walled cysts of variable size

scattered in both the lungs size 4.2* 3.7 cm 3 cyst in right lung and 6 cyst in the left lung, most of them containing crumpled membranes suggestive of pulmonary hydatid cyst and 2 present in liver which measures 6*5.2 cm. Usg abdomen also done which confirms liver hydatid cyst. Echinococcus antigen was negative. Patient was started on tablet albendazole 400 mg twice daily and advised to follow up after 3 months. Patient came after 6 months she has taken albendazole during this time, now complains of haemoptysis, chest X-ray shows resolving of cyst, sputum afb was negative. Videobronchoscopy done which shows no active site of bleeding, BAL fungal culture and aerobic culture shows no growth. Patient was advised to continue albendazole for 6 more months.

Results: In between patient got pregnant and stopped albendazole on advise of local doctor. She came to us after after 1 year, repeat HRCT chest shows calcification of cyst. Patient was asymptomatic.

Conclusion: Multiple hydatid cyst involving lung and liver is managed conservatively without surgical intervention is rare entity. Surgery is the main treatment of hydatid cyst.



due to the same symptom, but the mediastinal lesion did not show significant interval change (Figure 1C). Pleural fluid analysis still revealed lymphocyte predominant exudates with low ADA level, and no malignant cells were visible. A PET-CT showed increased ^{18}F -fluorodeoxyglucose uptake in the same lesion (Figure 1D). To make a confirmative diagnosis, mediastinal biopsy was done through video-assisted thoracic surgery.

Results: The biopsy specimen showed finely branching filamentous materials which stained positive with Periodic acid-Schiff stain and surrounding neutrophilic reaction. Finally, he was diagnosed as mediastinal actinomycosis with secondary lymphocyte-predominant exudative pleural effusion. He was treated with intravenous amoxicillin/sulbactam for 7 days and discharged with a prescription of oral amoxicillin/clavulanic acid. After completing 3 months of treatment, he had no chest wall pain and no demonstrable lesion was found in the mediastinum.

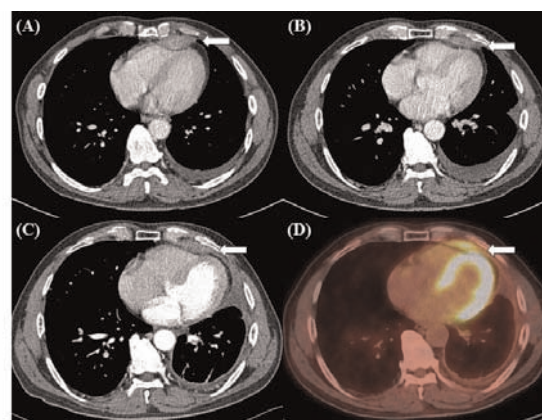


Figure 1. (A) An initial chest CT showed a soft tissue mass in left anterior mediastinum (arrow) and left-sided pleural effusion. (B) The size of mediastinal mass was slightly decreased after 8 months. (C) The mediastinal lesion did not show significant interval change at 14 month follow-up. (D) A PET-CT revealed increased ^{18}F -FDG uptake (SUVmax: 6.3) in the same lesion.

Conclusion: We report a case of mediastinal actinomycosis mimicking malignancy presented with recurrent lymphocyte-predominant exudative pleural effusion. In patients with recurrent and unexplained lymphocyte-predominant exudates, it may be worthwhile to consider finding hidden foci of actinomycosis.

AP274

A CASE OF PRIMARY MEDIASTINAL ACTINOMYCOSIS PRESENTED WITH RECURRENT LYMPHOCYTE-PREDOMINANT PLEURAL EFFUSION

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Background and Aims: Actinomycosis is a chronic suppurative granulomatous infection caused by *Actinomyces*. These pathogenic species may be involved in the three classical forms of cervicofacial, thoracic and abdominal actinomycoses. However, actinomycosis involving the mediastinum is extremely rare.

Methods: A 67-year-old male was admitted due to left side chest pain. He had left-sided pleural effusion, which was identified as lymphocyte-predominant exudates. The pleural fluid adenosine deaminase (ADA) level was 17 IU/L, and there were no malignant cells in cytology. A chest CT showed a soft tissue mass in left anterior mediastinum (Figure 1A). Biopsy was recommended, but he did not agree and was discharged. He revisited after 8 months, and size of the mediastinal mass was slightly decreased (Figure 1B). After 6 months, he was readmitted

AP275

EFFECTS OF INTRAVENA N-ACETYLCYSTEINE ON NEUTROPHIL, PROCALCITONIN, C REACTIVE PROTEIN AND LENGTH OF CLINICAL IMPROVEMENT IN COMMUNITY ACQUIRED PNEUMONIA

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Background and Aims: Community acquired pneumonia (CAP) causes high mortality and morbidity worldwide. Neutrophil, procalcitonin (PCT), and C reactive protein markers may be helpful in establishing the diagnosis, prognosis, therapy and clinical response to pneumonia. Intravenous N-Acetylcysteine (NAC) at a dose of 1200 mg/day is given as anti-inflammatory. To analyze effects of N-Acetylcysteine on neutrophil, PCT, C-reactive protein, and duration of clinical improvement in CAP patients.

Methods: Quasy experimental clinical trial with pretest and posttest design of 27 CAP patients in Dr. Moewardi hospital Surakarta from January 2018 to March 2018. Samples taken by purposive sampling were divided into two groups: treatment group got empirical therapy and 1200 mg/day of intravenous N-Acetylcysteine and the control group received only empirical therapy. The decrease in inflammatory was

measured by neutrophil, procalcitonin serum, leucocyte, CRP, and length of clinical improvement.

Results: Neutrophil values were decreased in control group $-3.623 \pm 3.18\%$ and treatment group $-8.435 \pm 5.37\%$ ($P = 0.011$). Serum PCT decreased in control group -0.023 ± 0.11 ($P = 0.00$) and treatment group -0.529 ± 0.669 ng / mL and decreased of CRP in control group -0.94 ± 1.09 and treatment group -1.07 ± 0.81 mg/L ($P = 0.28$). We found clinical improvement in control group $6.00 \pm 1,826$ and treatment group $5.36 \pm 1,082$ ($P = 0,488$).

Conclusion: Intravenous N-Acetylcystein 1200 mg/day for additional therapy decreased Neutrophil, procalcitonin and CRP levels on CAP

AP276

CHARACTERISTICS OF PATIENTS WITH HIGH MYCOBACTERIUM-AVIUM COMPLEX ANTIBODY

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Background and Aims: Nontuberculous mycobacterium (NTM), especially mycobacterium-avium complex (MAC) is increasing in the world. The principal criteria to diagnose NTM require multiple isolation of same NTM species from biological samples, absence of Mycobacterium tuberculosis and presence of clinical manifestation. Recently, an enzyme immunoassay (EIA) that detects serum immunoglobulin A antibody reacting to the glycopeptidolipid core antigen of MAC was developed, this EIA kit is using for rapid diagnosis of MAC and for differentiating MAC from pulmonary tuberculosis. The aim of this study is to clarify whether the antibody can be a supplementary diagnosis of MAC severity comparing with the clinical features and chest computed tomography (CT).

Methods: We investigated the 82 patients (74.4% were female, the mean age was $71. \pm 0.0$) with MAC met current the ATS/IDSA microbiological criteria between May 2015 and May 2018. All patients were evaluated the characteristics, chest CT findings and mycobacterium-avium complex antibody. Image findings were classified as nodules, consolidation, cavity and bronchiectasis, and we have compared with the antibody level and image features in each group.

Results: There were 29.3% of the cases below the cut off value (0.7U/mL). In the group of low mycobacterium-avium complex antibody, there were significantly observed the cases with immunosuppressed underlying disease (45.8% vs 32.8%, $P < 0.05$). In the group of high mycobacterium-avium complex antibody, the prevalence of female was higher (77.6% vs 66.7%), and the age was younger (70.2 vs 73.1 years). In image findings, bronchiectasis was significantly observed.

Conclusion: It was considered that we should be careful, because there were the cases in which the value of mycobacterium-avium complex antibody measured low.

AP277

IFN- γ RESPONSE TO PPD STIMULATION IN NON-TUBERCULOUS MYCOBACTERIAL PATIENTS MAY DISTINGUISH ACTIVE STAGE FROM CHRONIC ONE

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Background and Aims: The incidence of non-tuberculous mycobacterial (NTM) disease is reportedly increasing globally. In Japan, the incidence rate was 14.7/100,000 person-years in 2014, and 2.6 times higher than in 2007. The antibiotic treatment is prolonged, usually 1–2

years, because of the modest long term response rate. Some patients remain asymptomatic, but most patients progress over time gradually, and deciding to treat or observe is sometimes difficult. The immune response against NTM infection is not fully understood. Therefore, we assessed the cytokine response in NTM patients related to mycobacterial antigens stimulated peripheral blood mononuclear cells (PBMCs).

Methods: Outpatients (defined or suspected of NTM) were recruited at the Nagasaki University hospital. We isolated PBMCs and stimulated them with mycobacterial antigens. After overnight incubation, we did surface and intracellular cytokine staining. Cytokine responses (IL-2, IL-10, IL-13, IL-17A, TNF- α , IFN- γ) were analyzed with multicolour flow cytometry.

Results: We recruited 15 patients (3 males and 12 females). The mean age was 65 years old. They were all non-HIV patients. 4 patients had immunosuppressive drugs. 2 patients had latent tuberculosis infection. The pathogens were 8 *Mycobacterium intracellulare*, 6 *M. avium*, 1 *M. abscessus*, and 1 unknown. 7 patients were under treatment, 5 were after treatment, and 3 were non-treated. The disease status was stable except for one patient. In this patient stimulated with PPD, IFN- γ response was more elevated than other patients (IFN- γ producing CD4+ T cells/All CD4+ T cells ; 0.27% vs 0.053%). TNF- α responses were elevated in all 15 patients stimulated with PPD. TNF- α responses were also elevated in 11 patients stimulated with ESAT-6/CFP-10.

Conclusion: The cytokine responses may vary according to the status in NTM infection. Vigorous IFN- γ response to PPD in NTM patients may distinguish active stage from chronic one.

AP278

RETROSPECTIVE ANALYZE THE CLINICAL APPLICATION OF CRYPTOCOCCAL ANTIGEN (COLLOIDAL GOLD METHOD) TO DETECT PULMONARY CRYPTOCOCCOSIS

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Background and Aims: In recent years, the incidence rate of pulmonary cryptococcosis (PC) is increasing. Its clinical and imaging features are lack of specificity and the invasive biopsy is hard to be accepted, so the pathogenic detection rate is low and difficult to diagnosis this disease. Therefore, the use of cryptococcal antigen as an auxiliary immunological examination method is necessary. To study the sensitivity and specificity of colloidal gold method in the diagnosis of PC, in order to evaluate the clinical significance of the diagnosis of pulmonary cryptococcosis in the absence of pathological support.

Methods: Collect information of all patients who were suspected PC and examined by colloidal gold method. Calculate the sensitivity and specificity of colloidal gold method.

Results: There were 19 cases positive and 112 negative among the 131 cases of colloidal gold. In the positive cases, 13 patients were clinical diagnose of PC and others were not PC. The 112 negative cases were non PC patients. The sensitivity of colloidal gold method was 100% and the specificity was 94.92%. The positive predictive value was 68.42% and the negative predictive value was 100%.

Conclusion: In this study, the sensitivity of colloidal gold method was 100% and the specificity was 94.92%. The colloidal gold method has high value in the diagnosis and differential diagnosis of pulmonary cryptococcosis. And this method is stable at room temperature and its operation is simple, which needs 10 minutes to take the result. The positive predictive value was 68.42% and the negative predictive value was 100%. Therefore it can be used as an exclusive method for cryptococcal infection.

AP279

PNEUMONIA IN EARLY POST-KIDNEY TRANSPLANT PERIOD; A RETROSPECTIVE COHORT STUDY

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Background and Aims: Pneumonia is a major cause of mortality and morbidity in kidney transplant (KT) recipients. Anuradhapura District has the highest prevalence of chronic kidney disease of unknown origin (CKDu), which is the major cause of CKD in the country.

Methods: Forty-six recipients (41 males; mean age 43 years) have been followed up for average 17 (range 06–36) months at KT clinic, Teaching Hospital Anuradhapura since 2012. All patients who presented with pneumonia were admitted and managed in high dependency or intensive unit, by multi-disciplinary team including nephrologist, pulmonologist and microbiologist. All patients underwent sputum, blood and urine cultures and all who were intubated had tracheal aspirates or bronchial lavages performed. We accessed their detailed clinic and admission records to identify occurrence of pneumonia during early post-KT period.

Results: Forty-three had CKDu and three had diabetes mellitus leading to CKD in this cohort. Fourteen out of forty-six patients (30%) developed pneumonia during the study period. Majority of them (10 patients; 71%) developed pneumonia within the first year after KT. Bacterial pneumonia with *Pseudomonas* and coliforms were commonest, while two developed fungal pneumonia and one had smear positive pulmonary tuberculosis. Six (43%) died despite maximum possible care (Table 1).

All three patients with diabetes developed Post-KT bacterial pneumonia and one of them with resistant coliform growth on sputum culture succumbed to illness. Two patients with cultures showing no growth, were treated with combined antibiotics (to cover Gram negatives, MRSA and anaerobes) and antifungals, but also died. The patient developed tuberculosis did not have past tuberculosis.

Conclusion: We noted a high incidence (30%) of pneumonia in the early post-KT period in this cohort with predominant CKDu. Three were only three patients with diabetes and all of them developed pneumonia. *Pseudomonas* and coliforms were the commonest organisms responsible. Early post-KT pneumonia had a high mortality of 43%.

Aetiology	No	Comments	Outcome
<i>Pseudomonas</i>	04	Two had diabetes	Two died; Two recovered
Coliforms	04	One had diabetes	One died; Three recovered
<i>Moraxella</i>	01		Recovered
Fungal	02	Both also had mixed growth on sputum culture	One died; One recovered.
<i>Mycobacterium tuberculosis</i>	01	Also had <i>Pseudomonas</i> on sputum culture	Recovered
Culture negative	02		Both died

AP280

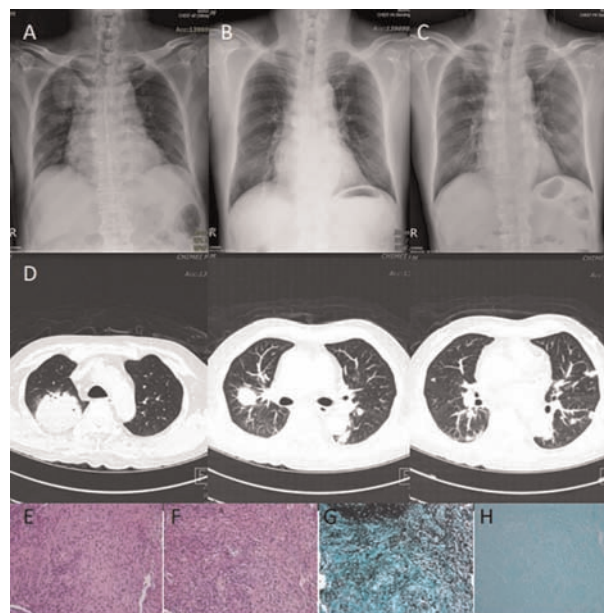
PULMONARY NOCARDIA INFECTION PRESENTING AS MULTIPLE LUNG MASSES

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Background and Aims: A man aged 59 years was referred to our department for evaluation of a solitary pulmonary nodule. He was

maintained on immunosuppressive regimen after renal transplantation. His chest X-ray showed a 5-cm irregular mass lesion in the right upper lobe and small nodular densities in bilateral lung fields (Figure 1A). Compared with the chest radiograph 5 months before (Figure 1B), the largest mass lesion had a rapid growth rate.



Methods: Contrast enhanced chest CT scan revealed a mass lesion at right upper lung field accompanied by multiple nodules in both lung fields (Figure 1D). There was mild erythematous change with mucosal swelling and purulent sputum at the bronchial orifice of apical segment of right upper lobe without endobronchial visible lesions under the flexible fiberoptic bronchoscope. The transbronchial biopsy showed chronic inflammatory infiltrates with no evidence of granuloma formation. Immunohistochemical analysis was negative to cytokeratin AE1/AE3, p40, and TTF-1. Special stains of PAS, GMS and AFB were negative for microorganisms (Figure 1E-H). On the 5th hospital day, *Nocardia* species was isolated from bronchial brushing specimen.

Results: After receiving TMP-SMX for 6 days, he developed an acute altered mental status with agitation and lower extremities weakness. The cerebrospinal fluid analysis revealed normal cell counts, glucose and protein, and the culture did not yield any growth of a microorganism. TMP-SMX was changed to ceftriaxone and doripenem on day 15 of the hospitalization. Within 5 days of the discontinuation of TMP-SMX use, he gradually returned to his baseline mental status. At the 2-month follow-up, the radiographic size of initial lesion had significantly decreased in size after treatment (Figure 1C).

Conclusion: This case highlights the importance of keeping in mind the possibility of pulmonary nocardiosis in immunocompromised patients and alerting patients about a rare side effect of TMP-SMX.

AP281

KARTAGENER'S SYNDROME: A RARE CASE REPORT IN MALE

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Background and Aims: A rare case autosomal recessive disorder Kartagener's Syndrome is a classic triad of sinusitis, situs inversus and bronchiectasis which a type of Primary Ciliary Dyskinesia (PCD). PCD

shows widespread disability in ultrastructure and ciliary motility where it affects the impaired function of movement and clearance of cilia.

Methods: Descriptive.

Results: We present the case of 32-year-old man with recurrent shortness of breath and phlegm cough since 1 year before admitted to hospital. He had a history of pulmonary tuberculosis treatment for 4 months and then stopped taking his medication because he feel no improvement. He had a history of colds, nasal congestion, and heart abnormalities since childhood. Patient did not go to doctor because symptoms resolve after taking self-purchased drugs. On general examination patient is anaemic with grade 2 clubbing, cyanosis, no pallor, icterus and pedal edema. His pulse was 122x/mins regular, respiratory pressure 120/80 mmHg in right arm supine position and oxygen saturation 90.7% with NRBM 10 lpm. On cardiovascular examination, apex beat was felt on right 5th intercostals space 1 cm lateral to midclavicular line and on auscultation of heart, heart sound better heard on right side with no murmur and gallop sign. Abdominal examination obtained tympanic note on percussion in right hypochondrium. X-Ray shows bronchiectasis. HRCT shows that patient had dextrocardia with opposite visceral abdomen. Waters x-ray shows that patient had a sinusitis on frontalis sinistra and sinus maxilaris bilateral. All these things lead to Kartagener's Syndrome.

Conclusion: The available information on various aspect of this disease in order to delineate the therapeutic objective more clearly. Early diagnosis is important for maintain of pulmonary function, quality of life, and increase in life expectancy in this disease.

AP282

CLINICAL EFFICACY AND COST-EFFECTIVENESS ANALYSIS OF CEFEPIME OR PIPERACILLIN/TAZOBACTAM BOTH WITH CIPROFLOXACIN IN MICU PATIENTS WITH SEVERE PNEUMONIA

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Background and Aims: Patients with severe community-acquired pneumonia have high mortality rate (up to 50%). Cefepime and piperacillin/tazobactam are active against *Pseudomonas aeruginosa* as well as *Streptococcus pneumoniae* but not recommended as primary therapy unless the patient has risk for *P. aeruginosa*. But risks of *P. aeruginosa* are not well established and it may be difficult for house staff to make a clinical decision. Furthermore no cost-effectiveness of antibiotic strategies have been reported.

Methods: Patients with severe community-acquired pneumonia who was admitted in MICU have been recruited from Dec. 1, 2016 to Aug. 31, 2017. Patients who had absolute neutrophil count less than 1000/mm³ and received antibiotic therapy less than 72 h were excluded. Each group received either cefepime or piperacillin/tazobactam, both with ciprofloxacin and changed to narrow spectrum antibiotics.

Results: 48 patients were screened and 43 patients (90%) were assessed. 21 patients were assigned to cefepime group and 22 were piperacillin/tazobactam group. APACHE II score were 18.7 ± 7.2 and 19.7 ± 7.9 ($P = 0.67$). Clinical success rates were 86% and 82% for patients treated with cefepime and piperacillin/tazobactam, respectively and 3 (14%) and 4 patients (18%) were died. Also there were no statistical significance in terms of frequency of concomitant antibiotics, antibiotics duration, numbers, duration of mechanical ventilation and MICU days. Pretreatment organisms were *P. aeruginosa* 3, *Acinetobacter* spp. 2, *K. pneumoniae* 1, *S. pneumoniae* 1, coagulase negative staphylococcus 1, methicillin-sensitive staphylococcus aureus 1, and *M. pneumoniae* 1. 9 patients (43%) in cefepime group and 5 (23%) in piperacillin/tazobactam group were superinfected ($P = 0.08$). Costs of

cefepime group was \$ 1165 ± 199 , and that of piperacillin/tazobactam group was \$ 893 ± 152 ($P = 0.28$).

Conclusion: There were no significant differences in clinical efficacy and cost-effectiveness in both groups. They would be acceptable strategies in terms of mortality but have concerns for superinfection and cost.

AP283

IMPORTANCE AND EFFICACY OF CONCURRENT INTRAVENOUS COLISTIN WITH NEBULIZED COLISTIN FOR VENTILATOR-ASSOCIATED PNEUMONIA COMPARED WITH ONLY INTRAVENOUS COLISTIN

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Background and Aims: Ventilator induced pneumonia caused by carbapenem resistance in *Acinetobacter baumannii* (CRAB) occur frequently in intensive care unit. Recently, interest of nebulized antibiotic therapy has become increasingly worldwide. Because nebulized therapy has target treatment and lower toxicity. But, nebulized based therapy has high risk for failure of concurrent CRAB blood infection. We studied efficacy and problem intravenous (IV) and intravenous with nebulized colistin (IVNE)

Methods: We reviewed sixty patients with VAP caused CRAB. They treated with either intravenous ((IV, $n = 42$) and intravenous with nebulized colistin (IVNE, $n = 18$). We enrolled patients from January 2015 to December 2016 in Gachon University Gil Medical Center. We analyzed this patient based on medical record, retrospectively.

Results: Of 60 patients, eighteen patients were treated intravenous colistin with concurrent nebulized colistin (IVNE) and 42 patients were treated only intravenous colistin (IV). Of 60 years patients, Blood of seven patients cultured CRAB. All patients were IV group. There was no CRAB in blood of IVNE. Mortality rate of IVNE and IV were 33.3% and 61.9% and was statistically significant ($P = 0.042$). In IVNE group, length of colistin treatment was statistically significant longer ($P = 0.008$). But Day from admission to colistin treatment was significant lower ($P = 0.012$). There were no statically significant difference in acute renal failure and increased BUN/Cr.

Conclusion: In this study, we suggest that concurrent intravenous colistin therapy with nebulized colistin may be safe and effective treatment compared with only intravenous colistin.

APL008

THE EFFECT OF PROCALCITONIN-GUIDED THERAPY ON PRESCRIPTION AND DURATION OF ANTIBIOTICS AMONG PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA: A META-ANALYSIS

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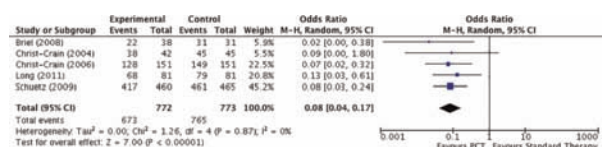
Background and Aims: Community Acquired Pneumonia (CAP), is considered as the sixth overall leading cause of death and the leading cause of mortality among infectious diseases. Bacterial aetiology is the most emphasized cause of CAP. Procalcitonin (PCT) may be helpful as a guide on when to prescribe antibiotics since it is expected to elevate in acute bacterial infections thus can help in preventing injudicious antibiotic use.

This study aims to determine the effect of PCT-guided therapy on prescription and duration of antibiotic administration among adult patients diagnosed with CAP. In terms of clinical outcome, all-cause mortality was determined.

Methods: Randomized Controlled Trials where patients diagnosed with CAP assigned to receive antibiotic treatment based on PCT results were looked into through online databases, cross-referencing and individual search. Number of patients prescribed with antibiotics, mean duration of antibiotic, and all-cause mortality were analyzed using random effects model.

Results: Total of five studies which fulfilled the inclusion and exclusion criteria were analyzed, with a total population of 1545 diagnosed with CAP, 772 patients on the PCT-guided group and 773 on the standard group. Number of patients prescribed with antibiotics was lower among the PCT-guided group than the standard group, with 673 (87.2%) patients vs 765 (99.0%) patients, respectively (OR 0.08, 95% CI 0.04–0.17). Among patients prescribed with antibiotics, those that were randomized within the PCT-guided group received antibiotics for 3.99 (95% CI 1.62–6.35) days less compared to those in the standard group. In terms on clinical outcome, there was no significant difference in all-cause mortality between the groups, 46 mortalities on the PCT-guided group vs 5 mortalities in standard group (RR 0.91, CI 95% 0.62–1.32).

Conclusion: PCT-guided therapy reduces antibiotic prescription and duration of use among patients with CAP managed at outpatient and medical wards compared to standard therapy without compromising clinical outcome.



Respiratory Neurobiology and Sleep 1

AP284

A CASE REPORT ON BILATERAL DIAPHRAGMATIC DYSFUNCTION DUE TO BILATERAL PHRENIC NERVE NEUROPATHY IN A 65-YEAR-OLD MALE WITH DYSPNEA ON SUPINE POSITION

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Background and Aims: Diaphragmatic dysfunction describes a spectrum of conditions resulting from weakness to complete paralysis of the diaphragm. When patients have diaphragmatic dysfunction, there is absence of the caudal displacement of the diaphragm during inspiration, thus compromising lung inflation. It is a rare cause of unexplained respiratory failure with a median delay for diagnosis of 2 years. However, there are a number of identified aetiologies that need to be ruled out in order to manage patients appropriately. For this reason, an algorithmic approach to diagnosis and management of diaphragmatic dysfunction is needed.

Methods: This paper reports a 65-year-old male who came in due to dyspnea in supine position associated with sleep disturbance and daytime sleepiness.

Results: The patient is a 20-pack-year smoker, with history of left diaphragmatic eventration s/p plication, respiratory failure requiring mechanical ventilator support, history of primary hyperparathyroidism with right

parathyroid adenoma, and paradoxical breathing on supine position. Patient was worked up revealing (1) elevated, dome-shaped right hemidiaphragm on Chest X-ray, (2) right parathyroid adenoma without noted nerve infiltration or compression along the tract of the brachial plexus and phrenic nerve on plain Neck and Chest CT scan, and plain Neck MRI, (3) moderate restrictive ventilatory defect with decrease in FVC by 30% when supine on Spirometry, (4) paradoxical movement on the right on diaphragm ultrasound (M-mode), and (5) severe bilateral phrenic neuropathy on EMG-NCV. Polysomnography documented obstructive sleep apnoea and possible sleep hypoventilation syndrome that improved with Average Volume Assured Pressure Support Mode (AVAPS) S/T mode. Patient was able to tolerate AVAPS S/T mode, he was liberated from nocturnal mechanical ventilator support and later underwent decannulation of tracheostomy tube.

Conclusion: Bilateral diaphragmatic dysfunction is a rare but important cause of unexplained respiratory failure and should be suspected among patients presenting with orthopnea, paradoxical breathing and sleep disordered breathing.

AP285

ABERRANT DNA METHYLATION LEVELS OF THE FORMYL PEPTIDE RECEPTOR 1/2/3 GENE PROMOTER REGIONS ARE ASSOCIATED WITH OBSTRUCTIVE SLEEP APNOEA

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Background and Aims: Formyl peptide receptors 1 and 2 can mediate endothelial dysfunction through affecting the production of reactive oxygen species and subsequent inflammation. Our previous study revealed that FPR1 over-expression and FPR2/FPR3 insufficiency play a role in the development of obstructive sleep apnoea (OSA). We hypothesized that epigenetic modification of the FPR1/2/3 gene promoter regions may underlie intermittent hypoxia with re-oxygenation (IHR) injury in OSA.

Methods: DNA methylation levels over 12 CpG sites of the FPR1/2/3 gene promoter regions and their gene expression levels in the peripheral blood mononuclear cells were determined by pyrosequencing and quantitative RT-PCR methods in 24 mild to moderate OSA patients, 20 severe OSA patients, 12 severe OSA patients under long-term continuous positive airway pressure treatment (severe OSA on CPAP), 16 matched primary snoring (PS) subjects, and 12 matched healthy non-snorers (HS).

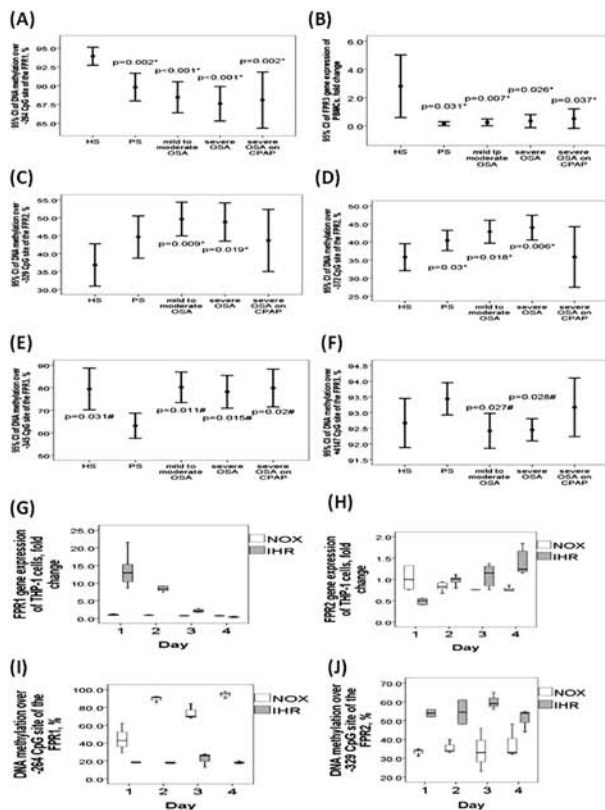
Results: Both DNA methylation levels over -264 CpG site of the FPR1 gene and FPR3 gene expressions were decreased in PS, mild to moderate OSA, severe OSA, and severe OSA on CPAP groups vs HS, while the former negatively correlated with FPR1/FPR3 gene expression ratios. Both -329 and -372 CpG sites of the FPR2 gene were hypermethylated in mild to moderate OSA and severe OSA groups vs HS, while the former negatively correlated with FPR2 gene expression. -345 and +4147 CpG sites of the FPR3 gene were hypermethylated and hypomethylated, respectively, in mild to moderate OSA and severe OSA groups vs PS, and the former negatively correlated with mean SaO₂/minimum SaO₂ and associated with memory impairment. *in vitro* IHR in human monocytic THP-1 cells result in FPR1 over-expression and FPR2 under-expression in association with DNA methylation changes over FPR1 (-264 CpG site) and FPR2 (-372/-329 CpG sites).

Conclusion: The development of OSA and its disease severity is associated with epigenetic modifications in the FPR1/2/3 gene promoter regions.

Table 1. Demographic, biochemistry, and sleep data of all the 84 study participants

PS=primary snoring, HS=healthy subjects (non-snorers), BMI=body mass index, AHI=apnea hypopnea index, ODI= oxygen desaturation index, SaO₂= arterial oxygen hemoglobin saturation, ESS=Epworth Sleepiness Scale, EDS= excessive daytime sleepiness, CKD=chronic kidney disease

	HS (n=12)	PS (n=16)	Mild- moderate OSA (n=24)	Severe OSA (n=20)	Severe OSA on CPAP (n=12)	p value
Age, years	50.9±9.3	47.1±8.0	47.4±12.4	46.5±15.3	52.4±10.8	0.384
Male Sex, n (%)	11 (91.7)	11 (68.8)	19 (79.2)	18 (90)	10 (83.3)	0.449
BMI, kg/m ²	24.3±2.8	25.9±3.2	26.3±3.2	26.8±2.2	26.3±3.2	0.188
AHI, events/hour	NA	3.8±3.3	18.7±6.2	59.4±18.9	60.3±15.6	<0.001
ODI, events/hour	NA	1.2±1.2	8.0±8.5	48.2±23.1	50.6±20.0	<0.001
Mean SaO ₂ , %	NA	96.6±1.1	96.5±1.2	93.6±3.3	93.1±2.3	<0.001
Minimum SaO ₂ , %	NA	91.1±3.1	86.3±6.7	70.6±12.1	71.9±10.6	<0.001
Snoring index, counts/hour	NA	141.6±177	206±215	335±236	239±244	0.079
ESS	NA	8.6±5.2	8.5±3.8	10.9±4.4	14.8±4.2	0.001
EDS, n (%)	NA	4 (25)	6 (25)	11 (55)	11 (91.7)	<0.001
Current smoking, n (%)	0 (0)	4 (25)	2 (9.1)	3 (15)	1 (11.1)	0.365
Cholesterol, mg/dl	NA	192.1±23.7	185.9±31.2	175.7±45.5	190±49.4	0.588
Triglycerides, mg/dl	NA	137.6±74.5	147.4±102	130.9±59.7	213.7±159	0.166
Hypertension, n (%)	1 (8.3)	4 (25)	6 (27.3)	3 (15)	5 (50)	0.066
Diabetes mellitus, n (%)	1 (8.3)	1 (6.3)	4 (18.2)	2 (10)	1 (11.1)	0.526
Heart disease, n (%)	0 (0)	0 (0)	1 (4.5)	2 (10)	1 (11.1)	0.524
Stroke, n (%)	0	2 (12.5)	1 (4.5)	0	0	0.29
CKD, n (%)	0	0	0	0	0	1



AP286

USING NOSAS SCORE TO PREDICT SEVERE OBSTRUCTIVE SLEEP APNEA IN A CLINIC-BASED POPULATION

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Background and Aims: The NoSAS score was developed as a screening tool to identify individuals with obstructive sleep apnoea (OSA) in a general population cohort. However, it has not been well studied in other clinical populations. We aimed to validate the NoSAS score in a clinic-based population and compare its performance to the Epworth Sleepiness Scale (ESS).

Methods: We conducted a retrospective chart review of 500 patients who were referred to the sleep clinic. The NoSAS score was calculated based on available demographic and anthropometric data in addition to presence of self-reported snoring. All subjects underwent a full polysomnography. A NoSAS score of ≥ 8 points and an ESS of ≥ 10 points were classified as high risk for OSA. We defined severe OSA as an apnoea-hypopnea index of ≥ 30 events/h.

Results: The prevalence of severe OSA was 52.6%. The number of patients who were classified as high risk by the NoSAS score and ESS were 240 (48.0%) and 279 (55.8%), respectively. Overall the NoSAS score performed better than the ESS. The sensitivity, specificity, and negative and positive predictive value of the NoSAS score to predict severe OSA was 64.3, 70.0, 63.8 and 70.4%, respectively. The sensitivity, specificity, and negative and positive predictive value of the ESS to predict severe OSA was 58.6, 47.3%, 50.7% and 55.2%, respectively. The area under the curve values of NoSAS score (0.724) was higher than ESS (0.544). However, both scores did not perform well as screening tools for severe OSA in view of their low sensitivities and negative predictive values.

Conclusion: Although the NoSAS score was superior to the ESS, both tools performed poorly in predicting severe obstructive sleep apnoea in a clinic-based population. Given the high prevalence of severe OSA in such patients, respiratory polygraphy or a full polysomnography may be needed to rule out sleep apnoea.

AP287

TOO LITTLE O₂, TOO MUCH HGB

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Background and Aims: Secondary erythrocytosis from OSA is a result of intermittent hypoxia that occur during sleep. This is often undiagnosed until patient already presents with symptoms. We are going to present a case wherein an apparently healthy man presented with bothersome symptoms from an underlying disease.

Methods: Case Report

Results: A 50 year old male consulted at the outpatient department with chief complaint of cyanosis during sleep, flushed face and headaches. He claims to be asthmatic as a child with no recurrent attacks and was apparently well until a few months ago when he started having headaches, his wife notices that he turns blue when sleeping. A few weeks prior to consult he noticed shortness of breath then flushing of the face and bulging red eyes. He sought consult wherein lungs were clear but oxygen saturation is 78% at room air. His ABG revealed hypoxemia at room air (pO₂ at 55), a stable left lung base fibrosis in chest X-ray,

moderate obstructive lung disease with significant response to bronchodilator, a severe obstructive sleep apnoea on polysomnography and a hgb of 212 and hct of 0.69 on CBC. He was immediately referred to a haematologist and underwent phlebotomy. He had immediate relief of symptoms and hgb decreased to 177, hct 55. He was also started on low dose ICS/LABA and Doxofylline and CPAP with PS of 13 and oxygen of 2 L per minute. On follow up, patient feels great, O2 sat of 96% at room air, normal PFT and sleep study showed moderate sleep apnoea. He was advised to continue CPAP and inhaler.

Conclusion: Based on this case and other OSA cases, secondary erythrocytosis appears to be more common in those with not known OSA. Awake and nocturnal hypoxemia seems to be more associated with this condition than severity of OSA as measured by AHI.

AP288

CPAP ADHERENCE IN ADULTS WITH NEWLY DIAGNOSED OSAHS AND RELATED INFLUENTIAL FACTORS: A STUDY IN CHANGSHA, CHINA

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Background and Aims: The purpose of this study was to assess CPAP adherence in Changsha (a representative Chinese city) adults with newly diagnosed OSAHS and assess the influential factors for CPAP adherence in this group.

Methods: A prospective longitudinal study was ongoing at the Second Xiangya Hospital and the Third Xiangya Hospital, CSU, Changsha, China. Consecutive 156 newly diagnosed OSAHS patients (138 males and 18 female, 118 severe and 38 moderate patients) were recruited for study participation. Following the diagnostic PSG, participants completed risk screening questionnaires including The Epworth Sleepiness Scale (ESS), The Health Literacy Screening Questionnaire (HLS). The Self-efficacy Measure in Sleep Apnoea (SEMSA), Sleep Apnoea Quality of Life Index (SAQLI). Participants completed a full-night, in-laboratory CPAP titration with PSG. After the CPAP titration, participants completed The Visual Analogue Scale (VAS) questionnaire about treatment. Participants returned to the sleep center for a scheduled research visit after 30 days of home CPAP treatment. The SPSS 13.0 analysis software was used.

Results: Only 55.8% patients (87 patients, including 80 severe and 7 moderate patients, 78 males and 9 female) had good CPAP adherence. There are difference between good and poor adherence patients in age, ESS, AHI, the lowest SaO₂, VAS, HLS and SEMSA (Table 1). The patients who are older, or with mild symptoms, or with dissatisfaction of initial treatment experience, or with lower risk cognition and lower health literacy had poorer treatment adherence.

Conclusion: CPAP adherence in Changsha adults with newly diagnosed OSAHS is poor. Age, severity of disease, satisfaction of initial treatment experience, health literacy, and self-efficacy of sleep apnoea (the perception of untreated risk of disease) are the main factors affecting CPAP adherence in Changsha patients with OSAHS.

Table 1. There are difference between good and poor adherence patients in age, ESS, AHI, the lowest SaO₂, VAS, HLS and SEMSA (values are mean ± SEM).

	good adherence	poor adherence	P
Age (years)	42.1±3.3	66.7±3.2	<0.05
AHI(events/h)	47.0±13.3	36.0±19.3	<0.001
Lowest oxygen saturation (%)	63±13	78±19	<0.005
ESS	13.5±5.6	10.2±4.6	<0.001
HLS	3.5±1.3	7.5±2.3	<0.005
SEMSA	80.5±13.8	73.5±8.5	<0.005
VAS	84.3±17.4	54.3±13.2	<0.001

AP289

HOW DOES THE OBSTRUCTIVE SLEEP APNEA INFLUENCE THE SLEEP EFFICIENCY, SLEEPINESS, AND NEUROCOGNITIVE FUNCTION IN PATIENTS WITH REM SLEEP BEHAVIOUR DISORDER

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Background and Aims: REM sleep behaviour disorder (RBD) may negatively influence sleep quality and cognitive function. Obstructive sleep apnoea (OSA) could result in chronic intermittent hypoxia and sleep fragmentation which would further promote daytime sleepiness and cognitive dysfunction. Though the high prevalence of OSA has been reported, the impact of concomitant OSA on sleep consolidation and daytime function in RBD patients is not clear. Therefore, this study aimed to meta-analyze the impact of OSA on the sleep efficiency, subjective sleepiness, and neurocognitive function in patients with RBD.

Methods: Studies investigating the OSA in patients with RBD were systematically retrieved by two independent researchers from MEDLINE, EMBASE and Cochrane Library from inception date to January 2018. The main outcomes included sleep efficiency, subjective sleepiness and neurocognitive function. The Subjective sleepiness was evaluated with Epworth Sleepiness Scale (ESS) while neurocognitive function was evaluated by Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). MMSE was converted to MoCA score to facilitate analysis. The effect of OSA was analyzed by random-effects meta-analysis and expressed as mean differences and 95% confidence intervals (95% CI). The heterogeneity was evaluated with I².

Results: The meta-analysis included 5 studies comprising of 373 RBD patients including 284 patients with OSA (RBD-OSA) and 89 without OSA (RBD-NOSA). The mean age was 62.3 y/o, 79.9% were male, and mean body mass index was 26.5 kg/m². The studies were homogeneous for all three outcomes (I² from 0 to 26%). The RBD-OSA had similar sleep efficiency (mean -2.31%; 95% CI -8.80 to 4.17; *P* = 0.26), ESS (mean -2.03, 95% CI -4.47 to 0.40, *P* = 0.58), and MoCA score (mean 0.15, 95% CI -3.57, 3.87; *P* = 0.45) with RBD-NOSA.

Conclusion: The meta-analysis showed concomitant OSA has no impact on sleep efficiency, sleepiness, and neurocognitive function in RBD patients.

Acknowledgement: The work was supported by grants from National Taiwan University Hospital (NTUH 107-19), and "Center for

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AP290

RETROSPECTIVE OBSERVATIONAL STUDY OF OBSTRUCTIVE SLEEP APNOEA IN WOMEN IN NORTHERN TERRITORY AUSTRALIA

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Background and Aims: We aim to identify the characteristics of female patient with obstructive sleep apnoea in Northern Territory Australia in both indigenous and non-indigenous women

Methods: This retrospective study included total of 306 women, both indigenous and non-indigenous Australian, who underwent diagnostic sleep study for suspected obstructive sleep apnoea at the Darwin Respiratory and Sleep Health from January to December 2015. All subjects underwent anthropometric measurements (height, weight, BMI, neck circumference), questionnaire for risk assessment of OSA (hypertension, heart disease, diabetes mellitus, depression, use of anti-depressants, smoking and alcohol use) and Epworth Sleepiness Score before the diagnostic sleep study. We used American Academy of Sleep Medicine guideline for severity assessment of OSA.

Results: A total of 306 women underwent sleep study; diagnosis of obstructive sleep apnoea was made in 102 (33%), which comprise 21 indigenous women (20%) and 81 non-indigenous women (80%). Severe daytime sleepiness with ESS more than 9 was reported by 56% of OSA diagnosed women. The mean age of all women who were diagnosed with sleep apnoea was 52 (min = 21.1, max = 80.1, SD = 13.3), comprising mean age 46.9 (min = 21.1, max = 75, SD = 13.9) for indigenous and 54 (min = 42, max = 79, SD = 14.6) for non-indigenous. Mean BMI of all OSA patients was 37. For indigenous patients with OSA, mean BMI is 37 and that of non-indigenous cohort was 36. Mean neck circumference of indigenous OSA patients was 42 cm whilst that of non-indigenous women was 38.8 cm. Mean AHI of all OSA patients was 37 (min = 4.8, max = 140, SD = 25.6). Indigenous women scored higher mean AHI 42.2 (min = 12.1, max = 130) compared to mean AHI 36.3 (min = 4.8, max = 140) of non-indigenous women.

Conclusion: Although lower proportion of indigenous women are diagnosed with obstructive sleep apnoea, the disease is more severe in them, associated with higher BMI and thicker neck circumference.

AP291

THE USE OF CONTINUOUS PULSE OXIMETRY IN THE DIAGNOSIS OF DEVENTILATION SYNDROME IN A CASE OF KYPHOSCOLIOSIS WITH CHRONIC VENTILATORY FAILURE

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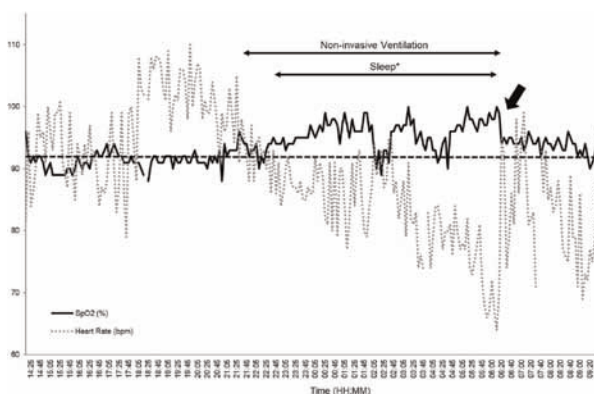
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Background and Aims: Deventilation dyspnoea (DD) following cessation of nocturnal non-invasive ventilation (NIV) has been described in individuals with severely impaired lung function. However, the pathophysiology is less well-understood and diagnosis is often challenging.

Methods: We describe the use of a wireless wearable ward-based continuous pulse oximetry and vital signs monitoring device (ViSi Mobile System, Sotera Wireless) in a case of DD.

Results: The patient was a frail elderly woman who presented with progressive dyspnoea. Significant past medical history included kyphoscoliosis with chronic hypercapnic respiratory failure on nocturnal NIV (6–7 h per night) for the 13 years preceding current admission. Clinical examination revealed kyphoscoliosis and signs of cor pulmonale. Chest imaging showed pulmonary infiltrates and bilateral pleural effusions consistent with fluid overload. This resolved with diuresis and pleural drainage. However, despite euvolemia, persistent dyspnea was observed following removal of NIV in the morning. Continuous pulse oximetry revealed mean (standard deviation) oxygen saturation (SpO₂) of 95.7 (2.3)% and 92.4 (2.1)% during NIV and when off NIV respectively; the findings correlated with arterial blood gas analysis showing partial pressure of carbon dioxide (PaCO₂) 43 mmHg during NIV and hypercapnia (PaCO₂ 59) when off NIV. There was a sharp decline in SpO₂ during removal of NIV in the morning (see Figure - Arrow). Alveolar-arterial oxygen gradient was normal throughout, which suggested no significant parenchymal disease or ventilation-perfusion mismatch. We suspected a component of respiratory muscle weakness but the patient was too weak to perform pulmonary function testing. The duration of NIV usage was lengthened and a small dose of opiate was administered in the morning following removal of NIV, which led to symptomatic improvement.

Conclusion: DD can complicate advanced kyphoscoliosis. The use of a simple continuous SpO₂ monitoring device allows for indirect trending of PaCO₂ and assisted in the diagnosis of DD in this case.



AP292

DYSPNOEA IMPROVEMENT IN PATIENTS WITH LUNG DISEASES IN A SINGLE SESSION OF MINDFUL BREATHING: A RANDOMIZED CONTROLLED STUDY

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Background and Aims: Mindful breathing has been practised in recent decades and there is a lack of study for it as a non-pharmacological method in improving dyspnea. This study was to assess the efficacy of mindful breathing in improvement of dyspnea score, oxygen saturation and respiratory rate in patients with lung diseases.

Methods: Sixty three inward patients, diagnosed with lung cancer, acute exacerbation of bronchial asthma (AEBA) or acute exacerbation of chronic obstructive pulmonary disease (AECOPD), were recruited and assigned randomly into intervention and control groups. They reported their dyspnea score according to Modified Borg Dyspnea scale while oxygen saturation and respiratory rate were measured. The parameters were assessed at baseline, at 5 mins and at 20 mins.

Results: Mindful breathing significantly reduced the dyspnea score among all patients in 5 min (OR = 12.886, 95% CI = 3.588, 46.282, $P < 0.001$) and 20 minutes (OR = 5.378, 95% CI = 1.832, 15.790, $P = 0.002$), oxygen saturation in 5 min (OR = 4.050, 95% CI = 1.137, 14.432, $P = 0.025$) and respiratory rate in 20 min (OR = 3.069, 95% CI = 1.094, 8.613, $P = 0.031$).

Significant early dyspnea score reduction was observed in 5 min in mindful breathing group among patients with lung cancer. ($P = 0.041$) In a subgroup of patients with AEBA, mindful breathing conferred significant sustained dyspnea reduction in 5 min ($P = 0.006$); in 20 min ($P = 0.003$) and early oxygen saturation in 5 min ($P = 0.039$). In mindful breathing group among patients with AECOPD, a significant reduction in dyspnea score was observed in 5 minute ($P = 0.034$) while delayed respiratory rate improvement was demonstrated in 20 min ($P = 0.035$).

Conclusion: Mindful breathing is a quick, easy and useful therapy and has a significant effect in dyspnea reduction among patients with lung diseases. Further studies with a larger sample size are recommended to discover more potential effects of mindful breathing in the subgroups of patients.

AP293

TREATMENT EMERGENT SLEEP APNEA: A CASE REPORT

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Background and Aims: While obstructive sleep apnoea is effectively treated with continuous positive airway pressure (CPAP), roughly 10% of initial CPAP titrations result in emergence of central apnoea's or hypopnoeas, a phenomenon referred to as treatment-emergent central sleep apnoea (CSA). Although the majority of treatment-emergent CSA resolves with ongoing CPAP therapy, some patients exhibit persistent CSA, creating a therapeutic challenge.

Methods: A 32-year-old male, sought consult due to morning headaches and poor concentration which affects his work. Associated symptoms were snoring, witnessed apnoea, daytime sleepiness, and easy fatigability. Past medical history and family history were unremarkable. Sleep history revealed that patient has sudden awakening with intense anxiety, awakens with headache, with back pain and with heartburn, has difficulty waking up in the morning, and has trouble falling asleep. Epworth sleepiness scale is 19. BMI is 38 kg/m² and neck circumference is 18 inches. Chest findings were unremarkable. STOP BANG score was 6/8. Echocardiogram and arterial blood gas were normal.

Results: On diagnostic polysomnogram, respiratory disturbance index (RDI) was noted to be 101.3 events/h, with 77% obstructive apnoeas, 13% central apnoeas and 10% hypopnoeas. Central apnoea index was 13.1. Lowest oxygen saturation was 89%. During the CPAP titration study, central apnoea index increased to 57.2. The patient then underwent a repeat therapeutic polysomnogram since the ending pressures of the first titration study failed to normalize the RDI. On repeat titration study, at bi-level positive airway pressure (PAP) with pressures of IPAP 13, EPAP 5, back up rate of 12, there was resolution of the central apnoea events.

Conclusion: Management of treatment-emergent CSA is controversial, and treatment recommendations are derived from clinical experience, small observational studies, and a limited number of small randomized trials. For this case, titration with bi-level PAP was helpful in relieving the central apnoea events.

Respiratory Structure and Function 1

AP295

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND RESPIRATORY FUNCTIONS

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Background and Aims: Since their ethiopathology and results shown similarities, the relationship suggested between the NAFLD and the impaired respiratory functions are shown for the first time by obtaining liver biopsy in this study.

Methods: 94 non-smoking patients 58♀, 36♂ who had NAFLD whose Activity Score (NAS) calculated for all patient after the biopsy. The control group 28♀&17♂out of 45 whose respiratory function test results (FEV1&FVC) received by spirometry.

Results: Biopsy results evaluated, steatosis degree and NAS score were negatively correlated with FEV1($r = -0.22$, $P = 0.033$ & $r = -0.363$, $P < 0.01$) & FVC($r = -0.271$, $P = 0.08$ & $r = -0.414$, $P < 0.01$), no correlation with lobular inflammation, aneurism, fibrosis. FEV1, FVC in all patients negative correlation with insulin resistance $r = -0.363$, $P < 0.001$ & $r = -0.602$, $P < 0.001$). 14 patients (14.8%) restrictive respiratory disease (FEV1/FVC ≥ 70 & FVC < 80). Two groups as non-alcoholic steatohepatitis (NASH) ($n:57$) and non-NASH ($n:37$), a significant difference found regarding insulin resistance, waist/hip circumference ratio, FEV1, FVC values.

Between groups FEV1/FVC ratio had no significant difference, restrictive pattern value (10.8% vs17.5 $P = 0.37$).

In NAFLD group, insulin resistance seen to be significant as an independent predictor factor ($P < 0.001$).

Conclusion: Patients with NAFLD, a restrictive respiratory disease seen relatively as a frequent co-morbidity; insulin resistance on these two organs is regarded as a probable mechanism.

As their ethiopathology and results shown similarities, the relationship suggested between the NAFLD and the impaired respiratory functions are shown for the first time by obtaining liver biopsy in this study.

AP296

THE WEIGHT LOSS THERAPY IMPROVED RESPIRATORY FUNCTION AND RESPIRATORY SYSTEM IMPEDANCE IN OBESE SUBJECTS

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Background and Aims: Obesity is known to have significant effects on pulmonary function. One of those features is forced oscillation technique (FOT) properties, so that higher respiratory system resistance (Rrs) and more negative reactance (Xrs) compared to subjects with normal body weight have been reported. In this study, effects of weight loss therapy on Rrs, Xrs, and other relevant parameters were examined.

Methods: R5 (Rrs at 5 Hz), R20, and X5 were assessed before and after weight loss therapy including exercise and diet for 4 weeks in 40 obese patients (M/F = 23/17, Age: 40. $\pm$ 3.5 years) using a commercialized FOT apparatus. With tidal quiet breathing through the mouth

piece, the measurements were completed after confirmation of 5 stable respiratory cycles. Spirometry was performed using a conventional spirometry. Fat mass (FM), skeletal muscle mass (SM), and fat free mass (FFM) were measured using bioelectrical impedance analysis.

Results: After the therapy, BMI and FM composition rate were significantly decreased from $44. \pm 0.9$ to $42. \pm 0.4 \text{ kg/m}^2$ ($P < 0.01$), and $42. \pm .0$ to $41. \pm .3\%$ ($P < 0.01$), respectively. SM and FFM composition rates were significantly increased from 26.9 ± 3.1 to $27.5 \pm 3.2\%$ ($P < 0.01$), and 57.6 ± 7.0 to $58.7 \pm 7.3\%$ ($P < 0.01$), respectively. Vital capacity (VC) and expiratory reserve volume (ERV) were increased from 3.6 ± 1.0 to $3.8 \pm 1.0 \text{ L}$ ($P < 0.01$), and from 0.7 ± 0.5 to $0.9 \pm 0.6 \text{ L}$ ($P < 0.01$), respectively. R5 was significantly decreased from $4. \pm .7$ to $3. \pm .5 \text{ cmH}_2\text{O/L/s}$ ($P < 0.01$), while X5 was significantly changed into less negative from -1.2 ± 0.9 to $-0.9 \pm 0.6 \text{ cm H}_2\text{O/L/s}$ ($P < 0.01$).

Conclusion: These results suggest that the weight loss therapy reduced BMI, FM and increased SM, VC, and ERV, which were accompanied by the change of R5 into decreased and X5 into less negative in the obese patients.

AP297

PRIMARY MEDIASTINAL SEMINOMA PRESENTING AS SUPERIOR VENA CAVA SYNDROME: A CASE REPORT

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Background and Aims: Primary mediastinal seminoma is relatively uncommon, occurring in men of the second to fourth decades. Signs and symptoms are usually non-specific and the disease is often misdiagnosed. The occurrence of superior vena syndrome is rare in reported cases of primary mediastinal seminoma.



Figure 2. CT scan of the patient showing a lobulated mass occupying the anterior and middle mediastinum.

Methods: A 24-year-old male presented with productive cough, dyspnea and puffiness of the face for 8 months. Work up revealed a mass noted on Chest X-ray. CT scan revealed, a $9.8 \times 12.0 \times 8.7 \text{ cm}$ lobulated mass occupying the anterior and middle mediastinal mass, partially encasing the ascending aorta. CT-guided aspiration biopsy was done but results were non-diagnostic. Beta HCG and serum AFP were normal. He was lost to follow up for several months until he became more symptomatic. Repeat cxr revealed pleural effusion on the right. Chest CT scan revealed a large lobulated, mixed attenuation mediastinal mass. CT guided biopsy was done but was non-diagnostic, hence patient underwent anterior mediastinotomy.

Results: LDH was slightly elevated, beta HCG and AFP were both normal. Histopathology revealed round cell proliferation with considerations of lymphoma and seminoma. Immunohistochemistry panel was done, CD117 positive, EMA negative and S100 negative confirmed the diagnosis of seminoma.

Conclusion: Normal beta HCG and AFB and immunohistochemistry results confirmed the diagnosis of a primary mediastinal seminoma.

The patient underwent several sessions of radiotherapy, with noted resolution of the symptoms of SVC. He was referred to oncology service for the initiation of chemotherapy.

AP298

THE CORRELATION BETWEEN RESPIRATORY FUNCTION AND GAIT ASYMMETRY IN STROKE PATIENTS

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Background and Aims: Stroke usually lead to lower respiratory function and induce restrictive ventilatory impairment. Hemiplegia and decreasing chest wall movement that cause restrictive ventilatory impairment are possibly associated with abnormal trunk movement during walking. However, little is known about the relationship between respiratory function and trunk movement during gait in stroke patients. Therefore, the aim of this study was to investigate the relationship between respiratory function and asymmetry of trunk movement during walking in the patients with stroke.

Methods: Twenty stroke patients (age; 56.3 ± 11.1 years, FEV_1 ; $66.6 \pm 34.5\%$ pred) walked 10 m wearing a tri-axial accelerometer (MG-M1110, LSI Medience, Japan) attached to the back at the level of the L3 spinous process. Medio-lateral and vertical acceleration were expressed as continuous waveforms and the bilateral surrounded area by waveforms was analyzed as Lissajous Index (LI). LI of 0 indicates perfect symmetry. %VC, FEV_1/FVC , PEmax, and PImax were evaluated as respiratory function in the patients with stroke. Pearson's correlation coefficients (r) were used to assess correlation between the LI and their respiratory functions.

Results: The mean and SD of LI is $37.1 \pm 35.7\%$. The means and SDs of %VC and FEV_1/FVC are $85.9 \pm 13.0\%$ and $70.4 \pm 20.7\%$, respectively. The means of SDs of PEmax and PImax are $47.6 \pm 18.0 \text{ cmH}_2\text{O}$ and $32.4 \pm 24.5 \text{ cm H}_2\text{O}$, respectively. LI was significantly correlated with %VC ($r = -0.765$, $P < 0.05$).

Conclusion: Our data suggest that decreasing lung capacity is closely related to asymmetry of trunk movement during walking in the patients with stroke. Further research is required to verify that pulmonary rehabilitation might improve trunk movement during walking in stroke patients.

AP299

LEFT BRONCHIAL ISOMERISM PRESENTED AS A SEVERE OBSTRUCTIVE VENTILATORY DISTURBANCE IN A HEALTHY ADULT

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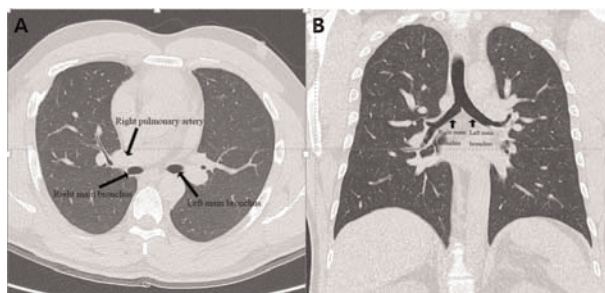
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Background and Aims: A 36-year-old man presented with abnormal pulmonary function tests which were incidentally found during preoperative evaluation of orbital wall fracture. Pulmonary function showed forced expiratory volume in one second (FEV1) of 1.84 L (45.8%), forced vital capacity (FVC) of 4.01 L (81.3%), and FEV1/FVC ratio of 46.0%. In this case, we report abnormalities of the bronchial structure in healthy patient without congenital abnormalities.

Methods: A low-dose chest computed tomography (LDCT) was performed to screen for lung cancer, which was requested by the patient.

Results: LDCT showed bilateral bilobed lungs with symmetric long bronchus and hyparterial right main bronchus, which indicated left bronchial isomerism. Pulmonary emphysema was not present in LDCT. Echocardiography and abdominal ultrasound did not reveal any structural abnormalities.

Conclusion: Bronchial isomerism is usually a component of congenital heterotaxy syndrome diagnosed in infancy and childhood. Left bronchial isomerism without heterotaxy is extremely rare in a healthy adult. The patient had no subjective respiratory symptoms despite severely declined pulmonary function.



AP300

RELATIONSHIP BETWEEN LOW-FREQUENCY INTERVENTION FOR INSPIRATORY MUSCLE TRAINING AND COUGH PEAK FLOW IN HEALTHY YOUNG ADULTS

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Background and Aims: This study assessed the relationship between inspiratory muscle strength and cough peak flow in healthy young adults and the effect of low-frequency inspiratory muscle training (IMT).

Methods: The subjects were 31 healthy young adults who were divided into an intervention group (16 people) and a control group (15 people). In the intervention group, IMT of 80% maximal inspiratory muscle load was performed 2 sets per day, twice a week. The control group did not receive any intervention. Maximum inspiratory muscle strength, cough peak flow as coughing power, respiratory function, maximum phonation time, thoracic extension difference, and grip strength were measured for all subjects at the baseline, after 2 and 4 weeks.

Results: There was a significant correlation between maximal inspiratory muscle strength and coughing power in all subjects ($\rho = 0.679$, $P < 0.001$). In the intervention group, the maximum inspiratory muscle strength significantly increased after IMT ($P < 0.001$). Cough peak flow did not change in both groups.

Conclusion: This study suggested that inspiratory muscle strength was related with cough peak flow in healthy young people. Low-frequency intervention for IMT improved inspiratory muscle strength, but secondary

effects, such as improvement in coughing power, were not observed. Further investigation is needed to identify more effective IMT intervention methods in the future.

AP301

DECLINE IN LUNG FUNCTION IS ASSOCIATED WITH ELEVATED LIPOPROTEIN A LEVELS IN KOREAN HEALTH SCREENING SUBJECTS WITHOUT CLINICALLY APPARENT DISEASE: A CROSS-SECTIONAL STUDY

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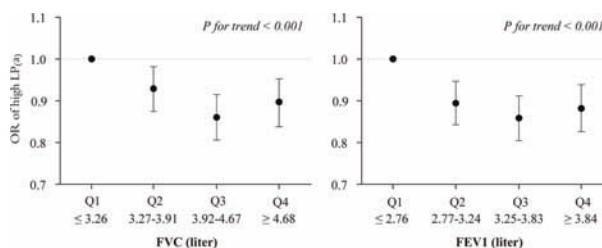
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Background and Aims: Reduced lung function and high lipoprotein a [Lp(a)] levels are both recognized risk factors for cardiovascular disease. However, relatively few studies have focused on the association between serum Lp(a) and lung function in the general population. Therefore, we evaluated the association between reduced lung function and high Lp(a) levels in Korean health screening examinees with no known medical disease.

Methods: We performed a cross-sectional study on 64,082 Koreans (33,049 males, $3 \pm$ years old) who underwent a health examination in 2015.

Results: The median Lp (a) level was 12 (6–25) mg/dL. The prevalence of high Lp(a) (defined as > 30 mg/dL) was 19.5%. Subjects with a high Lp (a) had both lower values of measured FEV1 and FVC (liter) than those with a low Lp(a) ($P < 0.001$). However, FEV1/FVC ratio was not significantly different between groups ($P = 0.112$). Comparison of the 2nd, 3rd, and 4th measured FVC (liter) quartiles with that of the lowest quartile (1Q) group (reference) on regression analysis revealed adjusted odd ratios (ORs) for a high Lp(a) of 0.928 (95% CI, 0.876–0.982), 0.860 (0.808–0.916), and 0.895 (0.839–0.954), respectively (P for trend < 0.001). In addition, adjusted ORs for high Lp(a) compared to reference was 0.894 (0.844–0.947), 0.857 (0.806–0.912), and 0.882 (0.8727–0.940) across the measured FEV1 (liter) quartiles in increasing order (P for trend < 0.001).

Conclusion: High Lp(a) levels were inversely associated with lung function in a healthy Korean population. Longitudinal follow-up studies will be required to validate our findings.



AP302

TRAUMATIC CHYLOTHORAX IN YOUNG CHILDREN: CASE SERIES AND MANAGEMENT

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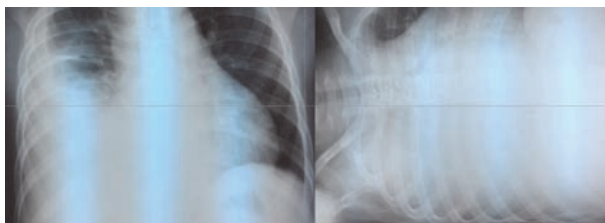
Background and Aims: To discuss evidence-based approaches in the management of chylothorax.

Methods: This is a case series of 6-year-old males with congenital heart diseases, underwent operation and later developed post-operative

chylothorax. First patient underwent ventricular septal defect closure and was managed with MCT diet. Second patient underwent Tetralogy of Fallot correction and was managed with MCT and Somatostatin. Third patient underwent Ventricular septal defect closure with diaphragmatic plication, right, was managed with MCT diet, somatostatin and later underwent surgical ligation of the thoracic duct.

Results: Chylothorax is a potentially serious complication of cardiothoracic surgery in children and may result in substantial morbidity. It is defined by the accumulation of chyle in the pleural space that occurs as a result of damage to the thoracic duct by rupture or laceration. Trauma is the leading cause of chylothorax, it is usually a cardiovascular or pulmonary surgical procedure. Once the diagnosis of chylothorax is made by pleural fluid analysis, investigations should be performed to outline lymphatic vessels, identify the site of chyle leakage and finally to ascertain the cause of chylothorax. Medium-chain triglycerides contain 6 to 12 carbon fatty acids, and are absorbed from the gastrointestinal tract directly to the portal circulation and transported to the liver for metabolism. Somatostatin is an endogenous hormone while Octreotide is a synthetic somatostatin analogue. Somatostatin and octreotide can be given as a continuous intravenous infusion or as an intravenous bolus, given twice daily. Surgical therapy is recommended in cases where despite conservative management the patient drains more than 100 mL/kg body weight per day in a child, leaks chyle at a rate of >1 L/day for 5 days, persistent chyle flow for more than 2 weeks, or if there has rapid decline in nutritional status despite conservative management. Various surgical procedures have been described including the direct ligation of the thoracic duct, pleurodesis, and placement of pleuroperitoneal shunt.

Conclusion: Development of evidence-based guideline for the management of postoperative chylothorax is important.



APL009

COMPARISON OF THE EFFICIENCY OF ORAL AIRWAY AND NASAL AIRWAY INSERTED IN THE ORAL AIRWAY DURING MASK VENTILATION

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Background and Aims: The purpose of this study was to investigate the efficiency of nasal airway inserted in the oral airway (ON airway) in securing the airway patency during mask ventilation.

Methods: Fifty eight patients undergoing general anaesthesia were randomly assigned to either oral airway group (group O) or ON airway group (group N). In both group, 2 mg/kg of propofol was infused intravenously and mask ventilation was performed in the sniffing position without head extension or jaw thrust. The patients were ventilated with a volume-controlled ventilator with O₂ flow of 10 l/min, tidal volume of 10 mL/kg (IBW), and respiratory rate of 10 /min. Before the start of mask ventilation, airway was placed in the oral cavity. Oral airway was used in group O and ON airway was used in group N. Peak inspiratory pressure (PIP), tidal volume and EtCO₂ were compared between the two groups. The location of airway tip was graded by fiberoptic bronchoscope as; 0: airway

obstructed by tongue, 1: epiglottis visible, 2: airway touches epiglottis tip, 3: airway passes beyond epiglottis tip.

Results: Compared with group O, group N significantly decreased the PIP (25.0 [18.0 – 29.0] vs 18.0 [16.0 – 19.0], $P < 0.001$, Group O and N, respectively) and increased tidal volume and EtCO₂ during mask. In the bronchoscopic findings, airway obstruction was more frequent in group N. ($P < 0.001$).

Conclusion: Compared with oral airway, nasal airway inserted in the oral airway facilitates the mask ventilation by promoting the patency of airway.

Tuberculosis 1

AP303

IMPACT OF ADDITIONAL ANTIBIOTICS ON IN-HOSPITAL MORTALITY IN PULMONARY TUBERCULOSIS COMPLICATED BY BACTERIAL PNEUMONIA: A PROPENSITY SCORE ANALYSIS

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Background and Aims: It is uncertain whether additional antibiotics with anti-tuberculosis agents are required to treat bacterial co-infection among patients with pulmonary tuberculosis. The aim of this study was to assess the impact of additional antibiotics on in-hospital mortality in patients with pulmonary tuberculosis complicated by bacterial pneumonia.

Methods: This study was a retrospective cohort using a propensity score analysis at National Hospital Organization Nishi-Beppu Hospital. The study population included patients who were admitted to the hospital for smear-positive pulmonary tuberculosis from January 2013 to December 2015 and whose sputum cultures were positive for general bacteria. Propensity scores were estimated based on the patient's background and clinical laboratory data. The mortality of patients who received additional antibiotics with anti-tuberculosis agents was analyzed after adjusting for other variables, including the propensity score.

Results: We assessed 66 and 57 tuberculosis patients treated with and without general antibiotics, respectively. Additional antibiotics tended to be administered to patients with a high level of C-reactive protein and neutrophil count, hypoalbuminemia, anaemia, and steroid treatment (area under receiver operating characteristic curve to predict treatment with additional antibiotics according to the propensity score = 0.829, $P < 0.001$). In the multivariate analysis, only age (adjusted hazard ratio, 1.094, $P = 0.004$) was associated with in-hospital mortality; however, the use of additional antibiotics had no effect on the prognosis of patients who received tuberculosis treatment.

Conclusion: Treatment with additional antibiotics may not improve the prognosis of pulmonary tuberculosis patients treated with anti-tuberculosis agents who develop complicating bacterial infections.

AP304

A NOVEL COMBINATIVE ADJUNCT THERAPY TARGETING HOST NUCLEAR RECEPTORS MINIMIZES TUBERCULOSIS TREATMENT REGIMEN

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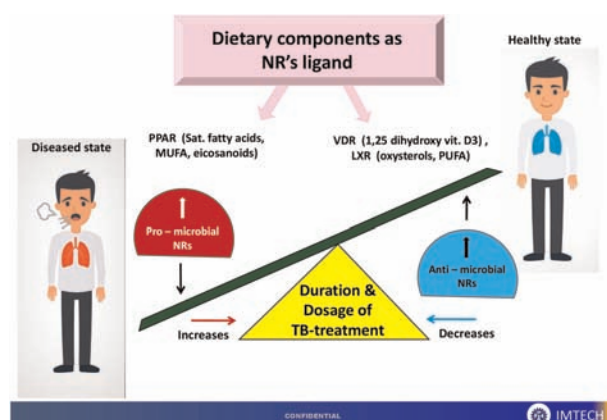
Background and Aims: Despite several novel drug discoveries and the considerable global effort, failure to achieve tuberculosis

(TB) eradication has now become a global plight. New disease prevention and treatment issues are being raised due to prevalence of increased drug resistance and synergistic interactions with other immune ailments like HIV and diabetes mellitus. The TB infection is an outcome of the poor immune status and is quite often described as poverty-related disease, linked with financial deprivation and social marginalization. This hints towards the crucial requirement of a healthy lifestyle and nutritious food for its prevention and cure. As microbes around us are evolving smartly, a bottom up approach concomitantly targeting host factors would be a better combinatorial course towards controlling TB prevalence and mortality. Therefore, the current study focuses on three nuclear receptors (NRs) : vitamin D receptor (VDR), liver X receptor (LXR) and rev-erb alpha (Rev-erb α) and comprises of a design that evaluates the chemotherapeutic efficacy of anti-tubercular drugs, alone or in different synergistic combinations with the ligands of contextually relevant nuclear receptors at their therapeutic dose.

Methods: The concluding results were attained by employment of bacterial viability assay.

Results: Besides leading to better *M. tuberculosis* clearance, viability assays showed that treatment with combination of these NRs ligands proved beneficial in reducing dosage of drugs and duration of treatment in-vitro.

Conclusion: Since these NRs can be targeted via nutrition, the combinatorial therapy involving amalgam of VDR, Rev-erb α and LXR ligands as a dietary supplement might prove helpful in reducing dosage or duration of present TB treatment. Moreover, the nutritional cocktail would be risk-free for HIV/diabetic patients harbouring TB infection as these NRs possess anti-diabetic and anti-viral effects. In a peroration, strengthening host body for the battle against TB would lead to improving the cure outcomes and minimizing the relapse rates.



AP305

PROFOUND CD4 LYMPHOPENIA IN A NON HIV PATIENT WITH MILIARY TUBERCULOSIS, PRESENTING WITH AN AIDS DEFINING INFECTION

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Background and Aims: South East Asia has one-third of the world's burden of Tuberculosis (TB). Patients with Tuberculosis manifest significant immunologic abnormalities, which may lead to co-infection with life threatening opportunistic pathogens. A critical marker of immunologic integrity is the CD4 cell count. Studies showed that HIV-negative patients with disseminated tuberculosis may have low CD4 cell count of up to

258–856 cells/cu.mm. In this case report, we present an HIV-negative patient with miliary TB and profound CD4 lymphopenia.

Methods: We have a previously healthy 34-year-old male, who came in acute respiratory failure. Patient presented with progressive dyspnea with fever, diarrhoea, weakness, oral sores and weight loss. Initial work-up revealed miliary TB on chest CT scan, candida growth on sputum culture, markedly elevated lactate dehydrogenase (LDH) and positive Sputum PCR for tuberculosis.

Results: Patient was managed as a case of severe pneumonia, miliary tuberculosis, fungal pneumonia, and was given Cefepime, Metronidazole, Levofloxacin, Fluconazole and quadruple antituberculosis medications. Despite treatment, he was persistently tachypneic with hypoxemia on non-invasive ventilatory support. Despite a negative sputum PCR for Pneumocystis jiroveci, Cotrimoxazole and Hydrocortisone were started, which improved patient's condition. CD4+ T cell count was 55 cells/cu.mm and HIV test was negative. On follow-up, he was symptom-free and has gained weight. Repeat HIV testing at 3 and 6 months turned out to be negative. Repeat CD4+ T cell count after completion of anti-tuberculosis medications increased to 277 cells/cu.mm.

Conclusion: Tuberculosis, especially the disseminated type, can cause profound lymphopenia, mimicking the effects of HIV. CD4 lymphopenia may cause opportunistic infections, as seen in patients with AIDS. It is important to realize the such effect can be seen also in military TB. Adequate treatment and close follow-up is important to rule out primary CD4 lymphopenia.

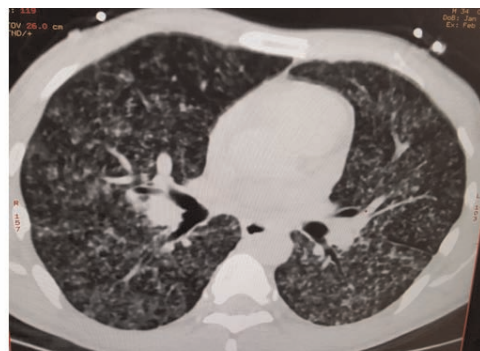


Figure 1. Chest CT scan showing Miliary Tuberculosis

AP306

THE PROGNOSTIC FACTORS AMONG ELDERLY PATIENTS WITH LUNG TUBERCULOSIS: A COMPETING RISK ANALYSIS

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Background and Aims: Japan has the longest life expectancy in the world and is the only developed country with a middle burden of tuberculosis. While advanced age has been suggested to be a prognostic factor in patients with tuberculosis, the characteristics that are associated with poor outcomes among elderly patients remain unclear. The aim of this study was to assess the prognostic factors among elderly patients admitted to a hospital for lung tuberculosis.

Methods: We retrospectively investigated 275 elderly patients (>65 years of age) who were admitted to the Nishi-Beppu National Hospital for bacteriologically-diagnosed lung tuberculosis from January 2013 to

December 2015, and analyzed the prognostic factors associated with tuberculosis-related death. Non-tuberculosis-related death was regarded as a competing risk.

Results: Forty and 19 patients died from tuberculosis-related and non-tuberculosis-related causes, respectively. Patients who died from tuberculosis-related causes were significantly older, and had a poorer performance status, a lower swallowing function, a lower oxygenation level and a lower serum albumin level in comparison to survivors. A competing risk regression analysis showed that a poor performance status (estimated sub-hazard ratio: 3.21, 95% CI 1.72–5.99, $P < 0.001$) and a low serum albumin level (estimated sub-hazard ratio: 0.33, 95% CI 0.15–0.74, $P = 0.007$) were significantly associated with tuberculosis-related death. Swallowing dysfunction had no effect on tuberculosis-related death.

Conclusion: This study revealed that a poor performance status and a lower serum albumin level predicted a poor prognosis among elderly patients with lung tuberculosis. Recent studies demonstrated that swallowing dysfunction significantly affected the prognosis of patients with community-acquired pneumonia. In contrast, the presence of swallowing dysfunction on admission did not appear to influence the mortality of patients with lung tuberculosis.

AP307

CORRELATION BETWEEN RADIOLOGIC ACTIVITIES ON CHEST CT WITH MICROBIOLOGIC RESULTS VIA BRONCHOSCOPY IN PULMONARY TUBERCULOSIS

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Background and Aims: Chest radiography usually has been used as the first diagnostic method when a person is suggested as pulmonary tuberculosis (PTB). Despite its advantage, chest radiography as the first diagnostic test for the diagnosis of active PTB is limited by poor specificity and reader inconsistency. Chest computed tomography (CT) provide more accurate information of presumptive PTB patients. However, there are no study suggesting a correlation of radiologic activities and microbiologic culture of mycobacterium tuberculosis (MTB) via bronchoscopy.

Methods: We retrospectively reviewed the records of all patients who underwent bronchoscopy because of suspected PTB between January 2012 and February 2015. All patients performed bronchoscopic washing or BAL and underwent AFB stain and culture, TB-PCR and gram stain. Using radiological criteria for determine radiologic activities on CT, we classified our patients in 4 groups.

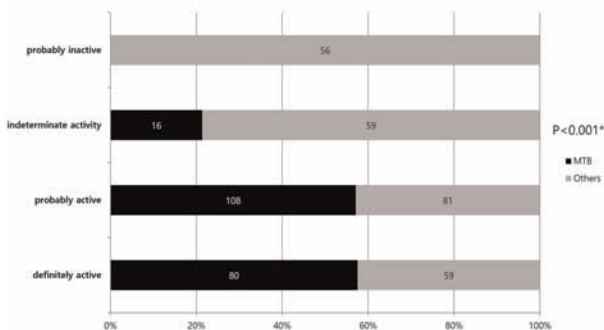
Results: Of 459 patients included, 204 had positive culture of MTB. Median age was 56.92 ± 17.5. 272 were finally diagnosed as pulmonary tuberculosis and 39 patients were nontuberculosis mycobacterium (NTM), 82 patients were pneumonia and 66 patients were other. Radiographic activities of our patients are 139 (30.3%) were definitely active, 189 (41.2%) were Probably active, 75 (16.3%) were Indeterminate activity and 56 (12.2%) were Probably inactive. There were significant correlation between the radiographic activity and culture-positive of MTB.

Conclusion: Our study suggests that radiologic activities based on chest CT findings correlated with the microbiologic diagnosis in patients with pulmonary tuberculosis. And chest CT is useful for diagnose radioactivity of pulmonary tuberculosis.

Table 1. Demographic and clinical characteristics of patients with suspected PTB on Chest CT (n=459)

	No. of patients (%)
Age, years	56.92±17.5
Male gender	258 (56.2%)
Comorbidity	
COPD	19 (4.1%)
Diabetes	77 (16.8%)
Hypertension	118 (25.7%)
Malignancy	63 (13.7%)
Cerebrovascular accident	16 (3.5%)
Ischemic heart disease	20 (4.4%)
HIV infected	1 (0.2%)
Lower respiratory tract specimens	
Bronchial washing	379 (82.6%)
Bronchoalveolar lavage	80 (17.4%)
Final Diagnosis	
Pulmonary tuberculosis (PTB)	272 (59.2%)
Microbiological confirmed PTB	209 (45.5%)
Histological confirmed PTB	5 (1.1%)
Clinically diagnosed PTB	58 (12.6%)
NTM* lung disease	39 (8.5%)
Pneumonia	82 (17.9%)
Others*	66 (14.3%)

Figure 1. Relative incidence of culture-positive of MTB according to radiographic activities. (n=459)



AP308

THE CORRELATION BETWEEN INTERFERON- γ AND INTERLEUKIN-17 LEVELS TO THE CHEST RADIOGRAPHIC INTERPRETATION IN RIFAMPICIN-RESISTANCE AND RIFAMPICIN-SENSITIVE PULMONARY TUBERCULOSIS

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Background and Aims: The tuberculosis incidence in Indonesia is the second largest in the world. It is still unclear how the role of cytokines to make the severity of the disease. Interferon- γ (IFN- γ) and Interleukin-17 (IL-17) are important cytokines in the immune response against Mycobacterium tuberculosis both in Rifampicin (Rif)-resistance and Rif-sensitive. This study aims was to determine the difference of these cytokines level in Rif-resistance and Rif-sensitive pulmonary tuberculosis (PTB) patients and their effect to form severity of the chest radiographic interpretation.

Methods: A descriptive analytic study. Fifty-eight subjects were selected: 27 Rif-resistance, 22 Rif-sensitive PTB patients and 9 healthy control (HC). Interferon- γ and IL-17 concentration was determined by Enzyme-Linked Immunosorbent Assay (ELISA) technique. The chest X-ray was conducted for PTB patients and the severity was interpreted.

Results: The level of INF- γ in Rif-Resistance vs Rif-sensitive PTB was 439.8 ± 52.029 pg/mL vs 336.68 ± 11.951 gp/mL and IL-17 level was $4.39 \pm .986$ pg/mL vs $4.0 \pm .935$ pg/mL. The level of INF- γ was 81.3 ± 6.33 pg/mL and IL-17 was $2.3 \pm .32$ pg/mL in HC. Both cytokines were not significantly different among all PTB patients ($P > 0.05$) but significantly different from healthy control ($P < 0.05$). The level of INF- γ in Rif-resistance and Rif-sensitive PTB to form severity of chest radiographs was not significantly different ($P > 0.05$). Neither with IL-17 level in Rif-resistance and Rif-sensitive PTB ($P > 0.05$).

Conclusion: The level of INF- γ and IL-17 were not significantly different in both Rif-Resistance and Rif-sensitive PTB patients but significantly different from HC. Interferon- γ and IL-17 had a low correlation to established the severity of chest radiograph both in Rif-Resistance and Rif sensitive PTB patients, although it were not significantly different. These two cytokines cannot be used to distinguish chest radiograph severity in Rif-resistance and Rif-sensitive PTB patients.

AP309

CLINICAL OUTCOMES OF TAILORED VS STANDARD ANTI-TUBERCULOSIS THERAPY IN PATIENTS WITH TUBERCULOUS LYMPHADENITIS

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Background and Aims: Although it is necessary to culture Mycobacterium tuberculosis from tuberculous lymphadenitis (TBL) to enable clinicians to tailor the therapy, based on the drug-sensitivity test (DST), substantial numbers of TBL remain culture-negative. Limited data are available regarding the treatment outcomes and recurrence rates after standard short-course anti-tuberculosis treatment in patients with culture-negative TBL. The aim of this study was to compare treatment outcomes and recurrence rates between a tailored anti-tuberculosis regimen based on individual DST result and a standard anti-tuberculosis regimen due to unavailable DST because of culture-negative in TBL patients.

Methods: We analysed the data of all patients with TBL from the TB registry database at five hospitals of Hallym Medical center, South Korea, during 2011–2015. The study population was divided into two groups according to regimen.

Results: Tailored and Standard anti-tuberculosis therapy were administered to respectively 44 and 163 patients with TBL. Drug resistance was detected in 3 (6.8 %) of patients with TBL, one case whom was multidrug-resistant. The treatment completion rate was not significantly different between the two groups (97.8 % vs 98.7 %). During a median 28-months follow-up, the recurrence rate was also similar in both groups (2.2 % vs 2.4 %).

Conclusion: Despite several limitations, these results support the hypothesis that immunocompetent patients with culture-negative TBL can be appropriately managed with a standard short-course anti-tuberculosis regimen, in this era of not increasing concerns about drug resistance.

AP310

NEUTROPHIL-LYMPHOCYTE COUNT RATIO (NLR) WAS ASSOCIATED WITH DISEASE ACTIVITY IN TUBERCULOSIS AND DIABETIC MELLITUS PATIENTS

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Background and Aims: Global data showed the high rates of Tuberculosis Diabetic Mellitus (TB-DM) incidence in the world, Asia as well as in Indonesia. Neutrophil-lymphocyte ratio (NLR) is a laboratory marker that can be used for systemic inflammation in TB-DM and also it is an available and cost-effective biomarker used in clinical practice that has been associated with recurrence and survival in various diseases, one of them TB-DM. It is necessary to cut off point NLR in TB-DM to know disease activity in Tuberculosis and Diabetic Mellitus Patients. The aim of our study is to investigate the value of neutrophil-to-lymphocyte ratio (NLR) as a possible marker to know disease activity in Tuberculosis and Diabetic Mellitus Patients.

Methods: This study is a retrospective cohort study with using secondary data between January 2016 and March 2018 taken with consecutive sampling in Cipto Mangunkusumo National Center General Hospital, Indonesia. Sampling was done by consecutive sampling with 181 patient. This study was analysed with descriptive analysis and ROC curve.

Result: Among the 181 patients in this study, 89 (49%) had TB-DM and 92 (51%) had TB non DM with complete neutrophil and lymphocyte data available. The area under curve ROC 0,726 with 95% CI got the cut of point NLR was 2.9. Patient with NLR > 2.9 ($N = 100$) and < 2.9 ($N = 81$).

Conclusion : In conclusion, NLR has attracted attention as a new inflammatory marker. The best cut-off value of NLR was 2.9 in predicting disease activity TBDM patients and this displayed a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy value (67, 66, 61.7, 71.7 and 66.8). The patient with NLR < 2.9 has immunocompetent and > 2.9 has immunocompromise. Many factors affect NLR was associated with disease activity in TB-DM.

AP311

THE COMPLIANCE AND SIDE EFFECTS OF 3HR THERAPY IN LATENT TUBERCULOSIS INFECTION

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Background and Aims: Isoniazid monotherapy for 9 months (9H) has been considered standard treatment of latent tuberculosis infection (LTBI). However, because of low compliance of this regimen, 4 months of Rifampin (4R), 3 months of Rifampin and Isoniazid (3HR), and 3 months of Isoniazid and Rifapentine has been used for the treatment of LTBI. The aim of this study was to evaluate the compliance and side effects of 3HR

Methods: We performed a retrospective cohort study at Chung-Ang University Hospital in Korea. During the January 2011 to December 2017, 352 populations who were diagnosed as LTBI were treated with 3HR, 4R or 9H.

Results: Among 332 patients, 96 (28.9%) were male and median age was 42.3 ± 1.65 . The treatment regimen of LTBI consisted with 3HR ($n = 290$, 87.3%), 9H ($n = 32$, 9.6%), and 4R ($n = 9$, 2.7%). Out of 332 populations, 265 (79.8%) completed the treatment. The cause of discontinuation of the treatment was lost-to-follow up ($n = 32$, 10.3%) and

side effects of the drugs ($n = 21$, 6.8%). The compliance of 3HR, 4R and 9H were 85.6%, 100% and 56.3%, respectively. The total number of side effects was 21 (6.8%), 3HR was 15(5.1%, hepatotoxicity 9, drug rash 5, GI trouble 1), and 9H was 7(21.8%, hepatotoxicity 5, drug rash 2)

Conclusion: The completion rate of 3HR was relatively good. However, relatively high rate of side effects must be considered when we used 3HR for the treatment of LTBI.

AP312

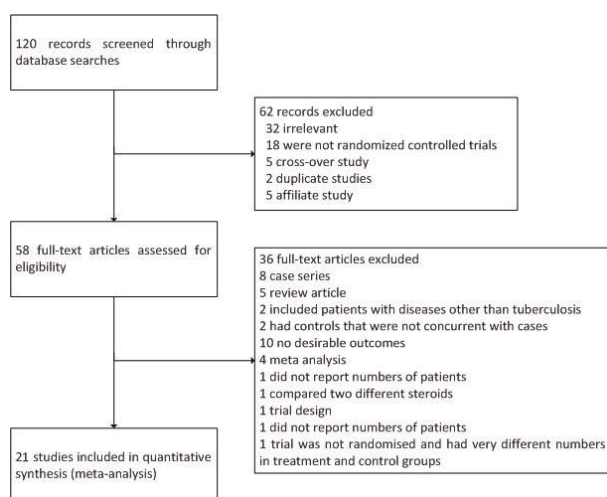
CORTICOSTEROIDS FOR MANAGING TUBERCULOUS SEROSITIS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background and Aims: The purpose of this study was to assess the effects of corticosteroids on mortality, side-effects, and sequelae of patients with tuberculous serositis.

Methods: We did literature search and meta-analysis on clinical trial studies published up to December 2017 from databases of the Cochrane Infectious Diseases Group Trials Register, the Cochrane Central Register of Controlled Trials, Medline, Embase, and Web of Knowledge databases. Combined relative risk (RR) and 95% confidence intervals (95% CIs) were calculated to evaluate the effects of corticosteroids. All analyses were performed by Stata 11.0 software.



Results: In total, 21 trials with 2487 participants were included in this report. We found that adjunctive corticosteroids, comparing with antituberculous drugs alone, were significantly associated with low risk of death in patients with TB serositis (RR = 0.83, 95%CI: 0.74–0.94, $P = 0.002$). However, corticosteroids did not reduce risk of death for HIV-positive TB serositis patients (RR = 0.87, 95%CI: 0.69–1.10, $P = 0.246$). The incidence of sequelae was significantly lower in corticosteroid group comparing with placebo group (RR = 0.72, 95% CI 0.61–0.87, $P < 0.001$).

Conclusion: Adjuvant corticosteroids could be effective in reducing mortality and sequelae of TB serositis. Further large placebo controlled trials are required to give more evidences for adjunctive steroid treatment in TB serositis.

IMPACT OF NON-TUBERCULOSIS MYCOBACTERIA COLONIZATION OR INFECTION ON MULTIDRUG RESISTANCE TUBERCULOSIS TREATMENT

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Background and Aims: Non-tuberculosis mycobacteria (NTM) infection was increasing all over the world. NTM culture rate was also increased up to more than 50% in Chest Hospital TB Laboratory in Taiwan. AFB stain and Mycobacteria Culture of sputum was the guidance of MDR-TB treatment. The result will be confused by NTM colonization and infection.

Methods: MDRTB cases treated in TMTC Southern area between 2007–2014 was enrolled. Sputum AFB stain and Mycobacteria Culture was checked at least one specimen monthly. Species Identification of Mycobacterium should be done if Mycobacteria culture was positive. Infection was defined as more than 2 specimen was the same NTM. Colonization was defined as only one NTM species. Risk factor like age, gender, severity of CXR, DM, renal disease and fluoroquinolone of NTM infection was evaluated.

Results: MDRTB cases was enrolled. NTM was cultured among 52.4% MDRTB patients (198/378). Among 196 NTM-culture patients, 43.4% (86/198) was NTM colonization, 23.2% (46/198) was NTM infection, 33.3% (66/198) had no species identification. Among the colonization, the most common pathogen was MAC (27/86), *Mycobacteria abscessus* (21/86), *Mycobacterium fortuitum* (17/86). Among the infection, the most common pathogen was *Mycobacterium abscessus* (27/46), *Mycobacteria abscessus* (10/46), MAC(3/46). The mean time of first NTM culture was 6.5 months. 43.9% (87/198) of NTM growth was beyond 6th month of MDRTB treatment. There was no CXR deterioration when the NTM was grew. There was no special risk factors among NTM colonization, infection and non NTM group. There was also no difference in MDRTB treatment success rate.

Conclusion: NTM colonization or infection was very common (52.4%) during MDRTB treatment. NTM would be encountered during the whole course of MDRTB treatment especially over 6 months after MDRTB treatment. *Mycobacterium* species identification was very important if we use *Mycobacterium* culture as the guide of MDRTB treatment.

AP314

EXTRA PULMONARY TUBERCULOSIS IN HIV PATIENTS: PROFILE & OUTCOME OF PATIENTS AT WESTERN VISAYAS MEDICAL CENTER PPMD DOTS UNIT PHILIPPINES JANUARY 2015 TO JUNE 2018

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Background and Aims: To find out the incidence and outcome of patients with Extrapulmonary Tuberculosis and Human Immunodeficiency Virus (HIV) enrolled at Western Visayas Medical Center (WVMC) PPMD DOTS Clinic from January 2015- June 2018.

Methods: Chart review of Treatment Form of patients enrolled at WVMC PPMD DOTS Unit from January 2015 to June 2018.

Results: There were 14 patients included in the study. Majority of patients were Suspect HIV AIDS patient SHAP 80%, PHAP Positive HIV AIDS 20%, all males, equally distributed at an age range of 19-29 yo = 50% and 30–39 years old = 50%. Most resided in the provinces outside

of Iloilo City 60% . Majority received prior BCG vaccination 70% . As to bacteriological status all were clinically diagnosed 100%. Location of Extrapulmonary TB was mostly in the cervical neck area presenting as lymphadenitis in 60% of cases followed by retinitis 14 % and perianal mass = 1 , inguinal mass = 1 and Gastrointestinal TB = 1. Most received TB Disease treatment regimen 2 HRZE and 4 HR in 78% cases. All were Genexpert negative. As to outcome 86% completed treatment, 1 died and 1 was lost to follow up.

Conclusion: Incidence of patients with EPTB and HIV is increasing. Thus there should be more public awareness regarding the various presentation of EPTB especially in HIV patients young adult groups aged 19–39.

AP315

A CASE OF TUBERCULOUS SPONDYLITIS FOLLOWING INTRAVESICAL BCG THERAPY

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Background and Aims: Treatment of tuberculous spondylitis is different from *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG.

But conventional polymerase chain reaction (PCR) used to identify mycobacterial species does not distinguish between *M. tuberculosis* and *M. bovis* BCG.

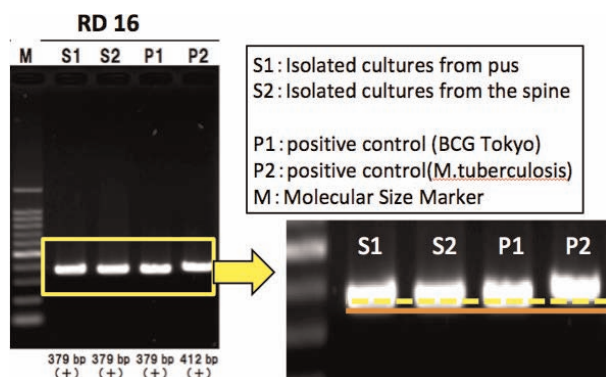
Methods: Identification was carried out using PCR and PCR-restriction fragment length polymorphism for the detected group of *M. tuberculosis*, and it was confirmed that it was *M. bovis* BCG.

Results: We directly identified *M. bovis* BCG genome.

See graphics.

Conclusion: By identifying that it is *M. bovis* BCG, we succeeded in treating tuberculous spondylitis with only internal treatment without surgical treatment.

An appropriate treatment can be examined by diagnosis using this PCR method.



AP316

PERFORMANCE OF GENEXPERT MTB/RIF ASSAY IN PULMONARY AND EXTRAPULMONARY SAMPLES IN REAL WORLD SETTING

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Background and Aims: Tuberculosis is a serious global public health issue, with the emergence of drug resistant TB (DR-TB) it poses an even greater risk. In order to curb this issue, World Health Organization (WHO) has suggested the usage of GeneXpert MTB/RIF assay in high risk patients. The objective of this study is to analyze the performance of GeneXpert assay in a “real world” setting in different types of sample.

Methods: All GeneXpert testing done in 2017 were examined and checked against the gold standard culture and drug sensitivity tests (DST) which were sent together with GeneXpert to ensure consistency of sample collection. Results were analyzed using SPSS®Ver24 Cross-Tabulation method.

Results: 120 samples were sent in 2017; 2 samples were rejected; 4 samples' results were missing. 23 results were excluded due to no DST were sent. There were 74 pulmonary and 17 extrapulmonary samples. GeneXpert result for 28 pulmonary samples were positive for MTB while none were positive from extrapulmonary group. There were 2 false positive and 2 false negative pulmonary samples. All extrapulmonary DST results were negative except for one pleural fluid sample returned as MTB. Therefore, sensitivity of GeneXpert assay for pulmonary samples was 95.7% while specificity was 92.9%. Sensitivity of GeneXpert assay for extrapulmonary samples was 100% while specificity was 100%. Furthermore, our findings were also analyzed for rifampicin resistance, 7 GeneXpert/RIF results were found to have rifampicin resistance, but only 2 of these samples' cultures (or 28%) returned as MDR-TB.

Conclusion: Based on our findings, we conclude that GeneXpert is highly sensitive and specific in detecting susceptible and DR-TB especially rifampicin resistance. Rifampicin resistance has been traditionally regarded as a surrogate marker for MDR-TB.⁽¹⁾ A study quoted 90% of all clinical isolates with RR-TB also positive for isoniazid resistance.⁽²⁾⁽³⁾ However, our findings failed to show this pattern.

AP317

LOW INCIDENCE OF DRUG INDUCED HEPATITIS IN 4 MONTHS RIFAMPICIN REGIMEN FOR THE PREVENTIVE CHEMOTHERAPY OF LATENT TUBERCULOSIS INFECTION

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Background and Aims: The proportion of foreign born patients with tuberculosis (TB) is increasing in South Korea. Refugees continue to flow into Korea. Refugees receive a screening of latent TB infection (LTBI) by Interferon Gamma Releasing Assay (IGRA), after their arrival in South Korea. The aim of this study is to analyze the incidence of drug induced hepatitis in the preventive chemotherapy with the four months rifampicin regimen, together with the status of the LTBI among the refugees from North Korea.

Methods: Cross-sectional study. The results of QuantiFERON-TB Gold In-Tube assays conducted after arrival in South Korea between 2014 and 2017 were reviewed and analyzed for the positive rate and preventive chemotherapy with the incidence of drug adverse events.

Results: Results of 4282 subjects were analyzed for LTBI, 814 males and 3,468 females. The mean age was 37.6 years. The IGRA positive rate was 62.3%, 74.4% for males and 59.6% for females ($P = 0.0000$) when indeterminate results were excluded. By age group, 38% of teens were positive and 58% were in their 20s. In multivariate analysis, males (aOR; 1.92, 95% CI; 1.57–2.34), age, TB related lesion on chest X-ray (aOR; 5.54, 95% OR; 4.07–7.53) were associated with the rate. Preventive chemotherapy was given to 79.9% (2,104/2,633) of IGRA positive

subjects and 2,103 patients received four months rifampicin regimen. 97.4% of them completed it. Twelve subjects (0.6%) had increased ALT more than three times higher than normal upper limit (41 U/L) in monthly periodic tests or as needed. Subjects with abnormal liver function in baseline tests were more likely to develop drug-induced hepatotoxicity during chemotherapy (aOR: 6.58, 95% CI; 3.61–12.00).

Conclusion: The LTBI rate by IGRA was serious in the refugees. The regimen of four months rifampicin seems to have lower drug induced hepatitis than isoniazid.

AP318

CLINICAL DIFFERENCES BETWEEN POSITIVE AFB AND NEGATIVE AFB IN LUNG TUBERCULOSIS PATIENTS IN INDONESIA

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¹INA RESPOND - NIHRD, Indonesia

Background and Aims: Indonesia is the second highest country in tuberculosis case, with the prevalence of 647 cases every 100,000 people. The common symptoms, for example, cough more than two weeks, fever, loss of body weight and night sweat are already known, but the clinical difference between acid fast bacilli (AFB) positive patients and negative AFB patients are still lack of data. The involvement of comorbidities has potentials in the changing of symptoms.

Methods: We evaluated 164 patients in this study, 99 positive AFB patients and 65 negative AFB patients. The descriptive analyses were performed to the demography characteristic, contact history, history of tuberculosis medication, comorbidities and also common symptoms.

Results: Positive AFB patients in Indonesia were more commonly found at age 18–60 years than age above 60 years ($P = 0.003$). There was no difference in BMI ($P = 0.47$) and also in the smoking habit ($P = 0.99$). Positive AFB were found mostly in patients with a history of tuberculosis medication, where the negative AFB were found mostly in primary lung tuberculosis ($P < 0.001$). There was no difference in contact history between two groups, and mostly there was no contact history ($P = 0.10$). HIV was found in 8.5% of tuberculosis patients (3% in positive AFB, 17% in negative AFB; $P = 0.001$). Diabetes mellitus was found in 27.4% of the patients (34% in positive AFB, 12% in negative AFB). Malignancy was found in 4.9% of the patients (0% in positive AFB, 8% in negative AFB; $P < 0.001$).

Conclusion: Differences between positive AFB and negative AFB patients were found in age and symptoms (cough worsen at night, loss of body weight, night sweat, fatigue). Diabetes Mellitus was mostly found in positive AFB patients.

AP319

KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING PULMONARY TUBERCULOSIS AMONG HIGH RISK HEALTH CARE WORKERS IN UST HOSPITAL

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Background and Aims: Tuberculosis is one of the top ten infectious disease in the Philippines, and is the sixth leading cause of morbidity and mortality in the country. There are risk factors enumerated in acquiring tuberculosis among patients, and there is little attention or note of the occupational risk encountered by health care workers in acquiring

this disease. The objective of this study is to determine the knowledge, attitudes and practices regarding pulmonary tuberculosis among health-care workers in UST Hospital.

Methods: This is a cross-sectional, descriptive study which targeted healthcare workers of USTH who are frequently exposed to patients suspected of having TB or respiratory secretions. A questionnaire was distributed and retrieved after 48–72 h. The results were then tabulated, tallied, and analyzed using Chi Square Analysis.

Results: There was a total of 156 participants including nurse aides, medical technologists, nurses, post graduate interns, residents and fellows. The knowledge of healthcare workers regarding basic principles of PTB is adequate. With regards to attitudes, majority of the respondents are willing to abide by the instituted regulations regarding prevention of spread of TB. Regarding practices there were poor adherence to the guidelines recommended by the WHO.

Conclusion: This study identifies key areas for training on TB and stresses the need for continuous re-training of all front-line health personnel. The authors recommend the following: 1) that the institution adapt guidelines designed for healthcare facilities to reduce incidence of healthcare related TB and 2) conduct regular seminars regarding PTB for healthcare workers.

AP320

CHARACTERISTICS OF TUBERCULOSIS PATIENTS WITH AFB SPUTUM SMEAR EXAMINATION POSITIVE AT PULMONARY HEALTH CENTER (BALAI KESEHATAN PARU MASYARAKAT) IN BANYUMAS, CENTRAL JAVA, INDONESIA KOLANDA MARIA^{1*}, HEIDY AGUSTIN¹, PUJI ASTUTI², JOKO SUSILO²

¹Pulmonology and Respiratory Medicine University of Indonesia-Persahabatan Respiratory Center Hospital, Indonesia, and ²Pulmonary Health Center BKPM Banyumas, Central Java, Indonesia

Background and Aims: Tuberculosis (TB) is still a health issue in Indonesia. Even though the medication are available, the basic problems like knowledge, attitude, behaviour, social economic, and demographic problems in Indonesia have been the obstacles in eliminating TB. Whereas, TB can affect social economic condition, because mostly TB cases found at productive age. Control of TB must be a government goal. From surveillance data at Central Java in 2011, we know that Banyumas had a higher number of patients with TB in Central Java. Banyumas was chosen as the sampling area in which highest rank of TB patients have been found here.

Methods: This study was the qualitative study using cross-sectional design. Sampling was accidental conducted from January until December 2014.

Results: Most cases were found in the middle of the year. Total recruited patients were 856 patients. Data showed 60% (515) patients were male, 94% (805) of them at productive age (15–64 years old). Out of all patients, 94% (804) were new cases. They received TB medication category one (without injection of Streptomycin). The examination history showed 46% (392) patients had AFB smear examination 3+ or >10 Acid Fast Bacilli (AFB)/oil immersion field in at least 20 fields, 31% (265) patients had AFB smear examination 1+ or 1–9 AFB/100 oil immersion power field, and 23% (194) patients had AFB smear examination 2+ or 10–99 AFB/oil immersion field in at least 50 field.

Conclusion: In 2014, the data from BKPM Banyumas showed that most TB patients were male. Most patients diagnose as TB new cases were at productive age. The majority of them also had a high bacterial load, which is highly infectious to other people. This data can help the government in Banyumas, Central Java, to improve the way to control TB.

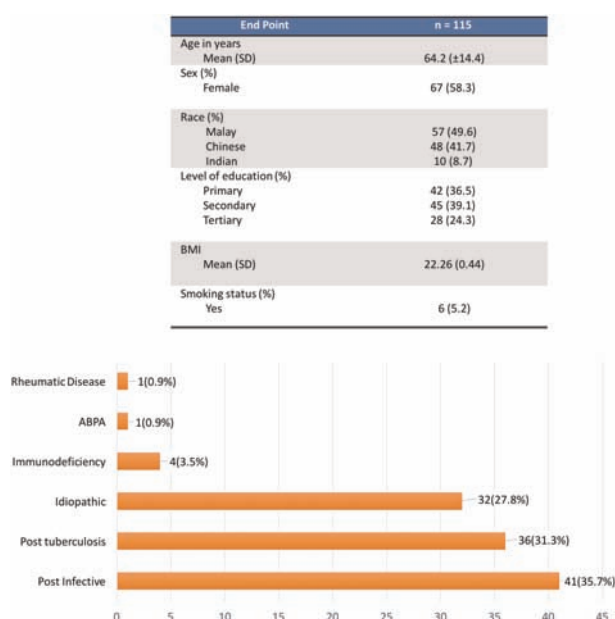
AP321

A CROSS-SECTIONAL STUDY TO PROFILE NON-CYSTIC FIBROSIS BRONCHIECTASIS IN MALAYSIA

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Background and Aims: Non-cystic fibrosis bronchiectasis has a diverse cause unique to the population under study. The prevalence of bronchiectasis is increasing especially in Asian population; however, the aetiology and profile of bronchiectasis in Malaysia as a high tuberculosis endemic area are unknown.

Methods: This study enrolled adult patients diagnosed with bronchiectasis as confirmed by high-resolution computed tomography (HRCT) at the National University of Malaysia Medical Centre, for the period of 6 months (November 2016 to April 2017). Aetiologies of bronchiectasis were determined by clinical history and radiological examinations including serum immunoglobulin levels, total immunoglobulin E (IgE) and *Aspergillus fumigatus* specific IgG measurement. Spirometry, HRCT and microbiological profile were also assessed.



Results: 115 patients with a mean age (±SD) of 64.2 ± 14.4 were enrolled. 67 (58.3%) were females with the population comprising of 57 Malays (49.6%) followed by 48 Chinese (41.7%) and 10 Indians (8.7%). 5.2% were smokers. The common aetiologies were post infective 41 (35.7%), post tuberculosis 36 (31.3%), idiopathic 32 (27.8%) and immunodeficiency 4 (3.5%). Mean FEV1 was 1.27 (±0.47), mean FVC was 1.61 (±0.53), mean predicted percentage FEV1 55.4 (±22.0), mean predicted percentage FVC 53.02 (±18.48). Mean FEV1/FVC ratio was 81.1% ± 22.1. Microbiologic profiling revealed *Candida sp.* in 30 (26%) of patients, *Mycobacterium tuberculosis* in 23 (20%), no growth in 20 (17%), *Pseudomonas sp.* in 8 (7%). The lowest mean (SD) FEV1 was observed in subjects with *Pseudomonas aeruginosa* ($P = 0.004$). Bronchiectasis distribution was most common in the right lower lobe in all aetiologies ($P = 0.031$) and significantly more common in post tuberculosis bronchiectasis ($P = 0.008$). Long term antimicrobial therapy reduces exacerbation rate per year ($P = 0.003$). 96.5% of patients reported exacerbations over the past 12 months with the mean rate of 4.08 ± 3.38 per year.

Conclusion: In conclusion, post infective and post tuberculosis causes were the most common aetiology for bronchiectasis. The mean

rate of exacerbations per year was high indicating high burden of this disease to the healthcare system.

AP322

FACTORS PREDICTING THE NEED OF INTENSIVE CARE IN PATIENTS WHO WERE ADMITTED FOR PULMONARY TUBERCULOSIS

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Background and Aims: In pulmonary tuberculosis (TB) patients, acute respiratory distress syndrome is a common cause in the intensive care unit (ICU) and is associated with high mortality and morbidity. Although high mortality in pulmonary tuberculosis patients requiring ICU care are well known, factors influencing ICU care from admitted general ward initially is not well known.

Methods: A nested case-control study was performed among TB patients recruited from July 2013 to March 2017 in National Medical Center in Korea. Cases included 32 patients with pulmonary TB admitted ICU from general ward and 55 controls were selected from 623 TB patients requiring hospital admission after matching with age, sex, and radiologic findings of extent of tuberculosis.

Results: Among 1:2 matched cases and controls, the range of age, sex and the extent of TB on radiologic findings were distributed even. Patients who were referred to ICU have lasted their symptoms longer before admission to hospital. The level of serum albumin (g/dL) and haemoglobin (g/dL) were lower in patients who had needed intensive care ($P < 0.001$ and $P = 0.005$, respectively). The higher level of C-reactive protein (CRP) was found in patients who were referred to ICU ($P = 0.005$). The most common cause for ICU referral was respiratory failure (87.5%). After adjusting the duration of symptom persistence before admission, BMI, and the level of haemoglobin and CRP, which were also satisfied to be put into the multivariate analysis, the level of albumin was found to significantly predict for the risk of intensive care within the admission period (Q1 albumin < 2.0; OR 17.78, 95% CI 13.32–240.32, and 2.0–3.0; OR 7.05, 95% CI 0.70–71.08, p for trend 0.04, respectively).

Conclusion: This study showed the level of albumin at admission was crucial to predict the admission of ICU care in patients with pulmonary TB.

AP323

ELIGIBILITY OF SHORTER REGIMEN (STR) AMONG MULTIDRUG RESISTANT TUBERCULOSIS PATIENTS IN PERSAHABATAN HOSPITAL, INDONESIA

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Background and Aims: Multidrug-resistant tuberculosis worsening global health problem. Indonesia is one of 10 MDR TB highest burden countries worldwide, with estimated 6,800 cases every year. Cure rate of MDR TB treatment were very low about 52%, and in our setting only 51% compare with high cost and length of treatment since then WHO recommended shorter regimen (STR) for MDR TB treatment that reduce duration of treatment from 20 to 9 until 11 months. Some studies showed that STR increase cure rate about 80%. In our Hospital we started treat patient using STR in September 2017 there for we still evaluate the outcome of this regimen, but in this report we try to evaluate characteristic of patient treated with STR compare with standard and individual regimen.

Methods: We performed a secondary analysis of MDR TB patient data treated in Persahabatan hospital From September 2017 to February 2018. Data were collected from electronic MDR TB data base. Patient who were eligible with WHO criteria for STR will be treated with this new regimen but in our setting we exclude patient with extensive lesion as unfavourable outcome group.

Results: There were 230 patient treated in MDR TB centre with mean age 40.74 ± 13.571 , 58% were male, 16.1% were primary MDR TB cases. Subjects who were eligible with STR were 69 (30%) and among them, 27.53% were new cases, this was significantly higher than patient treated with standard regimen (11.18%, $P < 0.05$). There were 30 pre-XDR cases detected by culture in this study, 5 of them were treated with STR at the beginning which actually excluded by WHO criteria for STR.

Conclusion: Number of MDR TB patient eligible for STR remains low compared with patient treated with standard and individual regimen.

AP324

ACQUIRED BRONCHOESOPHAGEAL FISTULA IN ADULT FILIPINO

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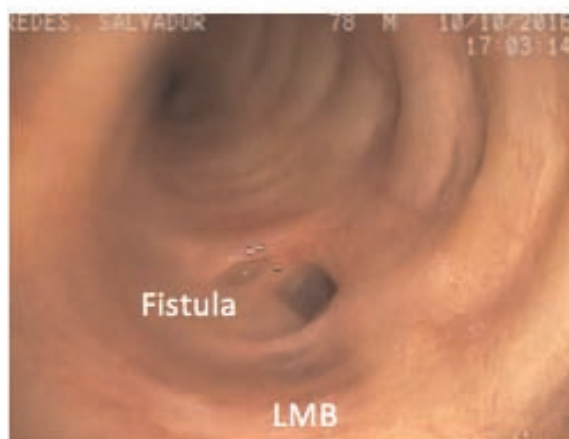
Background and Aims: An acquired bronchoesophageal fistula (BEF) in adult is a rarely encountered entity in clinical practice. It is a serious complication of malignancy and trauma. Although rare, acquired BEF can occur as a consequence of tuberculosis, HIV infection, mediastinitis, and syphilis. Patients usually present with recurrent lower respiratory tract infections and coughing. We report a rare case of bronchoesophageal fistula presenting as abdominal pain.

Methods: A 79-year-old man, non-smoker was referred to us with a 1-month history of abdominal discomfort. He had a history of pulmonary tuberculosis for which he completed treatment. Patient had no history of trauma or prolonged mechanical ventilation. He had clear breath sounds on auscultation. Chest X-ray showed fibro-hazed densities on both upper lobes secondary to previous Koch's infection.

Results: Barium swallow showed a fistulous communication between the oesophagus and left main bronchus. Esophagogastroduodenoscopy showed a 0.5 cm opening at 25 cm level with a visualized tract. Bronchoscopy revealed an opening between the 5th and 6th bronchial rings measuring 1 cm with communication to the oesophagus (Figure 1). Bronchial washing was negative for acid-fast bacilli. Surgery was discussed, however, patient refused. Patient suddenly developed ventricular fibrillation and expired.

Conclusion: An acquired BEF is a rare but serious complication of malignancy and trauma. Malignancy is the most common cause of which 77% are attributable to oesophageal tumours and 16% are secondary to pulmonary primaries. Of the non-malignant aetiologies, 75% are related to trauma from prolonged mechanical ventilation. The most characteristic symptom is paroxysmal coughing particularly after ingestion of liquids (Ono's sign). The development of BEF in tuberculosis is related to mediastinal lymph node involvement. This is a spontaneous BEF, as a definite underlying cause could not be identified except for the past history of pulmonary tuberculosis. A bronchoesophageal fistula developing as a delayed sequel of pulmonary tuberculosis is a rare phenomenon.

Figure 1. Bronchoscopic finding of fistula on the left main bronchus



AP325

SOLITARY PULMONARY NODULES DUE TO NON-TUBERCULOUS MYCOBACTERIAL INFECTION DIAGNOSED WITH VIDEO-ASSISTED THORACOSCOPIC SURGERY

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Background and Aims: The prevalence of nontuberculous mycobacteria (NTM) is increasing in Japan. Among the patterns of NTM pulmonary disease, solitary pulmonary nodule (SPN) is less common and often resembles primary lung cancer, leading to difficulty in differential diagnosis. The aim of this study was to identify the clinical features of NTM presenting as an SPN, which was diagnosed by video-assisted thoracoscopic surgery (VATS).

Methods: We enrolled patients with an SPN that was diagnosed as NTM disease between January 2006 and December 2016. The patients' clinical, laboratory, and radiologic findings were investigated. Furthermore, acid-fast bacilli culture of the resected lung specimens and the prognosis of the patients were analyzed.

Results: This study included 19 NTM patients with a mean age of 64 years; 12 were men and 7 were women. The pulmonary lesions were detected on regular check-up in 11 patients, during further examinations for other diseases in 7 patients, and during work-up of haemoptysis in 1 patient. Flexible bronchoscopy was performed on 9 patients and yielded negative results for acid-fast bacilli infection. Serum anti-mycobacterium IgA antibody was detected in 1 case. All cases underwent VATS resection because the lesions mimicked lung cancer in morphology or enlargement in size. The culture results of all resected lung specimens showed infection with *Mycobacterium avium*-intracellular complex in 17 patients, *M. xenopi* in 1 patient, and *M. szulgai* in 1 patient. None of the patients received drug therapy after VATS resection. All patients were followed-up postoperatively at a median duration of 4 years (range, 10 months to 10 years). There was no disease recurrence in this series.

Conclusion: VATS is useful for the diagnosis and management of NTM disease manifesting as an SPN resembling primary lung cancer.

AP326

LATENT TUBERCULOSIS INFECTION AND TREATMENT**STATUS OF NORTH KOREAN REFUGEES**YOUNG KIM^{1*}, SEUNG HEON LEE¹, HO JIN KIM¹, CHI YOUNG KIM¹, BYEONG KI KIM¹, CHOL SHIN¹, JE HYEONG KIM¹¹Korea University Ansan Hospital, Korea University College of Medicine, South Korea

Background and Aims: The World Health Organization reports that the incidence of tuberculosis in North Korea in 2016 is 561/100,000, seven times that of South Korea. More than 1,000 North Korean refugees are escaping to South Korea every year. The aims of this study is to identify the characteristics of latent tuberculosis infection (LTBI) test results of North Korean refugees and to confirm the actual status of LTBI treatment for North Korean refugees.

Methods: From November 2010 to March 2012, 172 North Korean refugees who were tested for tuberculosis infection by tuberculin skin test (TST) and found positive by more than 10 mm were analyzed.

Results: Of the 172 TST positive reactors, 34 (19.8%) were males and 138 (80.2%) were females. The mean age was 35.4 ± 1.0 years and mean body mass index was 22.3 ± 2.4 kg/m². The mean size of TST was 17 ± 4 mm and the number of subjects with BCG scar was 122 (70.9%). The mean TST size in males was 14 ± 4 mm and 18 ± 4 mm in females and was statistically significant when BCG scar and age were corrected. ($P < 0.001$). The Quantiferon Gold in Tube (QFT-GIT) was performed in 103 of the TST positive reactors and all 103 patients were positive. All 172 patients with LTBI were treated with isoniazid and rifampin. Of these, 55 (32.0%) discontinued treatment; one of them (0.6%) was pregnant and three (1.7%) due to adverse events. Thus 117 (68%) completed the LTBI treatment.

Conclusion: We could detect LTBI based on TST for North Korean refugees and completion rate of LTBI treatment was 68% in North Korean refugees. Further comparative studies with South Korean patients for LTBI and treatment are needed in the future.

APL010

PRIMARY MDR TB CASES IN WEST SUMATERAELSIS MARETA EDRIYENTI^{1*}, IRVAN MEDISON¹, YESSY SUSANTY SABRI¹¹Andalas University, Indonesia

Background and Aims: Multi Drug Resistance Tuberculosis (MDR TB) become new challenge in tuberculosis control. World Health Organization (WHO) has introduced new approach to detect MDR TB by using rapid molecular test. The aim of this study was to find out characteristics of suspected and confirmed MDR TB patient at Dr. M. Djamil Hospital, Padang and Lubuk Alung Pulmonary Center.

Methods: This is a retrospective descriptive study using MDR TB registry data (TB 06) Dr. M. Djamil Hospital Padang and Lubuk Alung Pulmonary Center from January 2014 to December 2016.

Results: This study found that total 416 patients was suspected MDR TB. Confirmed MDR TB was 33 (7.93%) patients, consist of new cases (primary) of resistance to rifampicin in 3 (9.1%) patients and previously treated (secondary) MDR TB in 30 (90.9%) patients. Those patients were treated as MDR TB patients with standardized regiment. The average of age MDR TB patients was 3 ± 1.98 years old and most of them were males 23 (69.69%). The risk factor of MDR TB mostly was relapse cases in 22 (66.67%) patients. From three primary MDR TB patients, two of them had diabetic mellitus and one has contact with confirmed MDR TB patients.

Conclusion: MDR TB patient mostly were previously treated cases. Two of new tuberculosis with MDR TB had diabetic mellitus.

Table 1. Suspected MDR TB Characteristics

Tabel 4.1 Karakteristik suspek TB MDR

Karakteristik	Riw OAT (-) n= 86		Riw OAT (+) n= 330		Total n=416	
	JUMLAH	%	JUMLAH	%	JUMLAH	%
Umur (rerata $\pm$ SD)	41,5 $\pm$ 14,3		45,1 $\pm$ 15		44,4 $\pm$ 14,9	
Jenis Kelamin						
Laki-Laki	70	81.40	240	72.73	310	74.52
Perempuan	16	18.60	90	27.27	106	25.48
BTA						
BTA Positif	44	51.16	230	69.70	274	65.87
BTA Negatif	42	48.84	100	30.30	142	34.13
Tes Cepat Molekuler						
MTB Not Detected	33	38.37	88	26.27	121	29.09
Rifampisin Sensitif	50	58.14	212	64.24	262	62.98
Rifampisin Resistan	3	3.49	30	9.09	33	7.93
Suspek TB MDR						
Kriteria 1	0	0.00	8	2.42	8	1.92
Kriteria 2	0	0.00	5	1.52	5	1.20
Kriteria 3	0	0.00	13	3.94	13	3.13
Kriteria 4	0	0.00	16	4.85	16	3.85
Kriteria 5	0	0.00	16	4.85	16	3.85
Kriteria 6	0	0.00	144	43.64	144	34.62
Kriteria 7	0	0.00	68	20.61	68	16.35
Kriteria 8	3	3.49	1	0.30	4	0.96
Kriteria 9	35	40.70	30	9.09	65	15.63
Kriteria Lain						
DM	26	30.23	7	2.12	33	7.93
Kerusakan Paru Luas	22	25.58	22	6.67	44	10.58
Komorbid						
HIV	35	40.70	30	9.09	65	15.63
DM	34	39.53	14	4.24	48	11.54

Table 2. Confirmed MDR TB Characteristics

Karakteristik	Riw OAT (-) n=3		Riw OAT (+) n=30		Total n=33	
	Jumlah	%	Jumlah	%	Jumlah	%
Umur (Rerata $\pm$ SD)	40,6 $\pm$ 15,503		38,8 $\pm$ 12,581		33 $\pm$ 11,975	
Jenis Kelamin						
Laki-Laki	1	33.33	15	68.18	16	64.00
Perempuan	2	66.67	7	31.82	9	36.00
Suspek TB MDR						
Kriteria 1	0.00		2	9.09	2	8.00
Kriteria 2	0.00		0.00		0.00	
Kriteria 3	0.00		3	13.64	3	12.00
Kriteria 4	0.00		2	9.09	2	8.00
Kriteria 5	0.00		1	4.55	1	4.00
Kriteria 6	0.00		12	54.55	12	48.00
Kriteria 7	0.00		2	9.09	2	8.00
Kriteria 8	1	33.33	0.00		1	4.00
Kriteria 9	0.00		0.00		0.00	
Kriteria Lain(DM)	2	66.67	0.00		2	8.00
Komorbid						
HIV	0.00		0.00		0.00	
DM	2	100.00	0.00		2	100.00

Asthma 2

AP327

DEVELOPMENT OF A COST-EFFECTIVENESS MODEL TO ASSESS ASTHMA INHALER ADHERENCE AND TECHNIQUE INTERVENTIONS

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Background and Aims: Real-world patients' medication adherence and inhalation techniques severely impact asthma clinical and economic outcomes, but have not been incorporated into previous asthma cost-effectiveness models. Advancements in smart, digital and eHealth-based inhalers development could offer new opportunities. This study aims to develop a model incorporating adherence and inhalation technique and determine the potential cost-effectiveness of adherence and inhalation technique enhancing interventions.

Methods: A Markov model with 6 health-states which consists of combinations of 2 asthma control status (controlled vs uncontrolled) along with 2 mortality states (asthma-related vs other cause) and exacerbation states (i.e. oral-corticosteroid burst, emergency department visit, and hospitalization) was developed for simulating the cost-effectiveness of adherence and inhalation improvement programs for patients with uncontrolled asthma. Bi-weekly health state transitions were used along with a lifetime horizon to determine the incremental cost-effectiveness ratio of three hypothetical scenarios (1. full adherence/good technique 2. full adherence/poor technique and 3. poor adherence/good technique) vs usual care (poor adherence/poor technique) within the U.S. payer perspective.

Results: Over a 60-year period, the full adherence and good technique group was associated with (discounted) \$107,309 costs and 18.82 quality-adjusted life years (QALYs), the full adherence and poor technique group was associated with \$107,936 costs and 18.80 QALYs, the poor adherence and good technique group was associated with \$106,517 costs and 18.74 QALYs, and the poor adherence and technique group was associated with \$103,667 costs and 18.74 QALYs. The incremental cost-effectiveness ratio of the full adherence good technique (full adherence poor technique and poor adherence good technique) vs usual care was \$41,831 (\$66,826 and \$1,056,016) per QALY.

Conclusion: Given the growing development of adherence and inhalation technique improving interventions (e.g. smart inhalers) in asthma, this study shows that attempts in improving adherence and inhalation technique for uncontrolled asthma patients can be associated with significant gains in QALYs at the standard willingness-to-pay threshold.

AP328

IMPACT OF OMALIZUMAB IN TREATMENT OF SEVERE ALLERGIC ASTHMA: PERSPECTIVE FROM SINGLE CENTER EXPERIENCE IN MALAYSIA

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Background and Aims: Omalizumab is a monoclonal anti-IgE antibody that has been shown to be an effective add-on therapy in severe

allergic asthma (SAA). However, there is little information about its clinical benefit among Malaysian patients. This descriptive study was sought to review real-life outcomes and safety of omalizumab in SAA.

Methods: We performed a retrospective review to assess pulmonary function (FEV1), asthma control by the ACT score and GINA classification, medication use and 'hospital exacerbation' in 12 patients who were treated with omalizumab at Hospital Raja Perempuan Zainab II for SAA. 'Hospital exacerbation' included emergency department visit and/or hospitalization due to exacerbation of bronchial asthma. Information was collected from medical records during follow up from 12-month pre and post-omalizumab initiation periods.

Results: All the 12 patients were classified as uncontrolled asthma (GINA), received high dose inhaled corticosteroid and long-acting β (2)-agonists prior to treatment with omalizumab. Nine (75%) patients were female, average age of 42.1 $\pm$ 13.3 year and allergic rhinitis was the commonest comorbidity (41.7%). The mean serum total IgE level was 921.4 IU/ML. The mean duration of omalizumab treatment was 2.5 years.

At 4 months; the ACT score increased significantly from 12.3 to 19.3 ($P<0.001$), oral corticosteroid requirement showed significant reduction from 58.3% to 8.3% and the GINA score improved to 58.3% (partially controlled asthma) and only 39.1% (uncontrolled asthma). The improvement sustained significantly for one year with multiple significance tests and Bonferroni correction. At 6 months, the mean FEV1 increased significantly from 56.0% to 69.8% ($P<0.026$). The mean hospital exacerbations reduced from 3 to 0.73 exacerbations per year using paired t test ($P<0.001$) with no side effects reported by patients.

Conclusion: Omalizumab is beneficial and safe as add-on therapy for SAA. In the setting of limited resource, local data on real-life outcomes and cost effectiveness of omalizumab therapy warrants further study.

AP329

PRODUCTION OF REACTIVE NITROGEN SPECIES IN ASTHMA-CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP

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Background and Aims: Asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO) has been focused on in the research field. However, the precise pathogenesis of ACO remains poorly understood and lacking in evidence. Excessive oxidative/nitrosative stress is thought to play a critical role in the pathogenesis of not only asthma but also COPD. In our previous reports, we demonstrated that nitrosative stress was enhanced in the airways of patients with severe asthma. The aim of this study was to investigate the imbalance of oxidants/antioxidants in the airways of patients with ACO.

Methods: Thirty healthy subjects, 33 asthmatic patients, 23 ACO patients were included in this study. The expression of inducible type of nitric oxide synthase (iNOS) and formation of 3-nitrotyrosine (3-NT), which are markers of nitrosative stress, in the sputum cells were assessed by immunostaining. The amounts of reactive sulfur species (RSS), which were newly identified antioxidants, were measured by a specific probe. The syntheses of RSS were evaluated by immunostaining. The amounts of pro-inflammatory chemokines in the sputum were measured by using a cytometric bead array. Furthermore, we examined the relationship between the levels of redox markers and the values of lung function.

Results: Immunopositive cells against iNOS, 3-NT and the synthases of RSS were significantly increased only in the ACO group compared with the other groups. The levels of RSS in the sputum were significantly decreased in the ACO group compared with the other groups. The amounts of IL-8 and MCP-1 were significantly increased in the ACO group compared with the other groups. Furthermore, the nitrosative stress markers and the levels of RSS were significantly correlated with the data of lung function.

Conclusion: These results suggest that imbalance of oxidants/anti-oxidants occurred in the airways of patients with ACO and it might be related to the pathogenesis.

AP330

TRIMETHYLAMINE-N-OXIDE REVERSES AUTOPHAGIC DYSFUNCTION IN THE LUNG TISSUES OF OVA-OVA BRONCHIAL ASTHMA MICE

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Background and Aims: Trimethylamine-N-oxide has been considered as an important regulator of bronchial asthma by improving airway inflammation, however the mechanism of Trimethylamine-N-oxide involved in improving airway inflammation remains not fully understood. In the present study, we investigated the effect of Trimethylamine-N-oxide on autophagy secondary to bronchial asthma in the lung tissues of OVA-OVA mice and in bronchial epithelial cell models.

Methods: Trimethylamine-N-oxide was administered in OVA-OVA mice and in tunicamycin-induced mouse bronchial epithelial cells, and autophagy markers were assessed via real-time PCR and western blot.

Results: The injections of Trimethylamine-N-oxide in OVA-OVA mice exhibited down-regulation of inflammatory cytokines and airway hyperresponsiveness, and improved airway inflammation compared with OVA-OVA mice receiving vehicle. Meanwhile, the administration of Trimethylamine-N-oxide reversed autophagic dysfunction. In accordance with these findings in vivo, Trimethylamine-N-oxide treatment also had a protective impact in bronchial epithelial cell in the presence of tunicamycin by regulation of mammalian target of rapamycin (mTOR) signalling.

Conclusion: Trimethylamine-N-oxide inhibits autophagy and improves airway inflammation in the lung tissues of OVA-OVA Mice and in bronchial epithelial cell models, which may be a promising therapeutic strategies of bronchial asthma.

AP331

THE CONDITION OF LUNG FUNCTION IN PATIENTS WITH ASTHMA DEPENDING ON THE BODY MASS

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Background and Aims: Currently, it is undeniably proven that obesity increases the risk of developing bronchial asthma and worsens control over it. Patients with asthma on the background of obesity are more often hospitalized and need higher volumes of drug therapy than patients with asthma and normal body weight. The ventilation capacity of the lungs in patients with asthma in combination with obesity is currently insufficiently studied. The purpose of the study is to examine the state of external respiration function in patients with bronchial asthma depending on the body mass by spirometry and body plethysmography.

Methods: The study included 67 patients with asthma of mild severity of partially controlled course (mean age 43. ± .5 years), 30 of them had normal body weight and 37—obesity of 1 degree. The control group consisted of 15 volunteers without bronchopulmonary pathology and obesity the study of respiration function was performed on the apparatus Master Screen Body (Care Fusion, Germany).

Results: It was found that the lung function parameters in patients with asthma with normal body weight did not differ significantly from the control group. In patients asthma with obesity, according to spirometry, a decrease in the forced expiratory volume after 1 second (FEV1) and the ratio of FEV1 to forced lung capacity (FVC) by 14 % ($P = 0.001$) compared with the control group, which is characteristic of obstructive disorders of . In these patients, according to body plethysmography, the residual volume (RV) was increased by 31% ($P = 0.03$) and the ratio of RV to the total lung capacity (TLC) was increased by 20 % ($P = 0.03$) compared to the control group, which indicates the dysfunction of the small respiratory tract and the formation of "air traps".

Conclusion: Thus, in patients with asthma of mild severity in combination with obesity, signs of bronchial obstruction and the dysfunction of the small respiratory tract were revealed.

AP332

FACTORS ASSOCIATED WITH EFFICACY OF TIOTROPIUM IN PATIENTS WITH ASTHMA

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Background and Aims: Tiotropium has been demonstrated to be effective in patients with asthma regardless of its severity at baseline, however, little is known about predicting factors, including specific symptoms, to efficacy of tiotropium. We aimed to clarify the efficacy of tiotropium for symptoms complained by patients with asthma or cough variant asthma (CVA).

Methods: This retrospective study recruited patients who were diagnosed as having asthma including CVA, and who were prescribed tiotropium between November 2014 to October 2017 for the first time at Kyoto University Hospital. We assessed the efficacy of tiotropium stratified by the presence of symptoms including cough, sputum, and dyspnea/wheeze based on their medical records. In addition, the associations of clinical indices, diagnosis and comorbidities with the efficacy of tiotropium were examined.

Results: A total of 201 patients (mean 59 years old, 63 males) were evaluated. Tiotropium was effective in 156 (78%) of them; the efficacy rate was significantly higher in patients with dyspnea/wheeze than in those without them (88% vs 71%, $P = 0.005$), and in patients with classical asthma than in those with CVA, respectively (81% vs 61%, $P = 0.009$). Meanwhile, there was no significant association between cough at baseline and the efficacy rate. Comorbid gastroesophageal reflux (GER) was negatively associated with the efficacy rate in all patients. This negative associations were also observed in patients with cough or in patients with CVA.

Conclusion: Tiotropium was effective in over two thirds of patients with CVA, and further effective in patients with classical asthma. In addition, it may be more effective in patients with dyspnea or without comorbid GER.

AP333

BRONCHIAL THERMOPLASTY SUCCESS IN ASTHMA-CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP: A CASE REPORT

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Background and Aims: Patients with asthma-chronic obstructive pulmonary disease overlap (ACO) have both clinical features of asthma and chronic obstructive pulmonary disease (COPD). Bronchial thermoplasty (BT) is a novel non-pharmacological, endoscopic treatment for patients with severe asthma. However, there is currently no guideline to suggest that BT is one of the treatments for patients with ACO.

Methods: We present a 52-year-old male with severe uncontrolled asthma and COPD who underwent BT treatment.

Results: After three stages of BT treatment, the patient's symptoms and lung function were significantly improved after treatment. Although the patient developed pneumonia after the third procedure of BT, it recovered very well after anti-inflammatory treatment and left no sequelae.

Conclusion: It is the first report to describe a patient with ACO who underwent BT treatment. It suggests that BT may be a new treatment for ACO and more studies will be needed to identify this in the future.

AP334

THE EFFICACY OF A STRUCTURED ASTHMA DISEASE MANAGEMENT PROGRAM IMPACTS ON OVERALL CONTROL OF ASTHMA & QUALITY OF LIFE OF ASTHMA PATIENTS

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Background and Aims: Asthma poses a huge disease burden in Singapore. Apart from deaths due to asthma, there is much morbidity due to disease exacerbations and days lost from work and school from asthma.

Aims: This study is to ascertain that a structured disease management program does impact on the over control of the asthma patients.

Methods: Systematic reviews have shown that patient education and optimizing drug treatment can have major sustained beneficial effects in patients. A structure management programme was implemented with nurse educators and data entry clerks being employed to the programme. 50% drug subsidies accord to patients who were prescribed with asthma medication.

Under the Programme: The asthma nurse educator will record all the necessary parameters and provide the necessary educational information and tools. She monitors the treatment and compliance with the help of Action Plans. All clinic attendances are monitored and in the case of failure of attendance, the nurse will contact the patient over phone and arrange a new appointment, or refer to the social worker if social intervention is required.

Results: Data was extracted from the data system from 2001 – 2007 with 20,000 patients enrolled in the program. Outcome indicators such as hospitalization, Nebulization, Days off from Work/ School, Days with wheezing/cough/sob, Nights with wheezing/cough/sob, Days off from Activity were collected. 1st visit was used as baseline and actual improvement at 4th visits in the outpatient clinics.

Conclusion: The intensive education and counselling provide to the patients, tracking of defaulters who default follow-up treatment and drug subsidies are the successful components in reducing hospitalizations, the need for nebulization and asthma symptoms.

Outcome Indicators	1 st visit	4 th visits	Reduction
Hospitalization	42.5%	4.2%	38.3%
Nebulization	82.1%	9.6%	72.4%
Days off from Work/ School	33.3%	12.3%	21.0%
Days with wheezing/cough/sob	85.2%	48.5%	36.7%
Nights with wheezing/cough/sob	79.3%	39.2%	40.1%
Days off from Activity	46.2%	18.9%	27.3%

AP335

PHYSICIANS' PERCEPTION ON PATTERNS OF DIAGNOSING AND MANAGING ASTHMA: A SURVEY IN MYANMAR

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Background and Aims: Myanmar ranks 4th in the world for asthma-related deaths and asthma ranks 9th in the most common causes of death in Myanmar.

Methods: This observational-survey analyzed data from 211 doctors including physicians and paediatricians from 10 cities across Myanmar to understand their perception on managing asthma along with the challenges faced in their daily practice.

Results: 32% doctors encountered minimum 5 patients with asthma daily. 70% doctors said most of their patients were >25 years old. Only 6.3% doctors used spirometry regularly for diagnosing asthma, 28% did not use lung function measuring tools. For patients with uncontrolled asthma, doctors did follow-up every month. Fluticasone was the most preferred ICS (65%-doctors); Salmeterol/fluticasone was the most preferred LABA/ICS (77%-doctors). Only, 40% doctors prescribed inhalation therapy to all their patients. Almost 62% doctors believed that >40% of their patients were apprehensive to use inhalers for which lack of awareness and cost of treatment were believed to be the most common reasons. 84% doctors preferred prescribing pMDI with or without spacer. 70% doctors preferred prescribing similar devices for reliever and controller medications both as they believed that using similar device would be easier for patients. Only 11% doctors perceived that >70% patients showed >80% adherence to inhalation therapy. Almost 60% doctors evaluated patients' inhalation technique when they suspected it to be wrong while others checked it at every visit. Major factors for poor asthma control were incorrect inhaler technique and non-adherence. High cost of medication and skipped medicines in absence of symptoms were major factors of non-adherence.

Conclusion: Use of spirometry can be increased for diagnosing and confirming asthma. pMDI-with or without spacer was the most preferred choice for managing asthma. Regular and repeated device technique demonstration can improve adherence and asthma control.

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THE POTENTIAL ROLE OF SERUM TGF- β AS A BIOMARKER FOR ASTHMA

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Background and Aims: Transforming Growth Factor (TGF)- β is a fibrogenic factor, which may induce airway remodelling in asthma. In contrast, TGF- β also has an immunosuppressive role by inducing the differentiation of regulatory T cells. To date, the significance of measuring TGF- β

in asthma has not been established yet. In this study, we investigated the relationship between the level of serum TGF- β and clinical background and other established biomarkers in asthma.

Methods: Patients were recruited from the outpatient clinic of Teikyo University Hospital ($n = 243$). The levels of serum TGF- β was measured by ELISA and the relationship between serum TGF- β and patient background, asthma control test (ACT) score, pulmonary function, peripheral eosinophil count, FeNO, and serum periostin was investigated.

Results: The level of serum TGF- β was significantly higher in atopic asthma. Although TGF- β was also significantly higher in patients who required admission, ER visit, and short-term burst of oral steroid, FeNO and serum periostin did not show such relationships. The levels of TGF- β tended to be higher in child-onset asthma without outgrow and inversely correlated with age of onset and %FEV1 in such patients.

Conclusion: The significant relationship between the level of serum TGF- β and the mode of onset, exacerbation, and fixed airflow limitation was observed, suggesting the detrimental roles of TGF- β in asthma pathology. As other established biomarkers did not show such relationships, TGF- β might serve as an independent biomarker for asthma.

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NOVEL ASSOCIATION BETWEEN ASTHMA AND OSTEOARTHRITIS

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Background and Aims: To identify the risk factor of asthma patients in respect of associated comorbidities, we compared the features among patients with asthma, chronic obstructive pulmonary disease (COPD), and controls.

Methods: Data were collected from the Korean National Health and Nutrition Examination Survey. Subjects who completed questionnaires and spirometry were enrolled, and prevalence of comorbidities were compared between subjects with asthma, COPD, and controls.

Results: Data from a total of 9343 adult > 40 years of age who completed questionnaire and PFT were retrieved from KNHANES from 2010 to 2012. Among them, 425 patients (prevalence $4.6 \pm 0.3\%$) had self-reported asthma, 1131 patients (prevalence $12.0 \pm 0.5\%$) were compatible with COPD by spirometer, and 2560 patients (prevalence $17.0 \pm 0.5\%$) had self-reported OA. Age of asthma patients (60.6 ± 0.9) were higher than control groups (54.2 ± 0.2), but lower than COPD patients (64.7 ± 0.4). The prevalence of osteoarthritis was higher in asthma patients ($31.9 \pm 2.8\%$) than COPD patients ($17.8 \pm 1.5\%$) or control groups ($16.2 \pm 0.6\%$). The association of OA with asthma was significant (OR 2.42; 95% CI, 1.87–3.14), but not with COPD ($P = 0.33$) in univariable analysis. Since age, sex, obesity, and smoking status is known as important confounding factors for both asthma and OA, these variables were adjusted for multivariable analysis. OA was still significantly associated with asthma (adjusted OR 1.85; 95% CI, 1.36–2.51), but not with COPD ($P = 0.40$) in multivariable analysis. Osteoarthritis medication had no statistically significant influence on asthma development ($P = 0.36$) in OA patients.

Conclusion: Osteoarthritis could be one of risk factor of asthma, and attention for history of asthma is required in patients with osteoarthritis.

A COMPLIANCE STUDY OF THE MANAGEMENT OF PATIENTS WITH ASTHMA AGAINST THE GLOBAL INITIATIVE FOR ASTHMA (GINA) GUIDELINES 2016

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Background and Aims: This study evaluated the outcomes of patients with asthma against the 2016 GINA Guidelines in an acute care hospital.

Methods: A retrospective study of all patients admitted with a confirmed diagnosis of asthma from 1st January 2016 to 31st December 2016. Data collection, comprising Asthma Control Test, asthma self-management education, nurse counselling, dosage of inhaled corticosteroids for asthma symptoms and mortality, were compared against the GINA Guidelines.

Results: Of the 132 patients, 43% ($n = 57$) were males and 57% ($n = 75$) were females. A majority of the patients 43% ($n = 57$) were Malays, followed by Chinese 37% ($n = 49$), followed by Indians 13% ($n = 17$) and 7% ($n = 9$) were Others. The mean and median ages of the patients were 46 and 44 respectively.

GINA Recommendation: Asthma Control Test is an objective, robust and validated method for monitoring asthma symptoms severity (Evidence A)

Indicator: 100% ($n = 132$) of the patients had undergone the asthma control test.

GINA Recommendation: Self - management education reduces asthma morbidity in both adult and children

Indicator: 100% ($n = 132$) of the patients had received counselling with self - management plans.

GINA Recommendation: Asthma education and training can be delivered effectively by a range of healthcare providers including pharmacist and nurse (Evidence A)

Indicator: 100% ($n = 132$) of the patients had received intensive asthma counselling.

GINA Recommendation

Medium/High dose inhaled corticoid-steroids (Evidence A), or Low dose inhaled corticoid-steroid (Evidence A), for troublesome asthma symptoms most days.

Indicator: 100% ($n = 132$) of the patients with confirmed asthma had medium or high dose inhaled corticoid-steroids or low dose inhaled corticoid-steroids.

GINA Recommendation: Overall mortality <1% in every 250 death worldwide.

Indicator

There was no mortality rate during the study period.

Conclusion: The management of patients with asthma was in compliance with the 2016 GINA Guidelines with no reported mortality rate.

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NEUTROPHILIC INFLAMMATION OF THE UPPER AIRWAYS IS A CHARACTERISTIC FEATURE OF MACROLIDE RESPONDERS IN PATIENTS WITH ASTHMA

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Background and Aims: Although macrolide antibiotics are known as a potential therapeutic option for severe asthma, the characteristics of

effective cases are not well understood. A low-dose macrolide therapy is effective in patients with diffuse panbronchiolitis where neutrophilic inflammation is existed in both upper and lower airways. Furthermore, macrolides also appear to be effective in neutrophilic rhinosinusitis. In this study, we investigated the effect of low-dose macrolide therapy in uncontrolled asthmatic patients who have also been diagnosed with chronic neutrophilic rhinosinusitis.

Methods: We recruited poorly controlled asthmatic patients (ACT score < 20 in spite of taking medium to high dose ICS/LABA) who have diagnosed with chronic neutrophilic rhinosinusitis. The existence of neutrophilic rhinosinusitis was confirmed by otolaryngologists. We assessed the effects of macrolides (erythromycin 400 mg/day or clarithromycin 200 mg/day, administered orally) on the reduction in the ICS dose while asthma control was maintained. Annual asthma exacerbation rates, symptom score (ACT), FeNO, were also assessed.

Results: Six cases (3 males, median age 49) started receiving macrolides. The sputum production was observed in all cases. 3 cases showed both high IgE level and positive for environmental inhalation antigen. The reduction of ICS doses was successfully achieved by the low-dose macrolide therapy in 4 out of 6 cases. In addition, macrolides reduced the number of exacerbation, and significantly improved ACT score (17.8 → 24.2, $P < 0.05$) compared to values before the administration. The concentration of FeNO was varied among the patients and that data was not improved by the treatment with macrolides.

Conclusion: These results indicate that coexistence of neutrophilic rhinosinusitis is associated with poor asthma control and that low-dose macrolide therapy is useful for controlling these patients. Our findings suggest that the type of inflammatory cells involved in the coexisting rhinosinusitis may be a predictive marker of the efficacy of low-dose macrolide therapy in patients with severe asthma.

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THE ASTHMA EXACERBATION AFTER INHALED CORTICOSTEROID WITHDRAWAL: THE ANALYSES OF THE NATIONAL HEALTH INSURANCE DATABASE

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Background and Aims: The current asthma guideline including Global Initiative for Asthma (GINA) 2017 recommended not to withdraw inhaled corticosteroid (ICS) in the adult asthmatics, but evidence remains unclear and the long-term use of ICS may induce side-effects. We analyzed patients with asthma who discontinued ICS after usage for 6 months or more, by using data of National Health Insurance Sharing Service (NHIS), which reflects real-world practice.

Methods: Among data extracted from NHIS between 2010 and 2011, the asthma was defined with the diagnosis of asthma and ICS medication possession rate > 50% in a year. The people with the diagnosis of COPD and long term systemic steroid users were excluded. The Asthma patients are divided into two groups, patients who continued ICS (ICS continuation group) and patients who stopped ICS more than 6 months (ICS withdrawal group). Moderate exacerbation was defined with the prescription of systemic steroid for 3 days or more and severe exacerbation was defined with hospitalization for asthma.

Results: A total of 1,160 asthma patients were identified as above definition. Among them, 278 stopped ICS for more than 6 months. In this ICS withdrawal group, 27 (9.7%) patients experienced moderate exacerbation. 25 (9.0%) patients had severe exacerbation. In ICS continuation group, 94 (10.7%) patients experienced moderate exacerbation, and 73 (8.3%) patients experienced severe exacerbation. The rate and the frequency of exacerbation were not different between two groups ($P = 0.65$ and $P = 0.22$, moderate, $P = 0.71$ and $P = 0.94$, severe).

Conclusion: Most of asthmatics did not have exacerbation even after the ICS withdrawal in real practice. However, the proportion of patients with exacerbation or hospitalization was not small. Therefore, prudent strategy is necessary to decide who should continue ICS, instead of ICS maintenance just based on asthma diagnosis itself.

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ASSESSMENT OF THE ACTUAL CONDITION OF ELDERLY ASTHMA

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Background and Aims: The population of Japan is declining after the peak in 2008. Also, the ratio occupied by 75 years or older is 13.8%. By the highest aging population and low birthrate, it is predicted that its ratio will rise to 20.2% in 2040. In a super-aged society, the increase of number of elderly asthma is predicted.

We investigated the actual situation about elderly asthma for making a future strategy to them.

Methods: We intended the patients with asthma who visited our outpatient clinic regularly from January to March 2017 ($n = 976$, female = 566, mean age: 63.8 years) retrospectively. The number of patients divided by age group were under 65 years ($n = 402$), 65–74 years (associate elderly, $n = 302$), 75–89 years (elderly, $n = 265$), 90 years or older (super elderly, $n = 7$), respectively. We analyzed patient's lung function, forced oscillation technique, FeNO, asthma control, blood eosinophils, serum IgE level. We compared some variables with the data of the patients with asthma in our outpatient clinic investigated in 2008.

Results: The percentage of 75 years or older was 27.9%. Because the same ratio was 21.6% in 2008, the aging of patients found to advance. Small airway damage became strong with aging, but the degree of damage became milder than in 2008. With aging, the ratio of poor control increased. The blood eosinophil count surpasses 5% and FeNO showed around 35 ppb in 75 years or older patients.

Conclusion: It was suggested the treatment for eosinophilic airway inflammation was necessary for acquiring improvement of elderly patient's control, because its inflammation was equivalent to non-elderly patients. Therefore, we have to consideration about how appropriate anti-inflammatory therapy is provided in an individual elderly patient with asthma.

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THE SITUATION OF SERVICE IN PATIENT WITH ASTHMA EXACERBATION, EXPERIENCE IN SECONDARY CARE HOSPITAL, THAILAND

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Background and Aims: The asthmatic patients in Thailand had hospitalization and emergency room visit from asthma exacerbation about 15 % and 21 % respectively which affect to patient outcome and quality of life so health provider should be known the situation of service in patient with asthma exacerbation for asthma exacerbation management effectively. To study the situation of service in patient with asthma exacerbation focus on rate of exacerbation, problem and cause of asthma exacerbation.

Methods: Action research study phase 1 by retrospective study from medical record in one community hospital during October 2014 to September 2015. Situation of asthma exacerbation was survey from patients with recurrent asthma exacerbation at least 2 times per year and in-depth interview healthcare providers, patient and caregivers.

Results: 346 patients have recurrent emergency room visited at least 2 times /year. 80.35 % with average age $2.7 \pm .43$ years old. The rate of recurrent asthma exacerbation $2.8 \pm .06$ times per patient. The average length time to recurrent asthma exacerbation was 51.0 ± 9.39 days. 283 patients (81.79%) were not prescribed inhale corticosteroid; in this group 108 patients (38.2%) had more than 3 times of asthma exacerbation and should be considered to start inhale corticosteroid. Content analyses from healthcare provider's perspectives about problems of asthma exacerbation were under diagnosis or delay diagnosis leading to delay treatment with inhale corticosteroid, non-adherence of medication and trigger. From patients or caregivers' perspective about problems of asthma exacerbation were weather change, no emergency bronchodilator supplies, loss follow up, incorrect technique of inhalation.

Conclusion: The situation of asthma exacerbation so healthcare provider should be concern for asthma exacerbation management effectively.

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BITTER TASTE RECEPTOR AND ITS ROLE OF RELIEVING BRONCHOSPASM FOR THE ASTHMATICS- AN EVIDENCE-BASED MEDICINE UPDATE, 2018

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Background and Aims: Bitter taste is sensed by type 2 taste receptors (TAS2Rs) which evoke G-protein cascade to release intracellular calcium and to activate transient receptor potential M5 (TRPM5) then stimulate vagal sensory fibre to complete communication with the brain. Two TAS2R agonists (chloroquine, quinine) inhibited mitogen-induced ASM growth for about 60% to 70% (P. Sharma 2016, LoE:[5])(level of evidence). Airway smooth muscle (ASM) relaxed by TAS2R agonists was observed under cryopreserved human precision-cut lung slices (hPCLSs) as a robust bioassay (Bai Y. 2016, LoE:[5]).

Methods: An EBM-based survey in Pubmed by searching keywords "bitter taste receptor", "asthma", "airway smooth muscle", limited in English language and human study, published date between 2016/Jan/1 to 2018/Apr/30 was done. EBM level is followed the Oxford centre for EBM 2011 edition.

Results: HEK-293T cell surface TAS2R14 expression increased by ~5-fold when β 2-adrenergic receptors were co-expressed and, with a prolonged β -agonist exposure, TAS2R14 internalized (Kim D. 2016, LoE:[5]). Using Phosphoinositide-specific phospholipase C (PLC) inhibitor, researchers found calcium mobilized through the Quinine-T2R-G $\alpha\beta\gamma$ -PLC pathway (Jaggupilli A. 2017, LoE:[5]). Most highly expressed ASM TAS2R10 and TAS2R14 subtypes were studied to find 15 and 23 single nucleotide polymorphisms (SNPs) for each other. A positive bronchodilator response (BDR) on -1897T>C (OR = 3.05, 95%CI 1.01–9.23, P-value = 0.04) and a low mean asthma control test (ACT) score on -815T>C (OR = 5.84, 95%CI = 1.94–17.61 P = 0.001) were associated in the TAS2R14 gene (S.Y. Yoon 2016, LoE:[3]). In ASM cells, TAS2R agonists decreased mitochondrial membrane potential and increased ROS and fragmentation. Inhibiting dynamin-like protein 1 (DLP1) reversed TAS2R agonist-induced mitochondrial membrane potential change and attenuated fragmentation and cell death (Pan S. 2017, LoE:[5]). Beta2AR increased surface expression of TAS2R14 but, by direct receptor-receptor desensitization of TAS2R14 function, prolong β -agonist activation offset TAS2R expression.

Conclusion: TAS2Rs and their agonists are novel targets for clinical asthma control. Further prospective study for effectiveness and responsiveness are potentially indicated.

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THE CHANGE OF NASAL RESISTANCE AT THE ACUTE NASAL CHALLENGE WITH COLD AIR IN ASTHMATICS WITH COLD AIRWAY HYPERRESPONSIVENESS

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Background and Aims: Cold airway hyperresponsiveness (CAH) is quite common for asthmatics and associated with TRPM8-dependent genetic predisposition (Naumov D. et al. *Respirology* 2017; 22, Suppl. 3:93–94, doi: 10.1111/resp.13207_20). It is diagnosed when the FEV₁ falls more than 10% after a test with isocapnic hyperventilation of cold air through the mouth. We aimed to assess the influence of cold air on the nasal resistance in asthmatics with CAH at the acute nasal provocation with cold air.

Methods: In 18 subjects with mild asthma (mean age $38. \pm .3$ years; FEV₁ = $96. \pm .5\%$ of predicted) with CAH (the drop of FEV₁ after 3-min isocapnic hyperventilation through the mouth with cold (-20°C) air was on average $-16. \pm .9\%$) the nasal breathing was assessed at frontal rhinomanometry and FEV₁ change was measured by spirometry before and after nasal test with 3-minute isocapnic hyperventilation with cold air.

Results: Initially all the subjects had a higher nasal resistance to the airflow under the pressure 150 Pa (R150): on average in the group on the right-hand side (Rr) it was $0.8 \pm .13$, and on the left-hand side (Rl) it was $0.6 \pm .13$ Pa/(mL/s). After 3-minute isocapnic hyperventilation with cold air through the nose the nasal resistance grew: Rr till $1.5 \pm .28$ Pa/(mL/s) ($P = 0.047$), Rl till $1. \pm .30$ Pa/(mL/s) ($P = 0.32$). In 4 subjects the nasal provocation with cold air led to the sudden obstruction of nasal breathing and the absence of airflow during 30 minutes. A significant drop of FEV₁ after nasal provocation with cold air was registered in 4 out of 18 subjects. On average in the group the change of FEV₁ was $-4. \pm .1\%$.

Conclusion: An acute nasal provocation with cold air leads to the increase of the nasal resistance in asthmatics with CAH and in each fifth patient to significant drop of FEV₁.

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POLY-UNSATURATED FATTY ACIDS METABOLOMICS STUDY REVEALS CHILDHOOD SERUM HETES LEVELS CLOSELY RELATED TO GLUTATHIONE PEROXIDASES IN ALLERGIC ASTHMA

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Background and Aims: Asthma is one of the most common chronic diseases in childhood and is the leading causes of morbidity. The prevalence of asthma disease has been increased rapidly in western and industrialized countries. It was reported that poly-unsaturated fatty acids (PUFAs), such as HETEs, were associated with the development of asthma disease. As well, Glutathione peroxidases (Gpx) and

lipoxygenases (LOX) play important roles in the metabolism of HETEs, and Gpx4 has been implicated as enzyme which regulates the redox homeostasis about HETEs. In this account, the metabolism of HETEs was elucidated in the asthma patients compared with healthy patients by using ultra-high performance liquid chromatography-quadrupole-time of flight/MS (UHPLC-Q-TOF/MS).

Methods: In this study, we enrolled 30 asthma patients and 30 healthy groups. All of the serum were participated using ethyl acetate and derivatized using (2-aminoethyl)trimethylammonium chloride hydrochloride (cholamine) reagent, then extracted and profiled by UHPLC-Q-TOF/MS and finally analyzed by Principal component analysis (PCA) and receiver operating characteristic (ROC) curve.

Results: The SIMCA-P software was used for the multivariate statistical analysis. PCA and orthogonal signal correction (OSC) partial least-squares-discriminant analysis (PLS-DA) were applied to distinguish changes between healthy and asthma human group. ROC curve was used to further confirm the main biomarkers in asthma group. Finally, 5 (S)-, 8(S)-, 11(S)-, 12(S)-, and 15(S)-HETE were significantly increased in asthmatic human group vs healthy human group. In addition, we predicted that Gpx4 overexpression could lead to the increase of HETEs.

Conclusion: By using derivatization and UHPLC-Q-TOF/MS profiling methods and analyzed by PCA and ROC curve statistical analysis, we can clearly distinguish the different metabolomics profiles between healthy and asthma human group. Finally, we can conclude that HETEs show significant differences between healthy and asthma human group, which may result from Gpx4 overexpression in the asthma patients.

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RESOLVIN E3 ATTENUATES ASTHMATIC INFLAMMATION IN A MURINE MODEL OF HOUSE DUST MITE (HDM) -INDUCED AIRWAY INFLAMMATION

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Background and Aims: Resolvin E series are derived from the omega-3 fatty acid eicosapentaenoic acid (EPA) and act as potent pro-resolving mediators of inflammation. Resolvin E3 (RvE3) is a novel lipid mediator recently identified as a member of the Resolvin E series, though the role of RvE3 for asthmatic inflammation is unknown. We investigated the role of RvE3 in a model of house dust mite (HDM) -induced eosinophilic airway inflammation in mice.

Methods: Allergic airway inflammation was induced by House dust mite (HDM) sensitization and challenge (Day 0–2, 14–17) in BALB/c mice. After the last HDM challenge (Days 17, 18), RvE3 was administered intraperitoneally. Leukocytes from the bronchoalveolar lavage fluid (BALF) were evaluated, and the lung tissue was used for assessment of expression of cytokine in the lung and pathological analysis.

Results: RvE3 treatment significantly decreased the number of total inflammatory cell, eosinophil, and levels of mRNA expression of Th2 cytokine. Histopathological analysis revealed RvE3 improved goblet cell hyperplasia in lung tissue.

Conclusion: RvE3 can facilitate resolution of allergic airway inflammation by regulating selective cytokines.

EFFECT OF NEBULIZED INHALED TRIPTOLIDE IN MOUSE MODEL OF ASTHMA

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Background and Aims: to investigate the effect of nebulized inhaled triptolide to airway inflammation in mouse models of asthma and the feasibility of applying triptolide through nebulized inhaling.

Methods: 24 SPF grade BALB/c female mice were divided into three groups of 8 in each group: Normal Saline Group (NS), Dexamethasone Group (Dex), Triptolide (TP) Group. In the process of sensitizing mice through Ovalbumin + Al (OH)3, animals in each group were treated with nebulized NS, intraperitoneal injection of Dex and nebulized triptolide respectively. Mice were sacrificed after 25 days, Bronchoalveolar lavage (BAL) and lung tissue were then collected, levels of IL6, IL10, IL17, IL23, TGF- β 1 were assessed and compared (ELISA). Transcriptional levels of IL-17, ROR γ t, FoxP3 among lung tissues were also assessed and compared (RT-PCR).

Results: In assessing BAL, the experiments find that there were significant differences ($P < 0.01$) among levels of IL6, IL10, IL17, IL23, TGF- β 1 in the three groups. IL6 level in NS Group is clearly higher than Dex Group and TP Group ($P < 0.01$). IL17, IL23 and TGF- β 1 demonstrate significant difference among the three groups between two means in the following order: Dex Group < TP Group < NS Group ($P < 0.01$), while IL10 shows the opposite trend among the groups. In assessing transcriptional level of lung tissue cytokines, the experiments find that the Ct value of IL17 in Dex Group was significantly higher than NS Group and TP Group ($P < 0.01$). Ct value of ROR γ t demonstrated significant difference among the three groups between two means in the following order: Dex Group > TP Group > NS Group ($P < 0.01$). Ct value of FoxP3 in NS Group was markedly higher than the other Groups ($P < 0.01$).

Conclusion: Inhalation of nebulized triptolide can play a role in suppressing airway inflammation. It curbed the levels of cytokine IL6, IL17, IL23, TGF- β 1, stimulated the expression of inhibitory cytokines IL10. At the transcriptional level, it decreased Th17 and increased Treg by influencing regulating factors ROR γ t and FoxP3.

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VALIDATION OF RISK FACTORS OF ASTHMA ATTACK QUESTIONNAIRE AMONG MALAYSIAN ADULT ASTHMATIC PATIENTS

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Background and Aims: Identifying the risk factors of an asthma attack and addressing those factors can prevent the asthma-related emergency department visits and hospital admissions. The main objective of this study was to assess the reliability and validity of newly designed risk factors of asthma attack questionnaire among Malaysian adult asthmatic patients.

Methods: This cross-sectional study was conducted at two Respiratory Specialist Clinics in Universiti Teknologi MARA (UiTM), Malaysia. The newly designed questionnaire was translated into Malay language by two independent bilingual experts. The translation process included: forward translation, backward translation, harmonization, cognitive debriefing and proof reading. The content validation was done by three experienced clinical experts; whereas, face validation was carried out by distributing

the questionnaires among 7 adult asthmatic patients. Post signed consent, the finalized Malay version of the questionnaire was distributed among 60 adult asthmatic patients. The data were extracted from the completed questionnaires and analyzed using Bond and Fox Software® (Rasch Model) and Statistical Package for Social Sciences (SPSS®).

Results: The item reliability and person reliability values were 0.90 (excellent) and 0.78 (good), respectively. The output tables of item construct showed that values for infit and outfit ZSTD (± 2), infit and outfit MNSQ (0.6 to 1.4) and PTMEA correlation (0.3 to 0.6) were within the acceptable range as specified by the Rasch Model. Hence, the newly devised translated questionnaire met the specifications of the Rasch Model for reliability and construct validity. Moreover, Cronbach's alpha value (0.751) proved the internal consistency of the questionnaire.

Conclusion: The risk factors of asthma attack questionnaire proved to be valid and reliable tool to identify the risk factors of asthma attack among adult asthmatic patients. Future work linking patient-reported risk factors and respective preventive strategies could be of value in reducing the emergency department visits and hospital admissions because of asthma attack.

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THE DIFFERENT RELATIONSHIP IN SINGLE NUCLEOTIDE POLYMORPHISMS OF CHITINASE 3-LIKE 1 (CHI3L1) GENE, CHI3L1 SERUM LEVEL, WITH BRONCHIAL ASTHMA AND ALLERGIC RHINITIS IN TAIWAN

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Background and Aims: Changes in the serum level of chitinase 3-like-1 (CHI3L1; also known as YKL-40) are correlated to the severity of asthma in European patients. Accordingly, CHI3L1 is believed to be a biological marker of asthma. In addition, the single nucleotide polymorphism (SNP) of the promoter-131C/G (rs4950928) of CHI3L1 gene is also related to asthma, although studies on Asian population revealed different results.

Methods: A total of 183 individuals were recruited for this case-control study. The venous blood samples of the patients were collected to determine the white blood cell (WBC) count, differential WBC count, eosinophil count, total IgE and eosinophil cationic protein levels, serum CHI3L1 level, and CHI3L1-131C/G genotype in order to clarify the relationship between the occurrence of asthma and CHI3L1 in an Asian population.

Results: In asthma patients in Taiwan, CHI3L1-131C/G genotype was not correlated with asthma ($P = 0.413$). However, the serum CHI3L1 level was significantly elevated in asthma patients, suggesting a correlation with asthma ($P = 2.10 \times 10^{-3}$). On the other hand, the serum CHI3L1 level was also correlated with asthma ($P = 0.013$), even in the asthma patients with a low IgE level.

Conclusion: The serum CHI3L1 level was indeed correlated with asthma, even in asthma patients with insignificant IgE expression. However, CHI3L1-131C/G genotype was not correlated with asthma in the study.

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EFFECTIVENESS OF A LONG-TERM COMBINED THERAPY IN PATIENTS WITH PERSISTENT ASTHMA DEPENDS ON THE PATTERN OF INFLAMMATION AND AIRWAY RESPONSE TO COLD AIR

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Background and Aims: The effectiveness of long-term controller therapy in patients with persistent asthma may depend on the morpho-functional profile of the effector cells of bronchial inflammation and the airway hyperresponsiveness features. We aimed to assess the effectiveness of a long-term therapy by ICS/LABA in patients with persistent asthma in the achievement of control depending on the airway response to cold stimulus and inflammatory pattern of bronchi.

Methods: The asthma control (ACT, points), lung function (FEV₁, MOC25-75, % pred), airway response (Δ FEV₁, %) to 3-minute isocapnic hyperventilation with cold air (IHCA), and cytological smears of the induced sputum (IS) were assessed in 109 subjects with mild asthma (mean age 41.0 ± 0.9 years) who had a long-term (6 months) controller therapy with formoterol/budesonide in the dose of 320/9 mcg/day.

Results: 60% of patients achieved a partial asthma control (≥ 20 points of ACT), on 22.4 ± 0.2 points (1 group); 40% of patients could not achieve the asthma control (on average 16.7 ± 0.1 points, $P = 0.00001$) (2 group). In patients of the 2nd group, compared to the 1st group, the indices of the forced expiration were worse (FEV₁ 90.7 ± 2.1 vs $95.1 \pm 2.3\%$; FEF₂₅₋₇₅ 62.1 ± 3.5 vs $75.2 \pm 4.2\%$, $P = 0.028$), and the drop of FEV₁ under IHCA was more intensive (-12.1 ± 2.0 vs $-7.0 \pm 1.6\%$, $P = 0.047$). In cytological smears of IS in the patients of both groups there were found high contents of neutrophils which were higher in the patients of the 2nd group (40.8 ± 2.8 vs $33.3 \pm 2.4\%$, $P = 0.046$), as well as there was revealed a tendency to the increase of a number of eosinophils (16.9 ± 2.2 vs $13.1 \pm 1.5\%$, $P = 0.15$) and goblet cells (0.12 ± 0.04 vs $0.05 \pm 0.01\%$, $P = 0.06$). The correlation between the contents of neutrophils in IS and airway response (Δ FEF₅₀) to IHCA ($r = -0.37$; $P = 0.029$) in the 2nd group was revealed.

Conclusion: Low sensitivity to controller therapy in asthma patients is associated with the mixed pattern of bronchial inflammation and cold airway hyperresponsiveness.

AP351

THE CORRELATION OF AIRWAY RESPONSES TO OSMOTIC AND THERMAL STIMULI IN ASTHMATICS WITH EXERCISE-INDUCED BRONCHOCONSTRICTION

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Background and Aims: The main triggers of exercise-induced bronchoconstriction are drying and cooling of airway mucosa. We aimed to define the correlation between airway hyperresponsiveness to dosed physical exercise (DPE) and the response to hyperosmolar and cold stimuli in patients with partially-controlled asthma.

Methods: 57 patients with partially-controlled asthma had 3 bronchial challenge tests: with hypertonic stimulus (HS) in 3-min inhalation of ultrasonically nebulized 4.5% NaCl solution; with cold stimulus in 3-min isocapnic hyperventilation with cold air (IHCA) and DPE on the treadmill LE 200C during 6–8 min at submaximal heart rate. All the tests were considered to be positive under fall of FEV₁ after the challenge by 10% from baseline. The 1st group included 29 subjects with the positive response to DPE, the 2nd group included 28 subjects with negative tests with DPE, IHCA and HS.

Results: In the 1st group the positive tests with HS and IHCA were registered in 10 subjects, the combination of the positive test with HS and negative with IHCA in 2 subjects, the combination of the negative test with HS and IHCA in 8 subjects, the combination of negative test with HS and

positive test with IHCA in 9 subjects. In this group the direct correlations between the change of FEV₁ after DPE and after IHCA were found out: at the 1st minute after DPE $r = 0.41$ ($P < 0.05$), at the 10th minute $r = 0.49$ ($P < 0.05$). The correlation between FEV₁ drop after DPE and after HS was not revealed. In the 2nd group there were not found any correlations between the changes of FEV₁ after DPE, IHCA and HS.

Conclusion: Airway cooling in a greater degree than drying is associated with bronchial smooth muscles response to exercises.

AP352

THE FIRST EQUATION TO ESTIMATE THE SIX-MINUTE WALK DISTANCE IN HEALTHY MALAYSIAN ADULT AGED 20 TO 40 YEARS OLD

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Background and Aims: The six-minute walk test (6MWT) is commonly used to assess functional exercise capacity in people with respiratory diseases. At least 30 regression equations to estimate the six-minute walk distance (6MWD) in different population (except Malaysian) has been published, with most of the equations were derived from individuals aged ≥ 40 years. Therefore, the aims of this study were to derive regression equation to estimate the 6MWD in Malaysian adults and compare the 6MWD measured in this sample with the 6MWD estimated using previously published equation.

Methods: Eighty-one adults (48 females) aged 20 to 40 years performed two 6MWTs using a standardized protocol. Best 6MWD from the two tests was used in the analysis. Heart rate was recorded each minute during the 6MWT. Other measurements taken include age, height, weight, blood pressure and spirometry.

Results: The 6MWD was 597 ± 74 m and males walked further than female ($648 \pm 6 \pm 9$ m, $562 \pm 5 \pm 5$ m, $P < 0.001$). The 6MWD was associated with height and percentage of predicted heart rate maximum (%pred HRmax); both $r > 0.5$, $P < 0.001$). The following equation explained 63.7% of the variance in the 6MWD, $m: 439 + (3.84 \times \%pred HRmax) - (82.2 \times \text{gender} [\text{males} = 0 \text{ and female} = 1])$. The 6MWD estimated using the equations derived from Caucasian population overestimated the 6MWD measured in the sample of Malaysian adults by 23 ± 64 m; $P < 0.001$).

Conclusion: This is the first study that derived regression equation to estimate the 6MWD in healthy Malaysians adults. The equations will facilitate interpretation of the 6MWD in clinical populations in Malaysia, particularly among those with diseases involving younger adults such as asthma and cystic fibrosis. Disparity between the measured 6MWD with that estimated using existing equation highlights the importance of using regression equations derived in a local sample.

Bronchoscopy and Interventional Techniques 2

AP353

COMPARISON OF RADIAL PROBE ENDOBRONCHIAL ULTRASOUND GUIDED AND BLIND TRANSBRONCHIAL LUNG BIOPSY IN DIFFUSE LUNG LESIONS

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Background and Aims: Currently, endobronchial ultrasound (R-EBUS) guided biopsy is widely used for the diagnosis of peripheral pulmonary lesions. But, the usefulness of R-EBUS guided transbronchial

lung biopsy (TBLB) for diffuse lung lesions is not known. We performed this study to evaluate the usefulness of R-EBUS guided TBLB.

Methods: This study was conducted as a retrospective, observational, and single institutional study. Patients who were admitted from January 2016 to December 2017 and underwent TBLB for diffuse lung lesions were included. We compared blind TBLB and R-EBUS guided TBLB groups. Diffuse lung lesions were defined as consolidation or ground glass opacity lesions involving more than one segment of the lung. In blind group, no fluoroscopy was used and in R-EBUS group, guided sheath was not used during TBLB.

Results: Total 129 patients underwent TBLB for diffuse lung lesions (61 patients in blind group and 68 patients in R-EBUS group). There were no differences in age, sex, and presence of emphysema between two groups. There was no difference between two groups in diagnostic yield based on biopsy results ($P = 0.272$). The number of specimen was 4.9 ± 1.7 in blind group and 6.3 ± 2.4 in R-EBUS group, and more samples were collected in R-EBUS group ($P = 0.003$). The procedure time was longer in R-EBUS group (22.2 ± 6.7 min) than blind group (15.3 ± 4.2 min) ($P < 0.001$). There was no difference in the amount of midazolam used between two groups. Pneumothorax, a complication of TBLB, occurred in four cases in blind group and none in R-EBUS group. The incidence of pneumothorax was significantly lower in R-EBUS group than blind group ($P = 0.032$). In the case of bleeding, there was no difference between two groups.

Conclusion: When performing TBLB for diffuse lung lesions, the diagnostic yield was not different between blind and R-EBUS groups. The procedure time was longer in R-EBUS group. But, the incidence of pneumothorax was significantly lower in R-EBUS group than blind group.

AP354

ANALYSES OF LUNG SOUNDS BEFORE AND AFTER THE TREATMENTS FOR LARGE AIRWAY STENOSIS

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Background and Aims: Every day we see many cases of dyspnea; however the causes are numerous. We think a stethoscope might become a useful method to diagnose large airway stenosis by analyses of lung sounds. Here we present the analysis by Adobe Audition® which is a computer software for music.

Methods: Lung sounds were recorded in a voice recorder, Linear PCM Recorder by Sony, through the bilateral chest wall using a pair of hand-made stethoscopes consisting of hard gum and an electret condenser microphone by Audio-Technica in Japan.

Results: (Case 1. Oesophageal carcinoma) A man in his seventies suffering from oesophageal cancer complained of dyspnea. CT revealed tracheal stenosis due to the carcinoma. The lung sound was a wheeze. Some sharp peaks were detected between 100 and 1300 Hz calculated by Fourier analysis. We placed an Aerostent®. Dyspnea decreased; however three months later stenosis recurred and the lung sound was wheezing with harmonic overtones. After inserting the second stent, wheezing disappeared. (Case 2. Bronchogenic cyst behind the right main bronchus) Lung sound was rhonchi with harmonic overtone heard only during inspiratory phase. The peaks were between 100 and 1300 Hz. After the thoracoscopic surgery, the adventitious sound completely disappeared. (Case 3. Kommerell diverticulum) We thought oozing blood around the stent of the thoracic aorta caused tracheal stenosis. So one more TEVAR stent was added under general anaesthesia. The adventitious sound gradually disappeared.

Conclusion: Here, we present some analyzed patterns of lung sounds, which differ according to each large airway stenosis. Data

analysis of these studies might help us to identify the large airway diseases in the future

AP355

RIGHT MAIN BRONCHIAL PLEOMORPHIC ADENOMA: A RARE CASE REPORT AND LITERATURES REVIEW ZHIXING ZHU¹*, DONGYONG YANG¹

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Background and Aims: Tracheobronchial pleomorphic adenoma is a rare disease which may be misdiagnosed and the proper diagnosis is usually delayed. This study is aimed to report the characteristics of tracheobronchial pleomorphic adenoma and review the relative references to enhance the knowledge of it.

Methods: A 38-year-old woman was admitted to hospital with complaint of progressive shortness of breath for 5 years. A chest CT enhanced scan revealed an endobronchial mass (oval, major axis: 1.42 cm and minor axis: 0.96 cm) located at the proximal part of the right main bronchus. Bronchoscopy identified a pink, broad-based, polypoid neoplasm with branching blood vessels on the smooth surface nearly completely obstructing the lumen of right main bronchus. The neoplasm was resected through combining an electrosurgical snare and argon plasma coagulation.

Results: Pathologic examinations showed an encapsulated biphasic lesion consisting of a mixture of epithelium and stroma with areas of hyalinization which confirmed the definite diagnosis of pleomorphic adenoma. The recovery was good without any procedure-related complications. The patient were free of clinical manifestations during the follow-up period for 3 years and no evidence of regenerative or residual neoplasm was found base on the follow-up chest CT enhanced scan and bronchoscopy.

Conclusion: Tracheobronchial pleomorphic adenoma is extremely rare, thus, its incidence, aetiology and prognosis are still unclear. Most of the clinical manifestations are cough, dyspnea, wheezing and shortness of breath. To those who are suffering from airway obstruction symptoms without clear course, we should take tracheobronchial pleomorphic adenoma into consideration. Chest CT, bronchoscopy, microscopy and immunohistochemical staining can facilitate the definite diagnosis. Surgical and endoscopic resection are two major treatments. Endoscopic resection especially the combination of an electrosurgical snare and argon plasma coagulation is worthy of being promoted due to its safety and efficiency. Because of the low possibility of recurrence and potential malignant transformation, careful follow-up after resection procedure is necessary.

location	therapy
endoscopic resection	
distal trachea	tumor was resected with rigid forcep and APC ⁽¹⁾
upper one-third of the trachea	tumor was resected with APC ⁽¹⁾
left main bronchus	tumor was resected with electrosurgical snaring ⁽²⁾
distal trachea	tumor was resected with APC, electrocautery and rigid bronchoscopic coring ⁽³⁾
left main bronchus	tumor was resected with electrosurgical snare and APC ⁽²⁾
right main bronchus	tumor was removed with diathermy snare ⁽²⁾
mid one-third of the trachea	tumor was excised with cold instruments ⁽¹⁾
surgical resection	
trachea	right thoracotomy with segmental resection and end-to-end anastomosis ⁽¹⁾
mid one-third of the trachea	collar incision with partial sternotomy and end-to-end anastomosis ⁽²⁾
left main bronchus	wedge bronchiectomy ⁽¹⁾
lower one-third of the trachea	tracheal resection and end-to-end anastomosis ⁽¹⁾
lower one-third of the trachea	right thoracotomy with circumferential resection and end-to-end anastomosis ⁽²⁾
distal trachea	tracheal reconstruction ⁽²⁾
trachea	segmental tracheal resection and end-to-end anastomosis ⁽¹⁾
upper one-third of the trachea	segmental tracheal resection and end-to-end anastomosis ⁽¹⁾
distal trachea	tracheal wedge resection ⁽¹⁾
distal trachea	primary anastomosis performed through right thoracotomy ⁽²⁾
mid one-third of the trachea	right thoracotomy incision and end-to-end anastomosis ⁽²⁾
hilum of the right lung	lobectomy ⁽²⁾

APC: Argon plasma coagulation

BRONCHOSCOPIC THERMAL VAPOUR ABLATION (BTVA) FOR SEVERE EMPHYSEMA: PRELIMINARY EXPERIENCE WITH A NOVEL INTERVAPOR® TECHNOLOGY IN A SINGAPORE TERTIARY HOSPITAL

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Background and Aims: Patients with severe pulmonary emphysema suffer from disabling dyspnea, respond poorly to medical therapy, and often are unsuitable for lung volume reduction surgery. In recent years, bronchoscopic lung volume reduction approaches, including endobronchial valve/ coil placement and thermo vapour ablation techniques, have been proposed as an alternative treatment. We present our preliminary experience with BTVA of a patient with severe emphysema using Intervapor® technology.

Methods: Our patient is a middle-aged gentleman who had COPD for the past 8 years. Lung function test showed severe obstructive pattern with significant air-trapping (FEV1 36% predicted, RV 265% predicted). Despite optimal inhaled bronchodilator therapy, he remained symptomatic (MMRC 3) and had frequent COPD exacerbations.

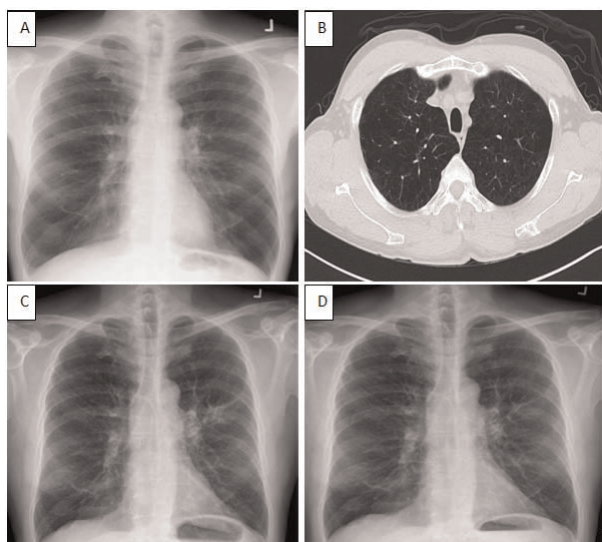
His chest radiograph (CXR) and computed tomography (CT) scan of the chest showed severe centrilobular upper lobe-predominant emphysema. Feasibility for BTVA was assessed based on CT analysis with Intervapor® technology and a personalized procedure programme was proposed.

Results: The patient underwent BTVA under general anaesthesia. A flexible bronchoscope was wedged in the anterior segment of the left upper lobe (LB3)- heated water vapour was delivered to the 3 subsegments in LB3; with a total procedural time of 30 minutes. There were no immediate post-procedural complications.

He had a moderate exacerbation requiring corticosteroids 1 week after procedure. CXR 1 month post-procedure showed a mass-like consolidation over the left midzone and he was prescribed antibiotics. Repeat CXR (Figure) 3 weeks later showed complete resolution of the consolidation with residual atelectatic changes, consistent with a localized inflammatory response followed by scarring of the lung parenchyma.

Symptomatically, he improved with a COPD assessment test score improving from 25 to 14 (2 months post-procedure). He had no further exacerbations and there was a 33% reduction in his weekly use of short-acting beta-agonists.

Conclusion: BTVA offers a promising and safe solution for symptom relief in end-stage emphysema patients.



AP357

EFFICACY AND INFLUENCE FACTORS OF INTERVENTIONAL BRONCHOSCOPY FOR THE TREATMENT OF SCARRING AIRWAY STENOSIS

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Background and Aims: Although an effective and critical therapeutic modality for scarring airway stenosis, the efficacy of interventional bronchoscopy differs among different studies. Thus, factors associated with the efficacy of interventional bronchoscopy and restenosis are not clearly understood. In this study, the clinical factors associated with the achievement of clinical success were specifically evaluated, and the variables associated with airway restenosis addressed.

Methods: Between January 2013 to December 2016, 301 patients with scarring airway stenosis from 18 tertiary hospitals, who were treated by interventional bronchoscopy were reviewed retrospectively. Airway stenosis characteristics and patients' performance status at baseline and after interventional bronchoscopy were recorded. The methods of interventional bronchoscopy included electric knife cutting, laser cauterization, balloon dilation, cryotherapy, and/or stenting. The interval days between the first two interventional bronchoscopy treatment (maintained patency time) were recorded.

Results: The final clinical stability rate of interventional bronchoscopy for the treatment of scarring tracheal stenosis was 67.8% (204/301). Stenosis sites ($P = 0.032$), dyspnea index ($P < 0.001$), and interventional method ($P = 0.005$) were independent predictors associated with the efficacy of interventional bronchoscopy treatment. The mean maintain patency time after the first interventional bronchoscopy treatment was 26.9 ± 30.9 days. Stenosis sites ($P < 0.001$), stenosis grade ($P = 0.001$), anaesthesia method ($P < 0.001$), and local drug usage ($P < 0.001$) were independent predictors associated with the maintained patency time after first interventional bronchoscopy treatment.

Conclusion: Interventional bronchoscopy is a useful treatment method for scarring airway stenosis. Enough attention should be paid to influence factors to improve treatment efficacy during the treatment process.

FEASIBILITY OF RE-BIOPSY BY ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL ASPIRATION (EBUS-TBNA) IN PATIENTS WITH PREVIOUSLY TREATED LUNG CANCER

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Background and Aims: Re-biopsy diagnosis is paramount in lung cancer patients with progressive disease after treatment. The endobronchial ultrasound-guided needle aspiration (EBUS-TBNA) was an important method for tissue acquisition. However, the role of EBUS-TBNA for re-biopsy in lung cancer was not clear. In this study, we investigated the feasibility of re-biopsy by EBUS-TBNA in lung cancer with suspected progression or recurrence after treatment.

Methods: Between November 2015 and October 2017, consecutive patients with suspected lung cancer progression or recurrence after treatment who underwent EBUS-TBNA were enrolled in National Taiwan University Hsin-chu Branch. The diagnoses were verified either by surgery or clinical follow-up.

Results: A total of 50 lymph nodes were sampled from 28 patients for suspected lung cancer recurrence ($n = 6$) or progression ($n = 22$) by EBUS-TBNA. The accuracy of EBUS-TBNA for the diagnosis of lung cancer progression or progression was 85.7% (24/28). The sensitivity, specificity, positive predictive value, and negative predictive value rate was 84.0%, 100%, 100%, and 42.9%, respectively. Logistic regression analysis revealed that lymph node size significantly influenced the diagnostic yield of EBUS-TBNA. The T790M mutation was identified in 5 (62.5%) of 8 patients with *EGFR*-mutant lung adenocarcinoma. There was no major complication noted in these patients.

Conclusion: EBUS-TBNA is a suitable re-biopsy method for patients with suspected lung cancer progression or recurrence.

AP359

TRACHEAL STENOSIS IN A YOUNG LADY FOLLOWING SHORT-TERM INTUBATION: MIMICKING ASTHMA

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Background and Aims: Among different causes of acquired tracheal stenosis, endotracheal intubation is most common. Complication is uncommon if duration of intubation is less than a week. The condition may mimic asthma and delay in diagnosis may occur especially when history is lacking.

Methods: A 28-year-old lady presented to us with the complaints of persistent dry cough and breathlessness for 6 months. She was seen by different physicians several times and was diagnosed as asthma. Despite getting optimum medications for asthma, her condition was deteriorating. On examination, she was anxious and dyspnoeic. Chest auscultation revealed breath sound vesicular with prolonged expiration and bilateral wheezes. SpO₂ 94% at room air, chest X-ray revealed normal findings. Rescue corticosteroid was started along with ongoing medications. Three days later, she presented with worsening dyspnoea. There was inspiratory stridor. Spirometry was consistent with fixed airway obstruction. On query, her husband told that she got admitted to ICU 2 months before the first appearance of present symptoms after suicidal ingestion of benzodiazepine tablet and was on invasive mechanical ventilation for 2 days. Fiberoptic bronchoscopy (FOB) revealed a smooth fibrous narrowing of

trachea at the level of 5th tracheal ring. Patient was sent for thoracic surgical evaluation and was advised for dilatation. Dilatation of stenosed area was done via rigid bronchoscope under general anaesthesia using oesophageal dilator.

Results: Her symptoms partially relieved. A second dilatation was done one month later and she was almost completely symptom free. She refused any further intervention/surgery. She was discharged with advice of periodic follow-up. FOB after 2 years revealed well maintained tracheal patency and she is now doing well without any further complaints.

Conclusion: Although resection and end-to-end anastomosis is the definitive treatment for tracheal stenosis, alternative methods may be tried to alleviate patient's symptoms where other facilities like APC, balloon or laser is not available.

AP360

COMPARISON OF DEXMEDETOMIDINE TO PROPOFOL FOR SEDATION OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION: A RANDOMIZED CONTROLLED TRIAL

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Background and Aims: Dexmedetomidine, a sedative agents via α_2 adrenergic agonist, provides light sleep-like sedation with little respiratory suppression. The study aims to evaluate the efficacy and safety of dexmedetomidine sedation compared with propofol in endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA).

Methods: Twenty patients requiring elective EBUS-TBNA were randomized into two groups. In study group (dexmedetomidine, $n = 9$), patients were sedative with dexmedetomidine 1 ug/kg infusion for 10 minutes and 0.5–1.4 ug/kg/h to maintain stable vital signs and The Observer Assessment of Alertness and Sedation scale (OAA/S) 3–2. In control group, (propofol, $n = 11$) the initial effect-site concentration was targeted to 2.0ug/mL (Schneider model, target-controlled infusion) ± 0.2 ug/mL to achieve stable vital signs and OAA/S 3–2. Vital signs, bispectral index (BIS) and recovery time were recorded. Patients' tolerance, awareness, cough and cooperation during bronchoscopy sedation were evaluated by 100 mm-visual analog scale (VAS, 0: no bother; 100: the worst intolerance).

Results: There was no difference in oxyhaemoglobin saturation between two groups. There was a trend that the lowest mean arterial blood pressure in study group was higher than control group ($81. \pm .8$ vs $71. \pm 6.6$ mmHg, $P = 0.09$). The lowest heart rate was significant lower in study group than control group ($57. \pm .9$ vs $71. \pm 2.5$ beat/min, $P = 0.03$). The mean BIS of sedation was significant higher in study group than control group ($83. \pm .8$ vs $74. \pm .5$, $P < 0.01$) and the recovery time was no difference. Tolerance and awareness during sedation were similar in both groups. The cooperation is better in study group with less cough compared to control group (VAS, $14. \pm 0.4$ vs $39. \pm 5.1$, $P = 0.01$; $17. \pm 7.9$ vs $48. \pm 6.4$, $P < 0.01$, respectively).

Conclusion: Dexmedetomidine provided a lighter sedation, reduced HR without compromised blood pressure and tolerance of patients undergoing EBUS-TBNA compared to propofol. Dexmedetomidine sedation provided better patient cooperation with less cough for of EBUS-TBNA.

DIAGNOSIS OF PULMONARY FUNGUS BALL USING ENDOBRONCHIAL ULTRASOUND-GUIDED

TRANSBRONCHIAL NEEDLE ASPIRATION: CASE REPORTS

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Background and Aims: Pulmonary mycosis, occurring in patients with normal immune function, may develop fungus ball and have a chronic course. The bronchoscopic diagnosis of pulmonary fungus ball is difficult, and the histopathological diagnosis of fungus ball is often achieved postoperatively. The present report discusses the use of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for the diagnosis of pulmonary fungus ball.

Methods: This investigation included two patients with a mass or nodular shadow in the lower lobe of the lung. EBUS images of the fungus ball were created using convex probe (CP)-EBUS and EBUS-TBNA was performed for the nodule located in the center of the low echoic mass/nodule.

Results: Case 1: A 72-year-old male with a 3-cm mass in the right lower lobe (S6) observed through chest computed tomography (CT). CP-EBUS revealed the presence of fungus ball in the mass detected in the right bronchus intermedius. EBUS-TBNA permitted the histopathological diagnosis of mucormycosis.

Case 2: An 80-year-old female with a 1.5-cm nodule with air crescent sign in the right lower lobe (S6) observed through chest CT. CP-EBUS revealed the presence of a 7-mm nodule in the center of the 1.5-mm fungus ball detected in the right basal bronchus. EBUS-TBNA permitted the diagnosis of aspergillosis (*A. fumigatus*) through histopathology and tissue culture.

Conclusion: This is the first reported use of EBUS-TBNA for the diagnosis of pulmonary mucormycosis or aspergillosis. Although the creation of images of a fungal ball by CP-EBUS may be challenging, use of EBUS-TBNA may be effective for the histopathological diagnosis of pulmonary fungus ball.

AP362

A CASE OF TRACHEOBRONCHOPATHIA OSTEOCHONDROPLASTICA OBSERVED ON ENDOBRONCHIAL ULTRASOUND

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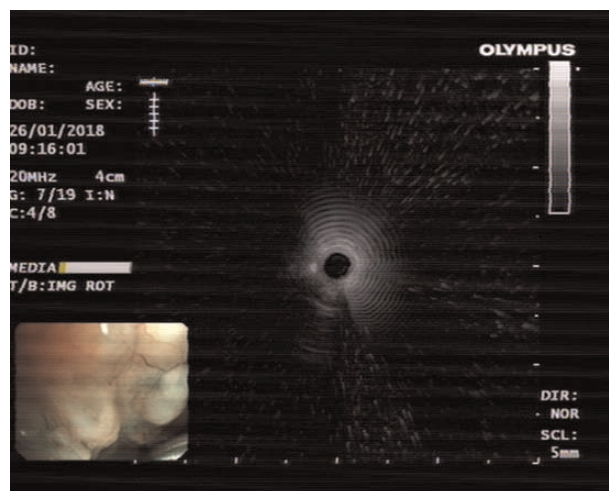
Background and Aims: Tracheobronchopathia osteochondroplastica (TPO) is a rare disease of the trachea and major bronchi that is characterized by multiple submucosal nodules with calcifications. The aim of the study is to study the imaging character of endobronchial ultrasound (EBUS) on TPO and enhance the acknowledge and diagnosis of TPO.

Methods: Reporting 1 patients with pathologically proved TPO, analyzing the clinical presentations, computed tomography of the chest, EBUS image and bronchoscopic features.

Results: The patient was asymptomatic. Chest CT scan and bronchoscopy in the patient showed multiple calcified nodules at the anterolateral wall of the trachea with typical sparing of the posterior membranous part. The submucosal hyperechoic foci was seen by EBUS.

Conclusion: We believe this is the first case about the EBUS feature of TPO after reviewing the literature. Awareness of TPO is significantly

important, especially in the patients with special CT image, and EBUS may be an effective approach for confirming the diagnosis.



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DIAGNOSTIC YIELD AND SAFETY OF EBUS-TBNA AND PERIPHERAL EBUS GUIDED TBLB UNDER MODERATE SEDATION: A SINGLE-CENTER RETROSPECTIVE AUDIT

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Background and Aims: Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) and peripheral EBUS guided transbronchial lung biopsy (EBUS-TBLB) can be performed under moderate sedation or general anaesthesia. Moderate sedation is logistically more convenient, but may result in greater patient discomfort, excessive patient movement, complications, and inadequate tissue sampling. Recent studies reported the diagnostic yield of EBUS-TBNA under moderate sedation to be 66.4–96%, while there is was limited information on the diagnostic yield of EBUS-TBLB. We thus aimed to describe the diagnostic yield and safety of EBUS-TBNA and EBUS-TBLB under moderate sedation.

Methods: All patients who underwent EBUS-TBNA and/or EBUS-TBLB under moderate sedation, between January 2015 and May 2017, at the National University Hospital Singapore were reviewed. Primary outcomes were diagnostic yield and safety of EBUS-TBNA and EBUS-TBLB. Diagnostic yield was defined by the proportion of patients who obtained a specific malignant or benign diagnosis from the procedure. Safety was determined from the presence of bronchoscopy-related complications, sedation-related complications, and readmission within 1 week after bronchoscopy for any delayed complications.

Results: 420 procedures were analysed (mean patient age 62.1 ± 13.1 years; mean bronchoscopy duration 61 ± 18.6 min). Mean sedation doses used were 50 mcg of intravenous Fentanyl and 2.5 mg of intravenous Midazolam. For EBUS-TBNA, the average number of lymph nodes sampled in each procedure was 1.7 (SD 0.8, min 1, max 5). For EBUS-TBLB, a total of 201 biopsies were performed. Diagnostic yield of EBUS-

TBNA and EBUS-TBLB were 70% and 87.1% respectively. Complications rates were low: transient bleeding 11.9%, transient hypoxia 0.5% and pneumothorax 0.1%. None required escalation of care post procedure, but 10 patients were hospitalised for respiratory complains or fever within 1 week after bronchoscopy.

Conclusion: EBUS-TBNA and EBUS-TBLB under moderate sedation are safe and have high diagnostic yields. These procedures should be considered as first-line sampling techniques.

AP364

ENDOBONCHIAL TREATMENT OF BRONCHOPLEURAL FISTULAS BY USING OVAL FORAMEN OCCLUDER UNDER VIRTUAL BRONCHOSCOPIC NAVIGATION: A CASE

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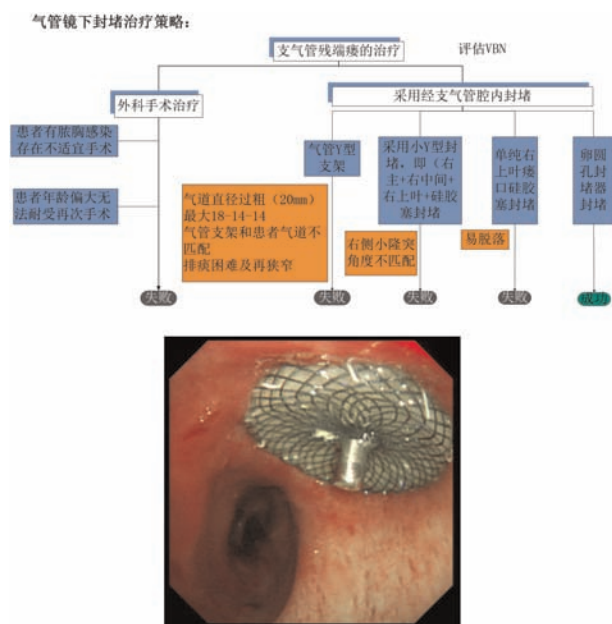
Background and Aims: To explore a new surgical method for the treatment of refractory fistula after transcatheter closure of bronchial endoscope.

Methods: The paper retrospectively analyzed the clinical data of one case diagnosed as stump bronchopleural fistula and right upper lung empyema after right upper pneumonectomy. After trying various plugging methods including silicone plugs and Y-silicon stents failed, the researchers tentatively applied the rigid bronchoscope combined with the flexible bronchoscope under general anaesthesia. Subsequently, the oval foramen occluder was built into the fistula to seal the fistula under virtual bronchoscopic navigation (VBN).

Results: The oval foramen occluder successfully blocked the right side of the upper lobe operation stump fistula mouth. One week later, the chest computed tomography fluoroscopy (CT) was re-examined and it was found that the right purulent cavity was significantly reduced. The patient without discomfort after the removal of thoracic tube was discharged smoothly.

Conclusion: The method of sealing postoperative bronchial stump fistula with oval foramen occluder under VBN provides a new strategy for the interventional treatment of refractory bronchopleural fistulas. Different types of occluders are chosen as the atrial septum occluder, the ventricular septal occluder, and the oval foramen occluder. According to the results of VBN assessment, the bronchial pleural fistula in the patient is characterized by a large fistula diameter and a thin wall. Moreover, oval foramen occluder has the characteristics of small left and right disc spacing and large volume of right disc, and it better matches the fistula mouth of the patient, which is the reason for the successful closure. Such type of occluder needs further improvement in the insertion method and the sealing effect. It is expected that the occlusion device dedicated to bronchial stumps will be available.

Key Words: Bronchopleural fistula, Oval foramen occluder, Virtual bronchoscopic navigation



AP365

PSEUDO-MEIGS' S SYNDROME: CASE REPORT

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Background and Aims: Interventional pulmonology is a rapid evolutionary area in pulmonary medicine. Flexi-rigid pleuroscopy is performed on patient with local anaesthesia under the aid of conscious sedation. Pleuroscopy is a safe procedure with estimated mortality rate around 0.09–0.34%.

Methods: A 29 year-old female presented to our clinic for her right recurrent effusion. She was diagnosed as tuberculosis (TB) 2 years ago with complete treatment. For fear of TB resistance, she was advised to have pleural biopsy for tissue TB culture. Also, chest computed tomography (CT) showed both pleural effusion and ascites. The chest CT did not suggest intrapulmonary lesions. When performing pleuroscopy, there was no lesions such as fibrinous adhesion nor organized fibrin as seen in pleural TB. The effusion revealed exudative in character. Patient then received a series of study including CA125 and gynaecological sonography. Patient then received uterine myomectomy intervention.

Results: The pleuroscopy biopsy did not suggest TB infection. The pleural effusion showed exudative in character. The sonographic study revealed a huge uterine mass (more than 10 cm) with high CA125, 510 U/mL. The effusion resolved after uterine myomectomy. She then was diagnosed as pseudo-Meigs' syndrome.

Conclusion: Pseudo Meigs' syndrome is not common at all. It represents a triad of pleural effusion, ascites, and a gynaecologic tumor except ovarian tumor. The tumor is usually benign. By definition, it lacks of evidence for tumor spreading in peritoneal or pleural cavities (negative pleural and peritoneal fluid cytology and/or no malignant involvement in biopsy samples) and both of ascites and hydrothorax must resolve after tumor removal.

CLINICAL IMPACT OF A NEW 25 GAUGE ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE IN LYMPH NODE STAGING

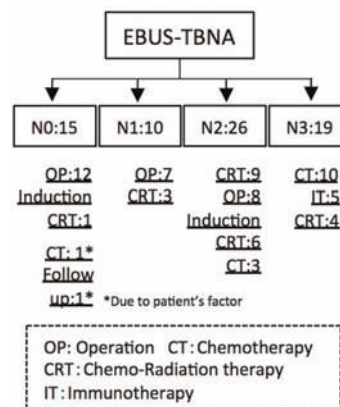
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Background and Aims: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is recommended not only for differential diagnosis but also for lymph node staging. Although 22 gauge needles have been widely used, some stations are often difficult to puncture due to its acute angle (e.g. #2R/L, #3p, #4L, and so on). Meanwhile, a smaller 25 gauge needle has been introduced in Japan at the end of 2016. This needle offers a structural advantage of better flexibility and puncturability. We aimed to validate the clinical impact of this new needle in lymph node staging.

Methods: This is a Cohort designed study enrolling consecutive patients who underwent EBUS-TBNA for lymph node staging using the 25 gauge needle at National Cancer Center Hospital from September 2016 to March 2018. Patients with confirmed stage IV disease were excluded. The following information were collected and analyzed: punctured lesions, sampling rates, results of the staging and the pathology, complications, and treatment policies.

Treatment Policy



Results: Of the 70 eligible patients, 315 punctures were made from 182 lesions (#2R: 20, #2L: 3, #3P: 4, #4R: 45, #4L: 28, #7: 35, #10R: 2, #10L: 4, #11s: 12, #11i: 6, #11L: 19, #12L: 4); by which 277 core tissues were sampled (the sampling rate was 87.9%). All of the lymph node staging were successfully performed without any severe complications; The results were: N0: 15, N1: 10, N2: 26, N3: 19, respectively. Clinical decisions for patients, except two, were determined according to the staging (Figure). On the other hand, 20 cases (38 lymph nodes) had to be verified pathologically by surgical resection. The overall sensitivity, specificity, positive predicted value, and negative predicted value were 88.9% (16/18), 100% (20/20), 100% (16/16), and 90.9% (20/22), respectively.

Conclusion: The new gauge 25 needle has a preferable sampling rate, diagnostic accuracy, and safety. This confers better decisions-making in selecting treatment policies for these patients.

AP367

REMOVAL OF THE HIGH-RISK BRONCHIAL OSSEOUS FOREIGN BODY UNDER VIRTUAL BRONCHOSCOPE NAVIGATION AND FORMULATION

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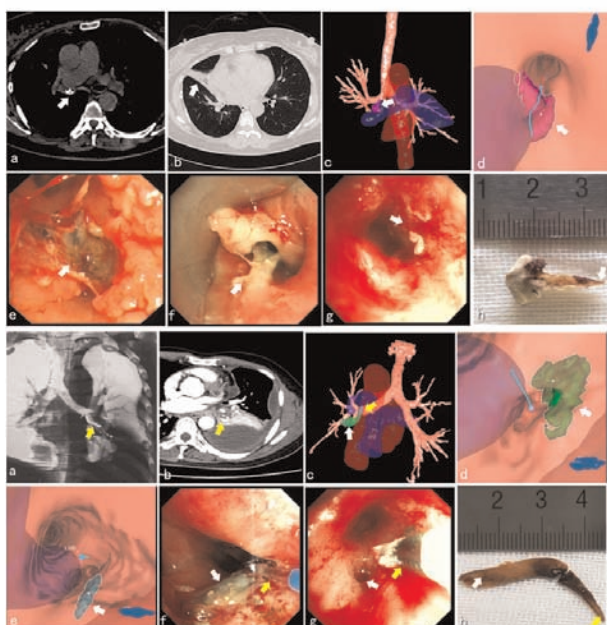
Background and Aims: We report two cases which the high-risk bronchial osseous foreign body was failed to be extracted through flexible bronchoscope but took out successfully with the help of virtual bronchoscope navigation technology. The foreign body was incarcerated in and penetrate the bronchial wall, close to pulmonary artery as well as aorta.

Methods: After the preoperative evaluation and formulation through virtual bronchoscope navigation technology, the advanced therapeutic endoscopic technique was used to extract the airway foreign body.

Results: The foreign bodies were extracted safely and effectively after comprehensive evaluation and surgical planning, thus avoid surgical thoracotomy.

Removal of the high-risk bronchial osseous foreign body under virtual bronchoscope navigation and formulation.

Airway foreign bodies result from aspiration is common in not only children, but also adults. It can be a big osseous foreign body which is incarcerated in or penetrate the bronchial wall. After many failed attempts through bronchoscopy, surgical operation seems to be the only way to deal with this situation, especially when it's close to the great pulmonary vessel. In clinical practice, however, many patients have no chance to receive surgery because of underlying diseases and high risk of complications. So extraction of foreign bodies through natural orifice of bronchus is still the focus of the respiratory endoscopic physicians. This paper reports two cases of patients admitted by ChangHai Hospital, in which the osseous foreign body is incarcerated in and penetrate the bronchial wall, close to large artery and failed to be extracted through flexible bronchoscopy. After preoperative evaluation and formulation with the help of virtual bronchoscope navigation technology, the osseous foreign body were completely, effectively and safely took out using the advanced therapeutic endoscopic technique.



Conclusion: With the help of LungPoint virtual bronchoscope navigation system, we extracted the foreign bodies safely and effectively after comprehensive evaluation and surgical planning, thus avoid surgical thoracotomy. Therefore, as for these kinds of high-risk airway foreign bodies, VBN is recommended as a new tool for preoperative evaluation, formulating surgical scheme or even real time navigation, its value remains to be further applied and summarized in clinical practice.

AP368

THE USEFULNESS OF PLEURAL BIOPSY IN PLEURAL EFFUSION

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Background and Aims: Pleural effusion remains a worrying situation because of the difficulty of etiological diagnosis. Sometimes it is difficult to differentiate between tubercular and malignant pleural effusion. Pleural biopsy is recommended for evaluation and exclusion of infectious aetiologies such as tuberculosis or malignant disease. We conducted a study to evaluate the role of pleural biopsy to determine the aetiology of a lymphocytic exudative pleural effusion.

Methods: It is a prospective study conducted over a period of 10 months from August 2017 till May 2018. Twenty-Six patients of a lymphocytic exudative pleural effusion were selected from Department of medicine "A", Calmette hospital. All included cases were underwent pleural biopsy by Abram's needle. Subsequently, the aetiology of effusion was determined by histopathological examination.

Results: A Total of 26 patients (mean age 57 years; male 42% female 58%) were included. The diagnostic yield was 73%. On histopathological examination, tuberculosis was found in 58%, malignancy 15% and non-specific inflammation in 27%.

Conclusion: Pleural biopsy in minimally invasive and low cost procedure. It is feasible with reliable result, especially in making the diagnosis of tuberculosis or malignancy origin. It is still very useful for low-income countries with high prevalence of TB like Cambodia.

AP369

A NEW TECHNIQUE FOR SELF-EXPANDING METALLIC Y-SHAPED AIRWAY STENTS DEPLOYMENT, SAFE AND SIMPLE

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Background and Aims: Self-expanding metallic Y-shaped airway stents (SEMYS) are frequently used for airway stenosis and fistulae caused by thoracic neoplasm. The standard deployment procedure of SEMYS requires rigid bronchoscopy and fluoroscopy, which are not widely accessible in less privileged areas.

Methods: We have developed a new technique for SEMYS deployment with moderate sedation, under flexible bronchoscopy and without fluoroscopic guidance. An 8 internal diameter endotracheal tube (ETT) is used to secure the airway and to guide the delivery system through the curves around the glottis. The ETT is cut open lengthwise in advance except its distal tip is kept intact. After intubation with the modified ETT, the guide wire is inserted through the ETT, and a flexible bronchoscope is inserted beside the ETT, and subsequently the delivery system is advanced along the guide wire all the way to the carina and deployed under bronoscopic monitor.

Results: By the time of submission, we have completed 16 cases of SEMYS deployment in this method with no major complications.

Conclusion: This technique, safe, simple and swift, improves accessibility of SEMYS in less privileged areas.

AP370

TRANSBRONCHIAL CRYOBIOPSY IN DIFFUSE

PARENCHYMAL LUNG DISEASE: A CHINESE PERSPECTIVE

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Background and Aims: Transbronchial cryobiopsy (TBCB) is an emerging technology of lung biopsy gaining much attention recently in the diagnosis of diffuse parenchymal lung disease. Our respiratory center is the first in China to introduce this technique, and we have made innovative adjustments to meet domestic demands in our experience of over 40 cases.

Methods: The procedures were carried out either with rigid and flexible bronchoscopes at the same time ("combined method") or with flexible bronchoscopes alone ("flexible method"), and no difference between the two methods was observed as for safety and productivity of the procedure. Deflated balloon catheters were not preventively placed except in the flexible method, and fluoroscopy is not utilized. We used 2 original classification systems for bleeding (categorization by the highest level of bronchial tree that blood reaches and categorization by the volume of blood collected by suctioning) in addition to the British Thoracic Society classification, and both new systems indicate severe bleeding with higher sensitivity than the latter.

Results: The procedural adjustments did not compromise safety of the procedure and quality of the specimens. A freezing time of 3–6 s was guaranteed in each biopsy, at least 3 samples were collected for each patient, and complications were under control.

Conclusion: Transbronchial cryobiopsy is a safe and promising approach for lung biopsy. The procedure with or without the rigid barrel were equally safe and productive, and the elimination of fluoroscopy does not compromise safety and productivity of the procedure.

AP371

NOVEL USE OF SPYSCOPE FOR PLACEMENT OF CATHETER IN RIGHT UPPER LOBE TO CONTROL BLEEDING DURING CRYOBIOPSY

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¹PVS Memorial Hospital, India, and ²KIMS Alshifa Hospital, India

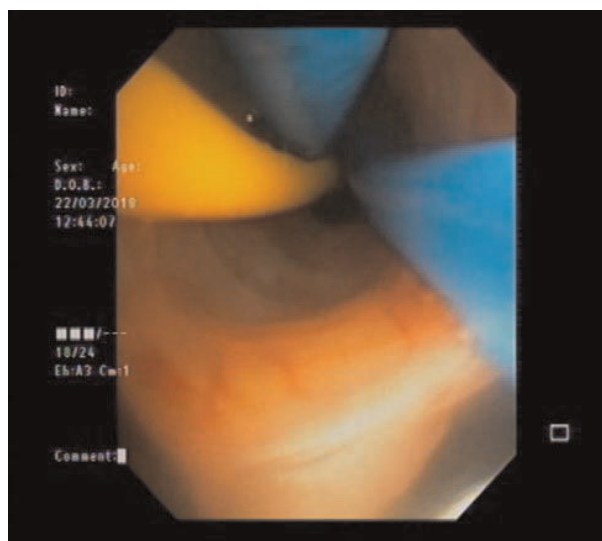
Background and Aims: The incidence of bleeding is more with transbronchial cryobiopsy. Placement of a bronchial blocker proximal to the biopsied segment, which is inflated after each biopsy to control bleeding while the bronchoscope is out of the airway is routinely used. This has the disadvantage of no vision during this period when the catheter inflation is done blindly. This loss of vision can sometimes be dangerous in patients with significant bleeding where further reintroduction of the scope or other measures for control of bleeding may fail. Moreover placement of bronchial blocker into right upper lobe is technically difficult due to angulation. We used Spyscope (Boston scientific) for placement of fogarty catheter into the upper lobe during cryobiopsy in our case.

Methods: Under general anaesthesia, a 7.5 sized rigid bronchoscope was inserted into the airway. A Spyscope attached to a fogarty catheter was placed into the right upper lobe bronchial segments. A fiberoptic

bronchoscope was introduced through the rigid bronchoscope into the right upper lobe. The flexible cryoprobe (erbe) was introduced into the working channel of the bronchoscope and cryo lung biopsies were taken. The fogarty was immediately dilated and kept in situ for 10 s. The Spyscope provided real time video of the airway while the bronchoscope was removed along with the cryoprobe for retrieving the tissue sample. The tissues sent for HPE showed non caseating granulomas suggestive of sarcoidosis.

Results: This technique highlights the advantage of using Spyscope for placement of fogarty catheter in the upper lobe and permits any haemorrhage produced during cryo biopsy to be controlled immediately but, the procedure requires general anaesthesia. However further studies are required to substantiate the advantage of using this novel technique.

Conclusion: We conclude that Spyscope can be used for the placement of catheter into the bronchial segments to control bleeding during cryobiopsy.



AP372

TWO YEARS EXPERIENCE OF INDWELLING PLEURAL CATHETER PLACEMENT FOR MALIGNANT AND RECURRENT PLEURAL EFFUSION IN SONGKLANAGARIND HOSPITAL ASMA NAVASAKULPONG¹

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Background and Aims: Indwelling pleural catheters (IPCs) are established as one of the major tools for the management of malignant or recurrent pleural effusions. Their role has expanded from second-line treatment for malignant effusions with trapped lung or failed pleurodesis to include primary therapy for a number of conditions. IPCs are effective, both in terms of symptom control and costs. We have started using IPCs in our hospital for 2 years and reviewed all IPC placement cases for the efficacy of treatment and complication after IPC placement.

Methods: Retrospective review IPC placement cases from January 1st, 2016 to January 31st, 2018. Baseline characteristics and result of treatment were analyzed for descriptive analysis.

Results: Thirty three cases (22 female, 11 male) were retrospectively reviewed. The median age was 66 years old. 69.7%, 18.8%, 6%, 3% and 3% of cases were advanced stage lung cancer, gynaecologic malignancy, breast cancer, hepatic hydrothorax and amyloidosis, respectively. 54.5% of cases were ECOG 3. 69.7% of cases were trapped lung. Initially

performed weekly drainage in all cases. Mean duration of catheter in place was 79 days. The maximum duration of catheter in place was 245 days. 30.3% of cases were removed catheter after lung expansion. 12% of cases were successfully performed talc pleurodesis as outpatient basis. Complications were transient and correctable. Pain was the predominant complication occurring in 10% of cases lasting 2 days and not required catheter removal for the resolution of discomfort. 6% of cases had empyema thoracis and 1% of cases had cellulitis. Both empyema and cellulitis were successfully treated with antibiotic. 98% of cases were satisfied with catheter stay in place.

Conclusion: Indwelling pleural catheter placement is a useful tool for malignant or recurrent pleural effusion in low income country. It is safe and decreases dyspnic symptom and rate of hospitalization due to pleural effusion.

AP373

DIAGNOSING MALIGNANCIES IN THE LUNG: THE QUALITY OF A BRONCHOSCOPY SERVICE AT A TERTIARY HOSPITAL BAPTI ROY¹*, PETER WU¹

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Background and Aims:

Background: The British Thoracic Society standards for bronchoscopy and EBUS suggest the quality of a service be measured by an "urgent" procedure (including suspected malignancy) being performed within 7 working days, whilst maintaining diagnostic rates for biopsies of >85% for bronchoscopy and >88% for linear EBUS-TBNA, particularly for malignancy.

Aims:

Primary – (i) Assess wait times for "urgent" procedures and (ii) diagnostic rates for malignancy for bronchoscopy and linear EBUS-TBNA.

Secondary – Assess the percentage of biopsy samples which were sufficient for further molecular testing for malignancy.

Methods: Prospective data collection for all patients undergoing bronchoscopy or EBUS over a 5 month period. Cases were followed up for 6 months to confirm a diagnosis of malignancy. Diagnostic rates were defined as 'patients diagnosed with malignancy from bronchoscopic or EBUS biopsy' divided by 'total patients with malignancy confirmed after 6 months follow up'.

Results: 102 bronchoscopy and 48 EBUS cases were performed. Median wait time was 5 days for bronchoscopy and 6 days for EBUS. 56% of bronchoscopies were classified as urgent and 75% were performed within 7 days. Main reason for delay was proceduralist availability (50%). 90% of EBUS cases were classified as urgent and 65% were performed within 7 days. Main reason for delay was needing anaesthetist support (56%). Diagnostic rates for visible tumour with bronchoscopy was 45%, and there was significant variation in type and number of biopsies undertaken. Diagnostic rates for EBUS-TBNA was 92%. Suitable tissue for molecular testing was obtained in 91%.

Conclusion: Overall, only 60% of "urgent" procedures were performed within 7 days, falling short of current standards, highlighting the need for improved scheduling. Malignancy diagnostic rates and sampling adequacy for EBUS-TBNA meets current standards, however fibreoptic bronchoscopy appears to fall short. This may reflect variable sampling techniques during bronchoscopy and a need for standardisation.

BRONCHIAL LEIOMYOMA: A RARE BRONCHIAL TUMOR WITH UNCOMMON PRESENTATION OF RECURRENT HAEMOPTYSIS

MENG-CHENG KO¹*, CHEN-YIU HUNG¹

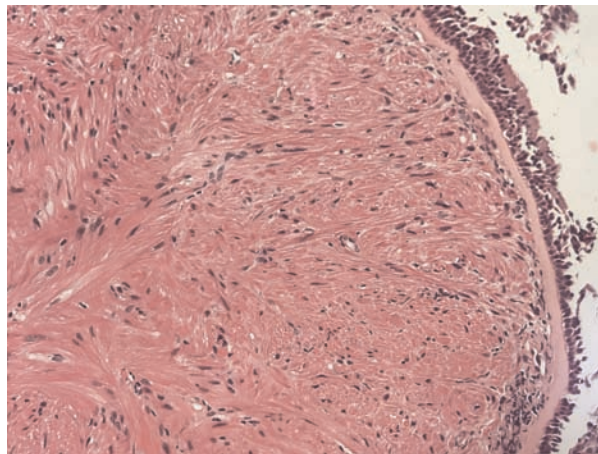
¹Chang Gung Memorial Hospital, Taiwan

Background and Aims: Benign lung tumor are uncommon which comprise 2–5% of all lung tumor. Bronchial leiomyoma is extremely rare. Slow growth rate, absence of haemoptysis, and central airway obstruction were observed as characteristics of benign bronchial tumours.

Methods: We report a 69 year-old cirrhosis female with mild bronchiectasis developed recurrent haemoptysis of unknown aetiology. According to clinical presentation, physical exam, and lab data, no evidence of infection sign, upper airway bleeding, or bleeding tendency was noted. Chest X-ray did not reveal tumor, ground glass opacity, pulmonary edema, nodular lesion, or cardiomegaly either. Since recurrent haemoptysis, chest computed tomography and flexible bronchoscopy were performed.

Results: Computed tomography showed no obvious lung or bronchial mass. However, one smooth, low vascularity, and soft mass lesion measured as 0.6 centimetre at the orifice of RB8 was found during white light bronchoscopy. Autofluorescence image from the same area was not notable for lack of autofluorescence. Biopsy reported bronchial tissue with submucosal nodular proliferation of intersecting fascicles of spindle tumoural cells with eosinophilic cytoplasm. Endobronchial leiomyoma was diagnosed.

Conclusion: Since the tumor lie in the proximal part of right lower lobe, cryotherapy for tumor removal may be suitable for this patient.



AP375

DIAGNOSTIC VALUE OF THORACOSCOPE FOR PLEURAL DISEASES IN INTERNAL MEDICINE

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Background and Aims: Pleural effusion is commonly encountered yet rarely accurately diagnosed by routine examinations during clinical practice of internal medicine. Patients plagued by pleural effusion of uncertain reason were examined by OLYMPUS LTF TYPE 240 electronic thoracoscope thus highlighting the diagnostic value of thoracoscope for pleural diseases in internal medicine.

Methods: From June 2017 to January 2015, clinical data of 81 hospitalized patients (male: 48; female: 33; age ranging: 25–65 years) plagued by pleural effusion of uncertain reason and examined by electronic thoracoscope were retrospectively collected and analyzed. Before electronic thoracoscopic examination, all cases were arranged for examinations including pleural routine, biochemistry, exfoliative cytology and pathogenic microbiology yet failed to be diagnosed of pathogenic reason. Accordingly, 500–1000 mL air were injected into thoracic cavity 1 day ahead of electronic thoracoscopic examination.

Results: Among 81 cases, 79 cases (97.5%) were accurately diagnosed by electronic thoracoscopic examination as shown in the following Results 32 cases of malignant tumor (40.5%) including 24 cases of pleural metastasis of adenocarcinoma and 8 cases pleural endothelioma, with typical presentation of varied tubercles resembling grape, cauliflower, effusion mass or diffuse incrustation under electronic thoracoscope; 41 cases of tuberculous pleurisy (51.9%) with typical presentation of diffuse pleural hyperaemia, multiple grey miliary nodules, pleural adhesion and pachynsis pleurae under electronic thoracoscope; 6 cases (7.6%) of nonspecific pleural inflammation under electronic thoracoscope; 2 cases of uncertain reason without obvious anomaly under electronic thoracoscope as pleural effusion were completed absorbed during 6-month follow-up. Adverse reactions of electronic thoracoscopic examination were classified as: 10 cases of fever (12.3%), 5 cases of pain of operative lesion (6.1%), which were transient and cured by symptomatic treatment. No severe complication.

Conclusion: Electronic thoracoscopic examination is advantageous to clinical practice of internal medicine owing to operation convenience, outstanding security and excellent efficiency, thus remarkably conducive to diagnosis of pleural effusion of uncertain reason.

AP376

CONCURRENT PROCEDURE OF PRIMARY TUMOUR BIOPSY USING NAVIGATIONAL EBUS BRONCHOSCOPY AND LYMPH NODE STAGE USING EBUS-TBNA IN LUNG CANCER

PATIENTS WITH PERIPHERAL AND MEDIASTINAL LESIONS
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Background and Aims: Recently, transbronchial biopsy (TBB) using virtual bronchoscopic navigation (VBN) combined with radial endobronchial ultrasound with a guide sheath (TBB with VBN-EBUS-GS) has improved the diagnostic yield of small peripheral lung cancer (PLC). Owing to these procedures, the examination time of TBB for PLC has been shortened in our institution. Further, we have been performing TBB with VBN-EBUS-GS for PLC and EBUS-guided transbronchial needle aspiration (EBUS-TBNA) for lymph node (LN) staging concurrently. However, an evaluation of these procedures performed concurrently has not been reported. We aimed to evaluate the effectiveness and safety of this one-stage combined procedure.

Methods: We retrospectively assessed 33 cases of lung cancer patients who underwent TBB with VBN-EBUS-GS for PLC and EBUS-TBNA for LN staging concurrently (one-stage procedure) and 31 cases where the procedures were performed on two days (two-stage procedure) from January 2012 to May 2016. The primary endpoints were the diagnostic accuracy of PLC and the total number of LN stations punctured.

Results: There were no significant differences in the median diameter of the major axis of the primary tumour and of the minor axis of the sampled LN between the group of one- and two-stage procedures for patient characteristics. Between the groups, diagnostic accuracy (78.8% vs 87.1%, $P = 0.512$), and the median number of LN stations punctured

(1.0 LN station vs 1.0 LN station, $P = 0.218$) were not significantly different. Total examination time (41.0 min vs 52.0 min, $P < 0.001$) and the median dose of midazolam per procedure (2.0 mg vs 2.5 mg, $P = 0.013$) were significantly different between the groups. There were three complications overall.

Conclusion: This study was the first evaluation on the effectiveness and safety of the one-stage combined procedure compared to the two-stage procedure in bronchoscopy. The one-stage procedure in bronchoscopy seemed to be equally effective and safer.

AP377

AETIOLOGY AND MANAGEMENT OF 131 PATIENTS WITH MAIN TRACHEAL STENOSIS

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Background and Aims: Based on the clinical data of 131 patients with main tracheal stenosis, the aetiology of the patients with main tracheal stenosis, the comparison of interventional therapy and the causes of tracheal restenosis were analyzed.

Methods: The clinical data of patients with primary tracheal stenosis attending the outpatient and inpatient departments of the Second Hospital of Jilin University were collected and analyzed, including causes of stenosis, treatment methods, tracheal restenosis factors and other indicators.

Results: 1. The aetiology of patients with main tracheal stenosis: tracheal tuberculosis was the main cause of benign tracheal stenosis, followed by tracheotomy and tracheal intubation, and the main cause of malignant tracheal stenosis was squamous cell carcinoma, The second was small cell carcinoma .

2. Multi-joint application of various interventional treatment methods, of which balloon dilatation is mainly used in many times and combined.

3. In patients with benign tracheal stenosis, balloon dilation and basal disease were found to be restenosis ($P < 0.05$) by single factor analysis; single factor analysis found no significant correlation between treatment, primary disease and sex and restenosis in malignant patients ($P > 0.05$). The multivariate logistic regression model showed that in patients with benign tracheal stenosis, the factors of restenosis were balloon dilatation and basal disease ($P < 0.05$).

Conclusion: 1. Tracheal tuberculosis accounts for the first place in the aetiology of benign main tracheal stenosis, followed by tracheal intubation and incision. The aetiology of malignant main tracheal stenosis constitutes the first place of squamous cell carcinoma, followed by small cell lung cancer.

2. For patients with scar stenosis, simple balloon dilatation can relieve symptoms, but the long-term effect is poor. It should be repeated and combined with cryotherapy, stent placement and T-tube placement treatment.

3. Patients with benign main tracheal stenosis who have underlying disease and applied balloon dilatation are prone to tracheal restenosis after interventional treatment.

Cell and Molecular Biology 2

AP378

VITEXIN MAY EXERTS ANTI-ALLERGIC INFLAMMATORY EFFECTS VIA ORAI1 CHANNEL INHIBITION

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Background and Aims: Th2 lymphocytes and mast cell are closely linked to allergic airway disease such as bronchial asthma and allergic

rinitis etc. These cells' activity is tightly regulated by intracellular calcium signalling. Therefore, understanding how Th2 lymphocytes and mast cell are regulated by calcium ion channels may provide new approaches in treating allergic airway diseases. In particular, the ORAI1 channel mediated intracellular Ca^{2+} increase is an important driver for the release and synthesis of allergic inflammatory mediators such as histamine, leukotrienes, and cytokines (IL-4, IL-13 etc.).

Spirodela polyrhiza (SP) extract has been reported to have anti-inflammatory and anti-allergic effects, such as the inhibition of pro-inflammatory cytokine secretion and mast cell degranulation. In this study, we examined the effects of the SP extract and its chemical constituents on the modulation of ORAI1 channels to evaluate their potential use as therapeutic agents for the treatment of allergic diseases.

Methods: A 30% ethanol extraction of SP (SP_{EtOH}) was prepared. T lymphocytes and mast cells were treated with the SP extract or its five chemical constituents including vitexin. Modulation of ORAI1 activity was measured using a conventional whole-cell patch-clamp technique.

T cell proliferation assay and β -hexosaminidase assay were performed.

Results: In Jurkat T lymphocytes, we found that 3 mg/mL SP_{EtOH} inhibited I_{CRAC} by $81.0 \pm 11.1\%$, while one of its constituents (vitexin; 100 μM) inhibited I_{CRAC} by $48.9 \pm 8.71\%$. Investigation of human primary T cell proliferation induced by co-stimulation with antibodies to cluster of differentiation 3 and 28 and of RBL-2H3 mast cell degranulation following IgE-antigen complex stimulation revealed that 100 μM vitexin inhibited both T cell proliferation (by $34.8 \pm 6.08\%$) and mast cell degranulation (by $36.7 \pm 0.07\%$); these effects were concentration dependent and no cytotoxicity was observed.

Conclusion: Vitexin represents a candidate for the development of therapeutic agents to prevent and treat allergic airway diseases.

AP379

INHIBITION OF NKCC1 MODULATES INFLAMMATION AND APOPTOSIS OF ALVEOLAR EPITHELIUM IN ISCHEMIA-REPERFUSION LUNG INJURY VIA NF- κ B AND P38 MAPK PATHWAYS

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Background and Aims: The expression of Na-K-2Cl cotransporter 1 (NKCC1) in the alveolar epithelium is responsible for fluid homeostasis in acute lung injury (ALI). Increasing evidence suggests that NKCC1 is associated with inflammation in ALI. We hypothesized that inhibiting NKCC1 would attenuate injury of alveolar epithelium after ischemia-reperfusion (IR) by modulating nuclear factor- κ B (NF- κ B) and p38 mitogen-activated protein kinase (p38 MAPK) pathways.

Methods: IR-ALI was induced by producing 30 min of ischemia followed by 90 min of reperfusion in situ in an isolated and perfused rat lung model. The rats were randomly allotted into four groups comprising two control groups and two IR groups with and without bumetanide. Human alveolar A549 cells were cultured in control and hypoxia-reoxygenation (HR) conditions with or without bumetanide.

Results: In IR-ALI, bumetanide attenuates the activation of epithelial phosphorylated-NKCC1, and significantly attenuated the increases in lung weight gain, vascular filtration coefficient (Kf), the ratio of wet weight to dry weight ratio (W/D) and the ratio of lung weight to body weight (LW/BW) in the IR group. Compared with the control group, NF- κ B p65 and p38 MAPK were increased after IR and HR, which were reduced by bumetanide. The expressions of Bcl-2 and caspase 3 were significantly

lower in HR group than in the control group, which were increased by bumetanide treatment.

Conclusion: Inhibition of NKCC1 by bumetanide attenuated ALI via NF- κ B and p38 MAPK pathways after IR. This interaction may associate with the inflammation and apoptosis of alveolar epithelium in IR-ALI.

AP380

ASSOCIATION BETWEEN CIGARETTE SMOKING STATUS AND COMPOSITION OF GUT MICROBIOTA IN KOREAN MEN

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Background and Aims: Cigarette smoking is known to affect gut microbiota. However, there have been few large scale studies on the relationship between smoking and gut microbiota in relatively healthy people. This study investigated the relationship between smoking status and the composition of human gut microbiota.

Methods: A total of 758 men were selected from a Korean health screening cohort and divided into three groups: never smokers ($n = 288$), former smokers ($n = 267$), and current smokers ($n = 203$). Variable V3 and V4 regions of the 16S rRNA were amplified, and de novo operational taxonomic unit clustering were performed using the UPARSE pipeline. Microbial composition analyses were conducted using QIIME2.

Results: Among the three groups, there was no difference in alpha diversity. However, Jaccard-based beta diversity among the three groups showed significant difference ($P = 0.015$). Pairwise PERMANOVA tests between never and former smokers did not show a difference; however, there was significant difference between never and current smokers ($P = 0.017$) and between former and current smokers ($P = 0.011$). Weighted UniFrac-based beta diversity also showed significant difference among the three groups ($P = 0.038$), and pairwise PERMANOVA analysis of never and current smokers showed significant difference ($P = 0.01$). In analysis of bacterial composition, current smokers had an increased proportion of phylum Bacteroidetes with decreased Firmicutes and Proteobacteria compared with never smokers, whereas there were no differences between former and never smokers.

Conclusion: Gut microbiota composition of current smokers was significantly different from that of never smokers, though there was no difference in terms of alpha diversity. Additionally, there was no difference in gut microbiota composition between never and former smokers.

AP381

THE ROLE OF SODIUM-POTASSIUM-CHLORIDE COTRANSPORTER IN LPS-INDUCED ALVEOLAR MACROPHAGE ACTIVATION

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Background and Aims: Alveolar epithelium plays an important role in both the development of and recovery from acute respiratory distress

syndrome. It has been well known the epithelium ion channels play important role in alveolar fluid homeostasis, under the regulation of inflammation cascades. Activation of sodium-potassium-chloride cotransporter NKCC1 may suppress AFC and may reciprocally modulate inflammatory response. Activation of alveolar macrophages has been recognized as an initiation in the pathogenesis of acute lung injury. In this study we investigated the changes of NKCC1 in macrophage of pneumonia patients and in a mouse macrophage cell line.

Methods: Six patients who were intubated due to acute respiratory failure were enrolled. After completing the informed consent, patients received a bronchoscopy to collect bronchoalveolar lavage fluid (BALF) within 48 h. The BALF was analyzed for alveolar Macrophage P-NKCC1 expression and cytokine production. In cell culture experiment, RAW 264.7 cells were stimulated with LPS (2ug/mL) and p-NKCC1 expression and cytokine production were evaluated.

Results: The expression of p-NKCC1 on alveolar macrophages was increased in patients with pneumonia/ARDS. The BALF protein, LDH, TNF- α , and IL-1 β were also increased. LPS stimulation significantly increased NF κ B expression in RAW 264.7 cells, while pretreated with bumetanide (NKCC1 inhibitor) inhibited the expression of NKCC1, NF κ B, and TLR4 and increased I κ B- α expression.

Conclusion: NKCC1 plays an important role in modulating the activation of alveolar macrophages.

AP382

THE HYPOXIA-INDUCIBLE FACTOR 1 α PROTEIN STABILIZER INHIBITS TRANSFORMING GROWTH FACTOR β -INDUCED EXTRACELLULAR MATRIX PROTEINS BEYOND CELL TYPES AND SPECIES

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Background and Aims: Combined stimulation of persistent hypoxia and transforming growth factor β (TGF β) cause acquisition of epithelial-mesenchymal transition (EMT). Although hypoxia-inducible factor 1 α (HIF1 α) activate the transcription of genes that might be associated with fibrosis development, several studies demonstrate that stabilized hypoxia-inducible factor 1 α (HIF1 α) protein expression might protect from acute lung injury. Thus, whether the stabilized expression of HIF1 α protein negatively regulate TGF β -induced extracellular matrix protein (ECM) production remains elusive. We reassessed the biological role of persistent hypoxia and stabilized HIF1 α expression on TGF β -induced EMT.

Methods: Firstly, we evaluated the effect of HIF1 α -stabilization on TGF β -induced ECM production in human alveolar/epithelial cells treated with prolyl hydroxylase 2 (PHD2) inhibitor. Next, we examined the effect of PHD2 inhibitor on TGF β -induced ECM production in human fibroblasts. Finally, we assessed the effect of PHD2 inhibitor on Rat lung epithelial cells.

Results: Our data showed that stabilized HIF1 α protein expression could repress TGF β -induced ECM production in not only epithelial cells but also fibroblasts. In addition, similar effects were observed in rat alveolar epithelial cells too.

Conclusion: Together, the data indicate that HIF1 α protein stabilization might be a hopeful target for providing a new therapeutic strategy for lung fibrosis.

HETERONEMIN INDUCES ROS-BASED MITOCHONDRIAL-MEDIATED APOPTOSIS IN LUNG CANCER CELLS

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Background and Aims: Substances from marine organism extracts demonstrate more effective at treating cancer cells. Previous studies had demonstrated heteronemin isolated from the sponge Hyrtios sp. induced autophagy and apoptotic cell death in human renal carcinoma cells. However, effects of heteronemin on reactive oxygen species (ROS) formation are still lacking.

Methods: 2'-7'-Dichloro-dihydrofluorescein diacetate (DCFH-DA) and fluorophore MitoSOX Red reagent followed by flow cytometry were selected to test changes of the cellular and mitochondrial redox state, separately. The apoptotic cell death was monitored by TUNEL assay and Annexin V/PI stain. Heteronemin treatment-related changes of protein expression of Bcl-2, Bax, caspase-3 and -9 were examined by western blot. Mitochondrial function was determined through monitoring changes of mitochondrial membrane potential via Rhodamine 123 reagent. Western blot analysis of the release of cytochrome C from mitochondria to cytosol was also conducted. The mitochondrial ROS inhibitor, mitoTEMPO, was used to test roles of mitochondrial ROS in apoptotic induction.

Results: Our data revealed heteronemin significantly suppressed the growth of human lung A549 cells, glioblastoma U87 cell; however, normal gingival fibroblast (HGF) cells were not affected. Heteronemin treatment upregulated Bad, cleaved caspase-3 and -9. The expression of cytosolic cytochrome c was also increased, along with increasing dose of heteronemin. In addition, oxidative stress of mitochondria and percentage of dissipation of mitochondrial membrane were increased after heteronemin treatment. Furthermore, supplementation with mitoTEMP, mitochondrial ROS scavenger, obviously inhibited apoptotic cell death of A549 cells.

Conclusion: Due to increased energy requirement, ROS generation and levels of anti-oxidant proteins are higher in cancer cells, resulting in high oxidative stress. Small molecules with ability to increase intracellular ROS can selectively kill malignant cells. Our results demonstrated for the first time that heteronemin inhibited growth of lung cancer cells via induction of mitochondrial ROS. Heteronemin showed the potential as a novel chemotherapeutic agent.

Clinical Allergy and Immunology 2

AP384

BRONCHOSCOPIC FEATURES OF RELAPSING POLYCHONDROITIS OF LARGE AIRWAYS AFTER TRACHEOSTOMY

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Background and Aims: Relapsing polychondritis (RP) is a rare systemic autoimmune disease characterized by inflammation of cartilaginous structures, particularly of the ears, nose, joints, and large airways. We

report two cases of airway RP that occurred after closure of tracheostomy and presented with similar CT and bronchoscopic features.

Methods: Patient A: a 70-year-old male had a tracheostomy during treatment for pneumonia but had its closure following recovery. Four months later, he developed fever, cough, and wheeze and the CT scan showed tracheobronchial wall thickening. Intravenous corticosteroids promptly eased the symptoms, but recurred after stopping the steroids. Oral prednisolone 20 mg daily was initiated before referral to us. Patient B: a 60-year-old male who underwent emergency surgery for intracranial haemorrhage was complicated by aspiration pneumonia and had a tracheostomy. Following recovery and tracheostomy closure, several months later he developed wheeziness which responded well to oral prednisolone 20 mg daily. CT scan showed thickening of the tracheobronchial walls.

Results: Both patients did not have the characteristic CT findings at the time of tracheostomy procedures. They were referred to our department for further investigation, with clinical suspicion of RP. Bronchoscopy was performed and we found striking resemblance upon airway observation with tracheobronchial wall swelling leading to loss of cartilaginous ridges and fish scale-like appearances. Confirmation of cartilaginous inflammation proved difficult by bronchoscopic biopsy though non-specific inflammatory changes were observed.

Conclusion: Up to 50% of RP cases involve the airways and impose risk of respiratory failure and death. Reports of preceding tracheostomy with subsequent onset of RP is scarce, and the bronchoscopic appearance of the airways in our cases were unique and have not been described previously. Obstructive symptoms after intubation or tracheostomy may be a sign of development of RP. Accumulation of case reports is warranted for prompt recognition and treatment of this potentially life threatening and poorly understood disease.

AP385

ONE-YEAR FOLLOW-UP STUDY OF PHARMACOKINETIC INTERACTIONS IN A TACROLIMUS-TREATED LUNG TRANSPLANT PATIENT

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Background and Aims: Lung transplantation is a well-established treatment for selected patients with end stage lung disease and the tacrolimus (TAC) based immunosuppressive therapy improves post-transplant survival significantly. This study was designed to assess the influence of multiple drug use on the trough concentrations of TAC during the first year after lung transplantation.

Methods: This study was conducted by tracking a lung transplant recipient. We analyzed the pharmacokinetic interactions between TAC and all other drugs for one year after lung transplantation. Assessment items included TAC daily dose (D), whole blood trough level (Co) and renal function. TAC doses were adjusted by keeping the TAC trough level within the

therapeutic range (5–15 ng/mL). We evaluated all suspicious drugs that had been mentioned in the literatures and in the actual clinical status.

Results: Our patient was a 57-year-old woman (36 kg, 155 cm, BMI 15.0) with idiopathic pulmonary fibrosis who had received bilateral lung transplantation on 1st Dec 2016. Seven drugs might affect the TAC trough levels including clarithromycin, diltiazem, esomeprazole, fluconazole, megestrol, metoclopramide and voriconazole in this patient. The stable average Co/D was 1.9 ± 0.7 in the second month after surgery. The drugs that significantly affect TAC were clarithromycin, fluconazole, megestrol and voriconazole. The maximum values of individual Co/D are 23.0, 18.1, 21.2 and 20.2 respectively. During the monitoring period, the patient maintained stable renal function without other adverse events.

Conclusion: TAC is mainly metabolized by cytochrome CYP3A4/5. Lung transplant recipients may receive anti-infective drugs such as clarithromycin, fluconazole and voriconazole which may inhibit the metabolism of enzymes and increase the TAC trough levels substantially. The medications for improving appetite in cachectic patients after surgery such as megestrol may also increase the absorption of TAC. It is very important to closely monitor TAC trough levels and adjust doses of TAC in time for the lung transplant recipients receive culprit drugs.

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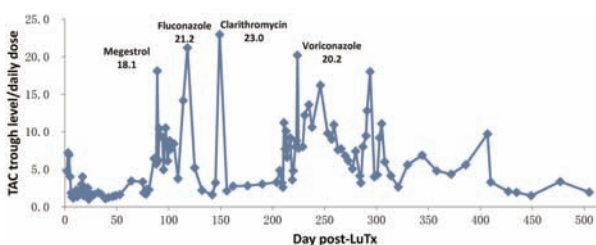


Figure 1. Change in tacrolimus (TAC) trough level and daily dose ratio over time in a lung transplant recipient

AP386

ASIA-PACIFIC SURVEY OF PHYSICIANS ON ASTHMA AND ALLERGIC RHINITIS (ASPAIR) – INDIA RESULTS

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Background and Aims: The Asia-Pacific Survey of Physicians on Asthma and Allergic Rhinitis (ASPAIR) aimed to assess physicians' perceptions and management practices of patients with coexistent asthma and allergic rhinitis (AR).

Methods: This was a cross-sectional survey of general physicians who routinely treat asthma patients (at least 10 a month), in China, India, Malaysia, Philippines, Thailand, and Vietnam. Here we present the data for physicians from India. General physicians ($n = 98$) and paediatricians ($n = 102$) across India were interviewed in-person about their attitudes and beliefs about co-existent asthma-AR, how they manage patients, and their understanding of the GINA and ARIA guidelines.

Results: Most physicians (88%) in India agreed that asthma and AR can co-exists and that patients suffer worse symptoms with both conditions vs one alone. 86% of physicians agreed that guidelines provide sufficient information for treating uncontrolled disease, yet 59% thought that treating

both conditions at the same time effectively was difficult and revealed that 43% of their asthma patients are treated with only quick relief medications and. Even though 85% of physicians agreed that both the asthma and AR symptoms should be treated, a fifth of surveyed physicians managing the most troublesome condition first and only 68% believed that intra-nasal corticosteroids (INS) and inhaled corticosteroids (ICS) should be given concurrently to patients. 55% of the surveyed physicians thought that patients prefer oral medications over inhaled medications and nasal sprays and approximately 36% of believed that the initiation of INS and ICS should be delayed in children for both asthma and AR.

Conclusion: The results from the ASPAIR survey in India highlight the need for increased communication and awareness for appropriate management of co-existent asthma-AR, particularly regarding use of INS and ICS, to improve patient outcomes.

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AP387

METABOLOMIC PROFILING OF SERUM DURING ALLERGEN IMMUNOTHERAPY IN ASTHMATIC CHILDREN

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Background and Aims: Metabolomics was a valuable tool for the discovery of biomarkers and for the elucidation of complex mechanisms in asthma. The aim of this study was to investigate the changes of arachidonic acid metabolites in dust mite sensitized children in allergen-specific immunotherapy (AIT) by metabolomics methods.

Methods: In this study, we enrolled 15 asthma children, 15 Dust mite sensitized asthma children and 10 Dust mite sensitized asthma children, finished three years allergen immunotherapy. All of the serum were processed using ethyl acetate and derivatized using (2-aminoethyl) trimethylammonium chloride hydrochloride (cholamine) reagent, then analyzed and profiled by ultra-high performance liquid chromatography-quadrupole-time of flight/MS (UHPLC-Q-TOF/MS) and reported as relevant concentrations.

Results: The dust mite sensitized asthmatic children group 15 (S), -HETE, 12 (S) -HETE and 5 (S) -HETE showed much higher signal intensity than the healthy children group, suggesting that the three metabolites have the potential of new biomarkers. The dust mite sensitized asthmatic children group 15 (S), -HETE, 12 (S) -HETE and 5 (S) -HETE showed much higher signal intensity than the healthy children group, suggesting that the three metabolites have the potential of new biomarkers. Moreover, in the LOX pathway, the metabolites of asthmatic children were higher than those of the Healthy group. These important metabolite levels increased first and then decreased, OY was higher than 3Y, and 1Y levels were highest

Conclusion: This suggested that HETEs were the potential biomarkers of asthma and Gpx4 might play important role in the regulation of the content of HETEs in asthma human serum, and may be used as biological indicators of therapeutic monitoring during AIT treatment. Corresponding metabolic enzymes (COX and LOX), might be not only involved in asthma pathophysiology but also represent the therapeutic target for AIT.

Clinical Respiratory Medicine 2

AP388

THE ROLE OF HIGH ALTITUDE SIMULATION TEST (HAST) IN PATIENTS WITH PULMONARY DISEASE AND NORMAL OXYGEN SATURATION AT BASELINE

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Background and Aims: HAST is an objective and reliable diagnostic tool that predicts the need for supplemental oxygen during air-travel. The aim of this study is to evaluate the real need of oxygen therapy during air-travel in patients with lung disease and resting oxygen saturation (SpO₂) above 95%.

Methods: This is a retrospective review of all HASTs that were performed in our hospital between 1st January 2015 and 31st July 2017. We excluded pediatric patients and patients with non-pulmonary diseases (cardiac pathologies, neurological pathologies and patients with advanced chronic illnesses). We included patients with pulmonary diagnosis such as asthma, chronic obstructive pulmonary disease, bronchiectasis, lung fibrosis and lung cancer.

Results: A total of 276 HAST results were collected. 209 were for adults, out of which 77 had an underlying pulmonary disease and not on Long term oxygen therapy at home. The median age was 66 years, and 54% of the patients were female. Out of the 77 patients 56 had SpO₂ equal or above 95% and 21 had a SpO₂ below 95%. Among those with SpO₂ equal or above 95%, 45 patients (80%) needed supplemental oxygen therapy with average flow rate of 1.5 L/min. As for the other group with SpO₂ below 95%, all of them needed oxygen therapy during the HAST with an average flow rate of 2.5 L/min.

Conclusion: This study showed that 80% of the patients with pulmonary diseases and normal baseline SpO₂ who underwent HAST required supplemental oxygen therapy during air travel. Further studies are needed to elaborate more on performing routine HAST prior to air travel in patients with serious and/or advanced pulmonary diseases who have a normal oxygen saturation on room air.

AP389

HIGH ATTENUATION AREA ALONG THE BRONCHIAL WALL ON COMPUTED TOMOGRAPHY SUGGESTS THE IRON PILL ASPIRATION

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Background and Aims: The symptoms of iron pill aspiration are non-specific and delay in diagnosis and removal leads to marked mucosal inflammation, necrosis, and bronchial stenosis. Moreover, it is often difficult to make the diagnosis by identifying the aspirated tablets on computed tomography(CT) because the iron pill disintegrates easily after aspiration. We describe 2 cases of serious bronchial injury due to the iron pill aspiration, which showed characteristic high attenuation areas along the bronchial wall.

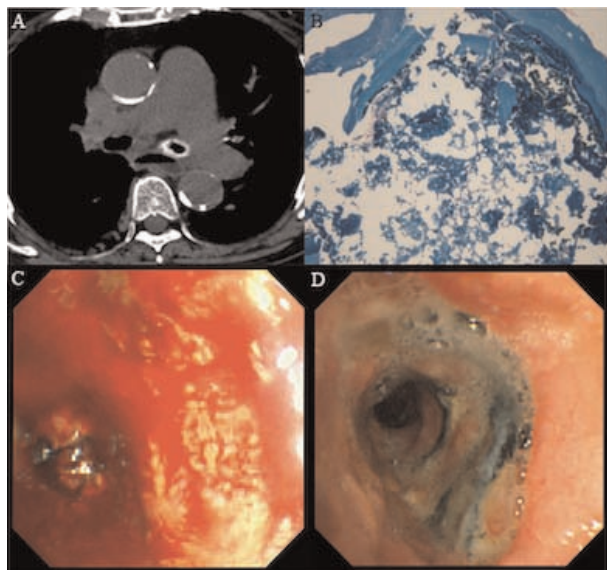
Methods: Case 1: A 91-year-old woman who was admitted to our hospital for dyspnea presented with bilateral wheeze despite normal chest radiograph findings. A chest CT scan showed stenosis of the left main bronchus and a high attenuation lesion around the bronchial wall (Figure 1A). Bronchoscopy revealed nearly total obstruction of the left main bronchus by a pill-like object, which stained positive for iron (Figure 1B). Furthermore, the endobronchial mucosa was haemorrhagic and yellowish-brown in colour (Figure 1C). A detailed history revealed her habit of taking iron tablets. One month after, bronchoscopy showed necrosis of the bronchial cartilage (Figure 1D).

Case 2: An 82-year-old man who had been on oral iron supplement for anaemia presented to our hospital with progressive cough and shortness

of breath. A chest CT scan showed a foreign body in the right middle lobe bronchus and same high density area along the bronchial wall. Bronchoscopy revealed similar bronchial injury and the biopsy tissue of bronchial mucosa demonstrated extensive inflammation, necrosis, and diffuse permeation by golden-brown fibrillary structures that stained positive for iron.

Results: Both cases showed the high attenuation areas along the bronchial wall corresponding with iron deposits and inflammations of the bronchial mucosa.

Conclusion: High density lesions along the bronchial wall on CT scan may serve as a clue to diagnosis, to be a suggestive of an iron deposition.



AP390

ACCURACY OF A SONOGRAPHIC SCORING INDEX IN THE CLASSIFICATION OF PLEURAL EFFUSION

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Background and Aims: Nowadays, there has been an increasing interest in the use of ultrasound for the evaluation of chest diseases especially in examining pleural effusions and sonographic appearances are helpful in determining the nature of pleural effusion. It will allow to diagnose a variety of thoracic disorders at the point of care and avoid waiting time to do therapeutic management right away, like inserting chest catheter/tube or do VATS and minimize costing for unnecessary tests in the analysis of the pleural fluid. In this context, the utility of sonographic appearances alone in the diagnosis of pleural effusion is now being well documented by using the Light's criteria as the reference standard.

Methods: Retrospective, Cross Sectional study

Presence of each of the sonographic features will be given a score of 1: homogeneously echogenic, echo floaters, fibrin strands, thickened pleura, consolidation, loculations, unilateral effusion.

Results: We have a total of 135 subjects and 76 have exudative effusion based on Lights criteria. Different cross tabulations were conducted to determine the accuracy of sonographic scoring index and a score of ≥ 3 points (42 subjects under exudative effusion) yielded the most acceptable

results significant at 0.005 ($P = 0.003$) with sensitivity of 55.3%, specificity of 71.2%.

Conclusion: Based on the results of the study, the sonographic scoring system is a fair test to diagnose exudative effusion. But if this test will be used, based on the coordinates of the curve, the cutoff value should be lowered to 2.5 to 3 to have a sensitivity of 55.3% and a specificity of 71.2%. Larger prospective studies are required in order to validate and improve present findings. Pulmonologist and Sonologist may work together at the same time when thoracentesis is to be done to yield better outcome.

AP391

NIPPV (NON INVASIVE POSITIVE PRESSURE VENTILATION) CAN IMPROVE THE CLINICAL OUTCOMES OF THORACIC SURGERY PATIENTS

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Background and Aims: In the past, non-invasive positive pressure ventilation (NIPPV) was used in chronic respiratory failure patients, such as spinal cord injury, congenital muscular dystrophy. The advantages of NIPPV are non-invasive and can decrease the complications of invasive ventilators, such as ventilator associated pneumonia and sedation used. In recent decades, NIPPV also can be used to treat acute respiratory failure. Evidences show that NIPPV had great benefits in COPD acute exacerbation, ventilator weaning of COPD patients, cardiogenic pulmonary edema and immunocompromised patients. The surgical wound pain usually influences the cough and respiratory function of thoracic surgery patients. These poor cough function can increase the occurrence of pneumonia and atelectasis that will prolong the admission days and cost subsequently. Recent research had shown that application of NIPPV in thoracic surgery patients can reduce the complication of post-surgery and accelerate the recovery of lung function.

Methods: A retrospective study had included total 182 thoracic surgery patients during 2015–2018. Control group was 97 patients and NIPPV group was 85 patients. NIPPV via mouth piece was used twice for all thoracic surgery patients daily for 3 days. Each time is 20–30 min.

Results: The length of hospital stay of control and intervention group was 10.11 ± 6.32 days vs 8.60 ± 4.58 ($P = 0.07$) respectively. For the lung resection subgroup, the length of hospital stay of intervention was significantly shortened as compared to control group. (9.86 ± 6.48 days vs 7.45 ± 3.36 days, $P = 0.01$) The percentage of post operation bronchoscopy intervention was also significantly decreased from 7.37% to 1.15% ($P = 0.03$) after NIPPV application.

Conclusion: NIPPV via mouth piece is a comfortable and simple method to provide lung expansion therapy. Post operation NIPPV intervention can significantly shorten the length of stay in lung resection patients and decrease the use the bronchoscope for airway toilet.

AP392

IMPROVEMENT QUALITY OF LIFE IN MEDIASTINAL SOLITARY FIBROUS TUMOR PATIENT: CHEMOTHERAPY PALLIATIVE PERSPECTIVE

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Background and Aims: Mediastinal solitary fibrous tumor (MSFT) is a rare spindle cell neoplasm. Approximately 1 to 8% of these intrathoracic tumours have been reported to occur in the mediastinum. The chief complaints of MSFT are cough, shortness of breath or chest pain, or may occur as asymptomatic incidental mass. The treatment of choice for solitary fibrous tumor is extensive surgical resection. However, when tumor cannot be removed surgically or when metastases occur, chemotherapy and/or radiotherapy can be proposed as palliative treatments.

Methods: Descriptive.

Results: A 19-year-old man, with chief complaint left chest pain and referred to his left back. The complaint is accompanied by a cough without sputum and hoarseness. In the immunohistochemical staining analysis, positive tumor cell cytoplasm results in vimentin, negative tumor cell cytoplasm in CK, positive tumor cell membrane on CD99, cytoplasm of focal positive tumor cells in EMA and negative tumor cells on CD34 which support a solitary fibrous tumor. Doxorubicin-ifosfamide regimen is the choice of chemotherapy palliative treatment in our case report. In the CT scan evaluation of thorax with contrast, we found stable disease (RECIST criteria) with quality of life according to EQ-5D-3L, 11111 indicated no problems in 5 dimensions such as mobility, self-care, usual activities, pain or discomfort and anxiety or depression.

Conclusion: Mediastinal solitary fibrous tumor is a rare spindle cell neoplasm, and the diagnosis requires pathological and immunohistochemical staining analysis. Chemotherapy and/or radiotherapy can be proposed as palliative treatments. EQ-5D is a simple tool that can be used to measure quality of life such as mobility, self-care, usual activities, pain or discomfort and anxiety or depression.

AP393

THE ROLE OF IMMUNOHISTOCHEMISTRY IN A MALIGNANT PLEURAL EFFUSION FROM AN OCCULT PAPILLARY THYROID CARCINOMA: A CASE REPORT

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Background and Aims: Metastatic pleural effusion as the initial manifestation in well-differentiated thyroid cancer is reported very rarely with prevalence to be less than 0.6%. Identifying the malignant cells in a pleural effusion from a thyroid primary is often challenging; hence cytomorphological studies can be helpful. Here, we report a case of papillary thyroid cancer initially presenting with massive pleural effusion.

Methods: This was a case of a 68 year old, female, known hypertensive, diabetic and hypothyroid who was noted to have worsening exertional dyspnea associated with weight loss, occasional cough and back pain on upper thoracic area. Chest X-ray was requested and showed massive pleural effusion.

Results: She underwent thoracentesis. Pleural fluid analysis were negative for malignant cells. She was readmitted for VATS with chest tube insertion and pleural biopsy. Histopathology report showed adenocarcinoma, moderately differentiated, metastatic and recommended immunohistochemical stains. Results were positive for CK 7, PAX 8, TTF-1, and WT-1 and negative for CK-20, GCDPF-15, GATA 3, Napsin A and CK 5/6. This favour lung and thyroid as probable site of primary malignancy. Fine needle aspiration biopsy of thyroid nodules was done and showed cytomorphologic features for papillary thyroid carcinoma. She also underwent CT guided biopsy of lung mass with immunostaining to rule out primary non-small cell lung carcinoma. Results showed

thyroglobulin to be negative but with strongly positive PAX-8 which favour thyroid carcinoma.

Conclusion: Malignant pleural effusions are caused most commonly in patients with breast, primary lung or lymphoid malignancy. Papillary thyroid carcinoma has generally good outcome but patient presenting with malignant pleural effusion is exceedingly rare and is associated with significant morbidity and worsening survival. Median survival had been reported to be from 3 to 12 months. Its clinical course has not been well described in the literature as well as its treatment recommendations.

AP394

SUCCESSFUL MANAGEMENT OF LEPTOSPIROSIS ASSOCIATED DIFFUSE ALVEOLAR HEMORRHAGE USING AN EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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Background and Aims: Acute pulmonary haemorrhage (APH) is an uncommon yet potentially fatal complication of Leptospirosis with 60–70% mortality despite maximum care. Authors present a case of a 34-year-old man with APH due to leptospirosis with refractory respiratory failure successfully managed with veno-venous ECMO.

Methods: A 34-year-old previously well labourer presented with a five day history of fever with myalgia and headache. On admission, he was febrile (101 F), tachycardia and had conjunctival injection. Examination of lungs and abdomen was unremarkable.

He was clinically suspected to have leptospirosis and initially managed with IV C. Penicillin. Investigations revealed thrombocytopenia, neutrophil leukocytosis, high total bilirubin, marginal elevation of transaminases, high serum creatinine. Six h later patient developed oliguria, hypotension and respiratory distress. ABG revealed a Ph of 7.46, pO₂ of 71 mmHg, PCO₂ 17.5, HCO₃ 12.8 mmol/L. Initial chest radiograph was normal. Patient was started on haemodialysis due to oliguric renal failure complicated with acidosis. Subsequent chest radiographs showed diffuse alveolar shadows suggestive of APH and he required assisted ventilation. Patient was treated with IV Methylprednisolone 1 g daily for three days and subjected to three cycles of plasma exchange. The patient's respiration deteriorated with progressive alveolar infiltration and arterial hypoxia despite maximum respiratory care. Patient was commenced on ECMO on the third day of admission and the procedure was continued for 6 days.

Results: After 14 days of supportive therapy he was successfully weaned off and he left the hospital fully recovered. Serology with a MAT revealed serovar bakeri with a titre of 1:640

Conclusion: DAH is a life threatening complication with a high morbidity and mortality. ECMO can be used as life saving measure when other supportive measures fail

AP395

RESPIRATORY EVENTS AND PROGNOSIS DURING PREGNANCY AND PERIPARTUM

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Background and Aims: The aim of this study was to investigate clinical features and identify maternal factors contributing to prognosis in women with pulmonary complications during pregnancy and the peripartum period.

Methods: Following a retrospective review of clinical data and radiographic findings between January 2006 and January 2016, 126 women diagnosed with pulmonary complications during pregnancy ($N = 79$) and peripartum within the first 4 weeks after delivery ($N = 47$) were enrolled in this study.

Results: Of the 126 patients, 113 (89.7%) required hospitalization. The median age was 32 years and the percentage of primiparous women was 49.2%. The most common respiratory complaint was dyspnea, followed by cough and fever. Pneumonia developed in 50 patients (39.6%), pulmonary edema in 31 (24.6%), pleural effusion in 28 (22.2%), active pulmonary tuberculosis in 13 (10.3%), and asthma exacerbation in 4 (3.1%). Among the 79 antenatal patients with pulmonary complications, 31 (39.2%) experienced pregnancy-related complications, 21 (26.6%) had an emergency C-section, and 29 (36.7%) had an adverse fetal outcome. Eleven patients (8.7%) developed acute respiratory failure requiring mechanical ventilation and the overall mortality was 1.6% (2/126) with no pulmonary complication-related deaths. Multiple regression analysis revealed the presence of pregnancy-related complications and younger fetal gestational age at diagnosis were independent predictive factors for adverse fetal outcomes.

Conclusion: Pulmonary complications during pregnancy and the peripartum period resulted in poor outcomes and the risk of adverse fetal outcomes was high, particularly in patients with pregnancy-related complications and younger gestational age at diagnosis.

AP396

COMPARISON THE PULMONARY CAPACITY IN LUNG TRANSPLANTATION PATIENTS WITH AND WITHOUT PRE-TRANSPLANTATION PULMONARY REHABILITATION

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Background and Aims: Lung transplantation is an option for some individuals with end-stage lung disease. Individuals living with end-stage lung disease already are deconditioned, with poor endurance and limited exercise capacity. Pulmonary rehabilitation (PR) of lung transplant candidates and recipients plays an important in optimizing physical function prior to transplant and facilitating recovery of function post-transplant. The role of pre- and post-lung transplant PR is to maintain and improve exercise capacity, lung mechanism, peripheral- and respiratory muscle function. The aim of this study is to compare the pulmonary capacity in lung transplantation patients with and without pre-transplant PR.

Methods: Lung transplantation patients were retrospectively included for study from June 2016 to March 2018 at a tertiary medical center in Taiwan. All of the lung transplantations received pre and/or post-transplantation PR. The PR program consisted of bronchial hygiene therapy, control breathing techniques and personalized exercises of 30–40 min per day for 3 months. Pulmonary function test and 6 minutes walking distance were measured 3 months before and after lung transplantation.

Results: Totally 7 patients were investigated including idiopathic pulmonary fibrosis in 4 patients, idiopathic pulmonary arterial hypertension in 2 patients, the chronic obstructive pulmonary disease in 1 patient and systemic sclerosis in 1 patient. These 7 patients were divided into two groups. The group 1 included 4 patients who were participated in pre- and post-transplant PR. The group 2 included 3 patients who were participated only post-transplant PR. At 3 months post-transplantation, the 6 minute walking distance, FEV1, FVC and FEV1/FVC between these two groups were 369 vs 191 m, 1.7 L (68%) vs 1.4 L (64.5%), 1.8 L (59%) vs 1.8 L (65%) and 92.3% vs 81.6%, respectively.

Conclusion: For the lung transplantation patients, pre-transplantation PR is effective and can improve exercise capacity with a significantly longer 6-minute walking distance.

LATE-PRESENTING CONGENITAL DIAPHRAGMATIC HERNIA IN A 4-YEAR-OLD MALE: AN INCIDENTAL FINDING

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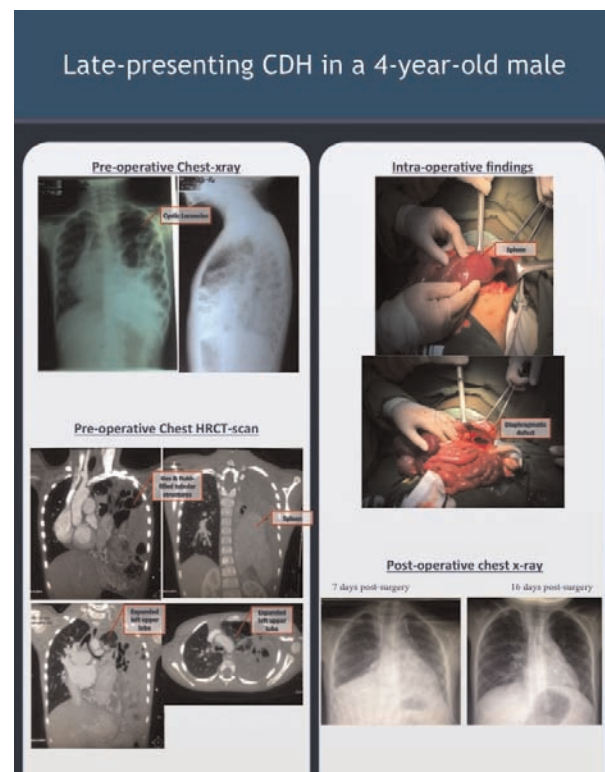
Background and Aims: Congenital diaphragmatic hernia (CDH) accounts for about 8% of the major congenital anomaly and contributes to 1–2% of infant mortality. CDH presents most frequently in the neonatal period. However, about 5–30% presents beyond the neonatal period or otherwise known as late-presenting CDH.

Methods: This patient is a 4-year-old male with an incidental radiologic findings of unilateral cystic lucencies. There was an unremarkable neonatal period. Episodes of tachypnea were noted during respiratory illnesses but the patient was playful in interim. He was also usually constipated. There was no previous admission nor any chest radiograph taken.

Three months prior to admission, the patient was admitted at a tertiary hospital for dengue fever and cough. Chest x-ray taken showed the presence of cystic lucencies on the left hemithorax. Referral to a pediatric pulmonologist was done. A high-resolution chest CT-scan taken showed the presence of left diaphragmatic hernia, Bochdaleck type.

Results: The patient was referred to surgery and repair was done after cardiopulmonary clearance. Post-operatively, the patient was extubated within 24 h and was given O2 support for 3 days. The patient was eventually discharged after 9 post-operative days.

Late-presenting CDH usually becomes symptomatic after 1 month of age. The current data suggests that these patients commonly presents with gastrointestinal symptoms. They also have vague symptoms thus are diagnosed late. In our case, the patient had intermittent episodes of tachypnea and constipation.



Regardless of its presentation, late-presenting CDH should be repaired as soon as possible. However, a cardiopulmonary evaluation should be done prior to surgery as associated anomalies in late-presenting CDH

ranges from 8.6–80%. In general, late presenting CDH has an excellent prognosis postoperatively.

Conclusion: Late-presenting CDH should be considered in any child beyond neonatal period presenting with respiratory and gastrointestinal symptoms. A chest radiograph should be a good screening tool for this patients with high-index of suspicion.

AP398

EVALUATION OF INHALED DRUG PROCEDURE AMONG PATIENTS WITH ASTHMA OR COPD

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Background and Aims: Patients suffering from obstructive lung diseases are increasing. Long-acting inhaler is the main stream of their treatment. Here, inhalation device operation manoeuvre was assessed by an out-of-hospital pharmacist, and evaluated in relation to patient characteristics.

Methods: Subjects were gathered from our clinic from May 2014 to July 2017. Steps in inhalation procedure are as follows; drug preparation, full exhalation, inhalation of drug, breath holding, relaxation, cleaning up. Depending on their familiarity, each step was evaluated by 0 to 3 points, then sum up the total points. The correlations were calculated between total procedure evaluation points and the patient characteristics.

Results: Total evaluation points' median was 18 (17–18) [9–18]. Older, male, more inhaler device use, high number of comorbidities patients tended to have lower points. Patients with asthma had higher points than COPD (full score; 91.7% vs 44.4%). About the devices; pMDI had the highest points, followed by Ellipta[®] and Turbuhaler[®]. Frequent inhalation training showed weak positive correlation ($r = 0.143$). Lower KPS population had their skill established more than higher KPS patients. This might occur because their procedure had the chances to be checked by their caregiver.

Conclusion: Frequent inhalation training is important for patients with obstructive lung disease, especially they are elderly, several device use, COPD and have high number of comorbidities.

Sex(N)	Female:11, Male:19
Diagnosis	Asthma:12, COPD:11, others:7
Karnofsky Performance Score (KPS)	90:15, 80:5, 70:4, 60:4, 40:4
	Median (range)
Age	74 (56-89)
Follow up frequency (N/year)	4 (1-4)
%FVC (%)	91.4 (50.2-112.0)
%FEV1 (%)	69.1 (46.5-110.0)

AP399

THE CAUSE OF DYSPNEA WAS DIAGNOSED DURING EMERGENT ENDOTRACHEAL INTUBATION: A CASE REPORT OF TRACHEA, STENOSIS

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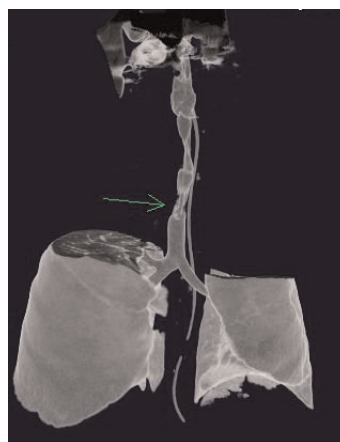
Background and Aims: A 59-year-old woman came to the emergent department of our hospital because of dyspnea for one day. The physical examination revealed stridor and wheezing. At the emergent

room, the blood gas showed respiratory acidosis. She was admitted to intensive care unit and non-invasive ventilation was given. She had no asthma or COPD history. Four months earlier before admission, she was injured in a traffic accident. She underwent endotracheal intubation and emergent surgery.

Methods: After ICU admission, intravenous antibiotics, intravenous methylprednisolone, and inhaled bronchodilator were prescribed. The otolaryngologist was consulted to screen the patient for any potential underlying vocal cord dysfunction, but the result was negative. Because her symptoms improved, she was transferred to the ordinary ward.

Results: Unfortunately, the patient developed respiratory distress and desaturation suddenly. We did emergent endotracheal intubation, but the endotracheal cannot pass through her trachea. A computed tomographic scan showed tracheal stenosis. Her symptoms were resolved after tracheal dilation and stent replacement.

Conclusion: In conclusion, post-intubation tracheal stenosis should be considered as a cause of unexplained dyspnea with hypercapnic respiratory failure.



AP400

SOCIAL MEDIA IN ACADEMIC PULMONOLOGY : #PCCP2018 EXPERIENCE

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Background and Aims: In the advent of modern technology, social media and web-based education, the Philippine College of Chest Physicians (PCCP) embarked on a program to educate its members to maximise the use of social media (particularly twitter) for its annual convention entitled Master Pulmonary Medicine with the hashtag #pccp2018. The annual convention was held last March 11–14, 2018. Focus was given to twitter to stimulate more engagement among the attendees in the convention particularly among the pulmonary fellows in training.

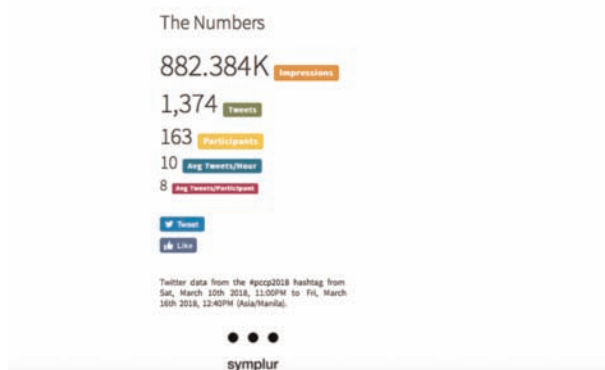
Methods: One major intervention that gave rise to the significant increase in twitter activity for PCCP is the GEEK (Generating Efficient ways to Enrich Knowledge) camp which ran three times prior to the convention. 103 attendees were introduced to various social media platforms and types of infographics, shown how to effectively utilise evidence-based articles, and to use google efficiently maximising its features. Ethical practice in social media was also an integral part of the course. Attendees include the officers, senior members and pulmonary fellows in training of PCCP.

Results: Based on Symplur data, tweets posted on the dates surrounding the convention generated 1374 tweets from 163 participants with 882,384 impressions.

Compared to #pccp2016 with 85 tweets and #pccp2017 with 57 tweets although they were not yet registered with Symplur. This reflected a 20× increase in the number of tweets, most likely also in the number of participants.

Conclusion: Instead of waiting to discuss about the information shared during the conference twitter can reach more people in more places through social media, which stimulates real-time interaction and exchange of ideas. The implementation of the GEEK camp significantly improved not only the attendance to the convention but also the interaction among the attendees based on the increasing number of tweets and the continuous activity of the PCCP twitter handle at the present time.

Table 1 Summary of Twitter data during the PCCP 2018 Annual Convention. Data from symplur



AP401

INHALER TECHNIQUE TRAINING FOR PATIENTS WITH RESPIRATORY DISEASES, SUPPORTED BY REHABILITATION THERAPISTS

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Background and Aims: The correct steps for use of inhaler devices are essential for the treatment of chronic obstructive pulmonary disease (COPD) and bronchial asthma. In our hospital, physical and occupational therapists have started to provide supportive inhaler technique training to the patients with COPD or asthma, in cooperation with medical doctors and pharmacists. The purpose of this study was to investigate the factors which affected the acquisition of inhaler technique after receiving the training.

Methods: From April 2015 to March 2017, there were 95 patients with COPD or asthma who had received inhaler technique training by physical and occupational therapists. We retrospectively investigated data on age, sex, inhaler device type, training times, cognitive functions, and inhaler technique through the clinical records. The inhaler technique was assessed face-to-face using dummy inhalers, with the standardized checklists for each device. Cognitive functions were assessed by Mini-Mental State Examination. We used Mann-Whitney U test to compare the median of continuous variables and Fisher's exact test to compare categorical variables.

Results: Before the training, 87% of the patients were evaluated and categorized into the incorrect steps group. After receiving the training, 67% of these patients acquired the correct steps for use of inhaler devices. The patients who acquired the correct steps were significantly younger ($P = 0.006$), and had higher cognitive functions than those who failed to master the steps ($P < 0.001$). The number of the training sessions tended to be larger in the correct users than in the incorrect users (median: 10 and 6, respectively; $P = 0.091$).

Conclusion: The results suggest that repeated training is effective for mastering the correct steps for use of the inhaler devices. Patients with high cognitive function were able to master the correct steps for the use of inhaler devices.

AP402

QUALITY ASSESSMENT OF CLINICAL PRACTICE GUIDELINES FOR RESPIRATORY DISEASES IN CHINA IN 2017

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Background and Aims: The overall quality of CPGs for respiratory diseases in China from 2013 to 2017 is slightly higher than CPGs from 1987 to 2013. It was pretty low and could be improved, especially in Rigor of development, Applicability and Editorial independence. Most guidelines were based on low-quality evidence. The development and publication of guidelines need to be refined effectively.

Methods: We searched WanFang Data, CNKI, VIP and CBM databases and websites like China Health and Family Planning Commission, Chinese Medical Association, China Association of Chinese Medicine, China Guideline Clearinghouse, Medlive and others. Assess the quality of eligible guidelines using AGREE II instrument.

Results: A total of 31 guidelines were included. The scores of the six AGREEII domains were: scope and purpose 59.4%, stakeholder involvement 25.3%, rigor of development 11.7%, clarity and presentation 59.1%, applicability 26.6%, and editorial independence 7.7%. Only 1 guideline was recommended for clinical use, 2 guidelines were recommended with modification and the rest were not recommended.

Table 1. AGREE II Domain Scores for the Guidelines Included

Domain	Mean $\pm$ SD (%)	Range (%)	Score $\leq 30\%$, No. (%)	Score $\geq 60\%$, No. (%)
Scope and purpose	59.4 $\pm$ 5.2	50.0 – 72.2	0 (0)	11 (35)
Stakeholder involvement	25.3 $\pm$ 8.1	16.7 – 65.3	28 (90)	1 (3)
Rigor of development	11.7 $\pm$ 10.2	4.2 – 53.6	28 (90)	0 (0)
Clarity and presentation	59.1 $\pm$ 4.7	51.4 – 73.6	0 (0)	11 (35)
Applicability	26.6 $\pm$ 6.8	18.8 – 54.2	23 (74)	0 (0)
Editorial independence	7.7 $\pm$ 18.5	0 – 100.0	30 (97)	1 (3)

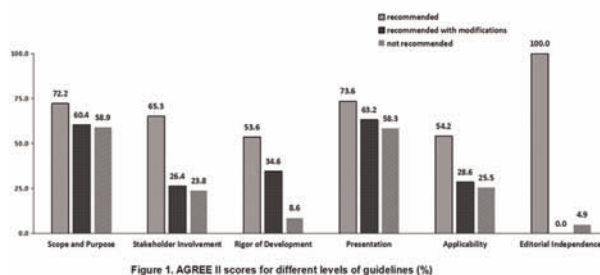


Figure 1. AGREE II scores for different levels of guidelines (%)

Conclusion: The overall quality of Chinese CPGs for respiratory diseases published in 2017 is low, particularly in stakeholder involvement, rigor of development, applicability, and editorial independence. More attention should be paid to the rigor of the guideline development method, the report specification, the practicality of the content and the

standardized training of the relevant development personnel in the formulation of the future CPGs.

AP403

CATAMENIAL PNEUMOTHORAX IN THREE FILIPINO FEMALES: A CASE SERIES

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Background and Aims: Catamenial Pneumothorax is a rare condition defined as a recurrent accumulation of air in the pleural cavity in reproductive age women without concomitant respiratory diseases, occurring in the period 72 h before or after the menses. The most common theory for pathogenesis is thoracic endometriosis, or the presence of ectopic endometrial tissue inside the thoracic cavity.

Methods: Case Series

Results: Between April 2017 and April 2018, three females were admitted to Cardinal Santos Medical Center, each presenting as sudden onset dyspnea during the menstrual period and diagnosed with catamenial pneumothorax. Two of them presented with recurrent cyclical dyspnea and a pertinent medical history of endometriosis. Two of the patients underwent chest tube insertion and all were given supplemental oxygen with eventual resolution of the pneumothorax. Two of the subjects were advised video-assisted thoracoscopic surgery and hormonal therapy. The last patient was admitted during her first episode of pneumothorax and is still being monitored for recurrence.

Conclusion: Catamenial Pneumothorax remains underdiagnosed but should be suspected in reproductive age women who present with cyclical dyspnea during the perimenstrual period. Treatment may involve oxygen supplementation; however, surgery remains the treatment of choice for Catamenial Pneumothorax. Due to the unique characteristics of the disease, it is recommended that treatment be conducted by multi-specialist teams.

AP404

FEATURES OF RADIOLOGIC DIAGNOSTICS OF RESPIRATORY CYSTIC FIBROSIS FIRST DIAGNOSED IN ADOLESCENCE

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Background and Aims: Respiratory cystic fibrosis (CF) at the age of 18 is diagnosed only in 3% from the general number of patients and in 11% from the number of adults. A provisional diagnosis is firstly done with computed tomography in the majority of cases. We aimed to assess the diagnostic efficiency of multispiral computed tomography (MSCT) with post-processing for the first identification of CF and to analyze typical radiologic patterns.

Methods: Under our observation during 7 years there were 8 patients with CF from 18 till 27 years old. To verify the diagnosis besides the sweat test there was done a genetic study. Four patients were diagnosed at the early childhood, and three only in adolescence first time. These patients had the disease disguised under recurrent bronchitis, obstructive pulmonary diseases, congenital polycystosis.

Results: The patients with CF diagnosed after 18 years old had a heterozygous mutation of the gene *CFTR* c.2657+5G>A, and the patients who were diagnosed in the childhood had a homozygotic type. Typical MSCT patterns for CF were systemized: bilateral total system damage of bronchopulmonary structures; intensive, more than 250% from the initial

sizes, dilation of bronchi of all generations with thickening and carnification of their walls; cross striation of the mucosa; sciagram patterns of "cricoids" under vertical projection of bronchi towards the axis of the tomographic section and "paired lines" under horizontal (coaxial with the tomographic section) placing of bronchi; filling of extended bronchi of all calibers with mucoid plugs; peribronchial infiltration and fibrosis of the lung tissue; mosaic perfusion; multiple round infiltrative focuses. Diagnostic sensitivity of the total of the patterns for CF was 100%, and specificity was 91%.

Conclusion: These patterns are quite specific for CF, which allows to conduct, taking into account the clinical data, a sure differential diagnosis with other respiratory diseases on the basis of MSCT data.

AP405

CORRELATION OF FORCED EXPIRATORY FLOW (FEF) 25-75% AND THE NUMBER OF PACK-YEARS AMONG SMOKERS

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Table I. Baseline Demographics and Clinical Characteristics

Characteristic (N=82)	FEV1/FVC ≥ 70 (n=29)	FEV1/FVC < 70 (n=53)	p value
Age, in years ($\bar{x} \pm SD$)	52 ± 13	64 ± 11	0.001
Gender			
Male	48	29	0.156
Female	5	0	
Weight, $\bar{x}$ in <u>kgs</u>	66.01 ± 14.80	69.56 ± 14.07	0.294
Height, $\bar{x}$ in <u>cms</u>	162.54 ± 6.87	165.93 ± 5.95	0.028
Body Mass Index (BMI) kg/m ²	25.04 ± 4.97	25.08 ± 4.69	0.971
Smoking history, pack years			
< 10 pack years	15	2	0.024
≥ 10 pack years	38	27	
Age started	17 (16-20)	17 (14-20)	0.380
Smoking duration	24.62 ± 13.90	34.17 ± 16.17	0.006
FEF $\bar{x}$ in ml	60.16 ± 18.82	25.85 ± 9.91	0.001

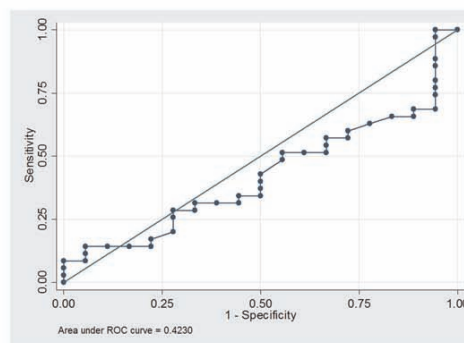


Figure 4: Accuracy of smoking pack-year in determining SAO among smoker with Normal FEV1/FVC

Background and Aims: Chronic obstructive pulmonary disease (COPD) is mainly due to cigarette smoking, this condition is characterized

by persistent airflow limitation, a condition characterized by persistent airflow limitation. A major site of airflow limitation in COPD is the small conducting airways. Small Airway Obstruction is a harbinger of COPD and abnormalities in the small airways in smokers may or may not have COPD. Thus the aim of the study is early detection of small airway obstruction and determine the Correlation of Forced Expiratory Flow (FEF) 25–75% and the number of pack-years among smokers.

Methods: Patient with smoking history is included and demographic and spirometry result (FEV1/FVC, FVC, FEV1, FEF25-75) are collected. Cut-off value of smoking pack-years with low FEF25-75 was determine and correlation among patients with normal and low FEV1/FVC was done.

Results: There was significant correlation of FEF 25–75 and smoking pack-years with inverse relationship ($r = -0.35$, $P = 0.0014$). The smoking pack-years cut-off value that will give low FEF25-75 was 16.5 smoking pack-years.

Conclusion: FEF25-75 may be use for early detection of small airway obstruction. This may help encourage smokers to quit earlier before significant airway obstruction symptomatology occurs and prevent further progression to COPD and other complications of smoking.

AP406

CHANGES IN CD4+CD25+FOXP3+ TREG CELLS AND INF- γ BETWEEN SUBLINGUAL AND SUBCUTANEOUS IMMUNOTHERAPY WITH HOUSE DUST MITE IN CHINESE PATIENTS WITH ALLERGIC RHINITIS

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Background and Aims: Few studies have compared the immunologic responses to specific subcutaneous (SCIT) and sublingual immunotherapy (SLIT). We aimed to compare these responses during a 1-year treatment between SLIT and SCIT in Chinese patients with allergic rhinitis sensitized to house dust mites.

Methods: Sixty-seven patients (age 5–55 years) with moderate-severe Dermatophagoides pteronyssinus (Der-p) and Dermatophagoides farinae (Der-f) allergic rhinitis and/or asthma were randomized (2:2:1) into SLIT ($n = 27$), SCIT ($n = 26$) and medication ($n = 14$) groups. Rhinitis and asthma symptom and medication scores, visual analogue score (VAS), serum Der-p specific IgG4 (Der-p-sIgG4), CD4+CD25+FoxP3+ regulatory T cells (CD4+CD25+FoxP3+ Tregs) and serum cytokines were measured.

Results: After 1-year treatment, a significant improvement of total rhinitis score (TRS), total rhinitis medication score (TRMS) and VAS occurred in both SLIT and SCIT, and total rhinitis symptom score (TRSS) was improved in SCIT ($P < 0.05$) compared with the medication group. CD4+CD25+FoxP3+ Tregs had a trend toward up-regulation in SLIT and inversely correlated with total rhinitis medication score ($P = 0.014$) and total rhinitis score ($P = 0.024$). Der-p-sIgG4 significantly increased in SLIT and SCIT ($P < 0.05$), and was 30 times higher in SCIT than SLIT after the 1-year treatment ($P < 0.05$). Serum INF- γ significantly increased in SCIT after 1 year treatment ($P = 0.011$) and had correlated with clinical improvement.

Conclusion: The CD4+CD25+FoxP3+ Tregs had correlation with clinical improvement in SLIT, while INF- γ had correlation with clinical improvement in SCIT.

COPD 2

AP407

CONSUMER-LED BETTER BREATHING SUPPORT GROUPS - A HEALTH AND SOCIAL ENTERPRISE

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Background and Aims: In 2013, The Canterbury Pulmonary Rehabilitation Working Group (PRWG) was involved in a SWOT (Strengths, Weaknesses, Opportunities, Threats) analysis of the current pulmonary rehabilitation (PR) service. Two of the key areas identified for review were programme delivery and education. The Working Group members believed they were doing a good job based on the objective outcome measures used, but the experiences and expectations of participants had not been explored thoroughly.

Methods: In September 2013 a Pulmonary Rehabilitation Consumer Focus Group was established. The group was formed from members of the different community exercise groups that support PR. In 2016, the consumer representatives and clinicians decided to try the consumer-led coffee and exercise support group model. This group would ensure all aspects (physical, social, psychological and spiritual) of one's wellbeing are cared for. The group includes 30 min, a light exercise session led by expert patient volunteers and a chat session afterwards to allow the attendees to voice their health concerns, share stories and coping strategies.

Results: Consumers have established four support groups in the Canterbury region: Rangiora, Shirley, Aranui and Templeton. Currently, these four groups are supporting more than 50 people living with chronic respiratory illnesses over a cup of coffee.

Conclusion: The consumer-led support groups have achieved multi-benefits to the participants and the health sector.

- These groups are independent and do not depend on external resources; this ensures their sustainability.

- The support groups improve the profile of respiratory illness in the community and provide an opportunity for everyone to come to learn and talk more about their experience with respiratory illnesses
- The remaining donations, after all expenses are paid for, is used to reinvest in the group members and other community charitable societies.
- The resource-independent structure allows public health funding to be released to support other more urgent areas

AP408

AN ACTION PLAN FOR SELF-MANAGEMENT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN SOUTH KOREA

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a common, chronic lung disease characterized by progressive and not fully reversible airflow limitation. A cornerstone of COPD management is preventing acute exacerbations of COPD that becomes more frequent and severe as the disease progresses, and breaking the cycle of recurrence.

Self-management has been highlighted as a potential approach that has yielded clear association with reducing the risk of acute exacerbations of COPD. Action plans offer a form of self-management to help individuals recognize and initiate early treatment for exacerbations, thereby reducing their impact. However, despite the existing clinical practice guidelines for COPD, there is little consensus on an action plan for self-management of COPD patients. This study was aimed to identify components of an action plan for self-management of COPD patients in the real clinical setting in South Korea.

Methods: This methodological study was conducted by the following steps: constructing the preliminary draft of an action plan from extensive literature reviews and existing clinical guidelines and recommendation regarding action plan and self-management for COPD patients; one-round Delphi method to find consensus within a group of 15 experts and 15 patients on the draft; testing content validity with 15 experts.

Results: Five components were included in the finalized action plan for self-management in COPD patients based on clinicians and patients input: (1) 10 questionnaires for self-monitoring of alteration in conditions (2) self-checking of body-temperature, pulse rate, and PEFR; (3) information on appropriate use of medications and changing medication when need that is tailored to an individual patient; (4) indications to visit a doctor/ emergency room; (5) information for family/primary care givers.

Conclusion: Further studies are warranted to explore alignment with clinical practice guidelines and feasibility of adaptations, to facilitate wide applicability, and evaluation of the effectiveness of the action plan identified in this study.

AP409

PREDICTIVE VALUE OF COMBINING RAPID DECLINE OF FEV₁ AND INFLAMMATORY BIOMARKERS FOR DEVELOPING COPD-A PROSPECTIVE COHORT STUDY IN BEIJING

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Background and Aims: To explore the predictive value of rapid decline in FEV₁, and baseline inflammatory cytokine for developing COPD

Methods: A prospective cohort study was conducted in Shichahai community, Beijing. 1261 Subjects aged 40–70 years old without history of lung disease and severe underlying disease were recruited. Between 2009 and 2012, We performed lung function tests twice at baseline and 3 years later, and measured SP-D level in blood. Rapid decline in FEV₁ was defined as over 50 mL decline in FEV₁ per year.

Results: 452 subjects completed all the visit, of which 88 subjects were excluded because of baseline FEV₁/FEV₆<70% or FEV₁<80%pred. 364 subjects were included in the final analysis, of which 37 subjects developed COPD during following up. COPD group had older age ($6 \pm .8$ vs $5 \pm .6$), higher ratio of smoking history (35% vs 21%), higher ratio of rapid decline in FEV₁ (64% vs 46%), lower baseline FEV₁/FVC ($0.7 \pm .07$ vs $0.8 \pm .06$) than non-COPD group. There were no differences in chronic respiratory symptoms, income class, educational level, comorbidity (hypertension, OSA), baseline level of SP-D, baseline FEV₁%pred, family history, occupation and statin take between COPD and non-COPD subjects. After logistic regression, only age was consistent positive associated with the development of COPD.

Conclusion: Age was associated with the development of COPD. The potential predictive value of rapid decline in FEV₁ and inflammatory biomarkers for COPD need further large scale study

AP410

CLINICAL CHARACTERISTICS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS DETECTED WITH COPD SCREENING IN THREE DIFFERENT RURAL AREAS IN JAPAN

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Background and Aims: Various simple questionnaires are used to detect undiagnosed patient with chronic obstructive pulmonary disease (COPD). The purpose of this study was to evaluate three different screening tools for detecting COPD patients in general population in three regions in Japan.

Methods: Different COPD screening tools were introduced for the general population in three rural areas, Hitachiomiya city in 2014, Yakushima town in 2015, and Hokuto city in 2016.

The criteria the subjects were suspected of having COPD in each area were as follows: the subjects who had a COPD Population Screener (COPD-PS) questionnaire score of 4 or above in Hitachiomiya city, the subjects who had a COPD-PS score of 4 or above and FEV₁/FEV₆ < 0.73 measured by handheld spirometer (Hi-Checker[®]) in Yakushima town, and the subjects who had a COPD-PS score of 4 or above and FEV₁/FEV₆ < 0.73 and smoking pack-year more than 20 in Hokuto city. The subjects suspected of COPD were recommended to perform spirometry at a medical institution. We retrospectively examined the clinical characteristics of COPD patients detected with these screenings.

Results: In the subjects who performed post-bronchodilator spirometry, the percentage of the patients who had a diagnosis of COPD in each area was 17.2%/72.7%/31.3%, respectively. Comparing the characteristics of COPD patients detected with each screening, the average age (73.0/73.5/74.0), the ratio of male (97.6%/92.5%/95.7%), the average COPD-PS score (4.6/4.6/4.9), and the average % FEV₁ (76.3%/71.6%/75.9%) were similar among three areas.

Conclusion: The majority of the patients who were detected with these COPD screening was mild cases. However, further examination is needed for more efficient screening.

AP411

IMPAIRED SKELETAL MUSCLE OXYGENATION IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Exertional dyspnoea is one major reason that limits activities of daily living in people with COPD which leads to reduced muscle strength further limiting exercise tolerance. Increased evidence suggested that exercise intolerance is not only contributed by inactivity associated decline in muscle strength, but also be related to altered metabolism and oxygenation in skeletal muscle. Thus, this study aims to compare changes in tissue oxygenation in the main skeletal muscles during exercise between people with COPD and normal health and to determine the potential contributing factors to exercise intolerance.

Methods: A total of twenty-six people were recruited. Of these, thirteen people had confirmed diagnosis of COPD (mean age: $6 \pm$ and % predFEV₁: $4 \pm 6\%$) and thirteen age-and-gender-matched healthy individuals participated as control. Participants were asked to perform a symptom-limited ergometry test to evaluate exercise tolerance. Two probes of Near-Infrared-Spectroscopy (NIRS) were attached to chest wall and quadriceps respectively to examine the levels of tissue oxygenation of these muscles under exercise induced stress.

Results: Comparing to healthy individuals, people with COPD has significantly lowered resting tissue oxygenation level in quadriceps by 11.6% ($P < 0.001$) but not in respiratory muscle ($P = 0.341$). After covariate adjustment, two-way-repeated-measure ANOVA demonstrated significant time $\times$ group interaction ($P = 0.02$) in tissue oxygenation of quadriceps with the most prominent differences observed immediately after exercise and at 5th minute of active recovery suggesting altered oxygenation during exercise. Spearman correlations showed that ergometry work rate was moderately correlated with resting tissue oxygenation level in quadriceps ($r_s = 0.52$, $P < 0.001$) and %predFEV₁ ($r_s = 0.72$, $P < 0.001$). %predFEV₁ and resting tissue oxygenation level in quadriceps explained 49% of variance of ergometry work rate ($F = 11.04$, $P < 0.001$).

Conclusion: Altered tissue oxygenation in quadriceps, but not in respiratory muscles, were observed in people with COPD. Such alteration, together with severity of airway obstruction, are the major contributing factors explaining 49% of variance of exercise tolerance in people with COPD.

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AP412

LOWER SERUM IMMUNOGLOBULIN FREE LIGHT CHAIN PREDICTS EXACERBATION RISK IN PATIENTS WITH COPD

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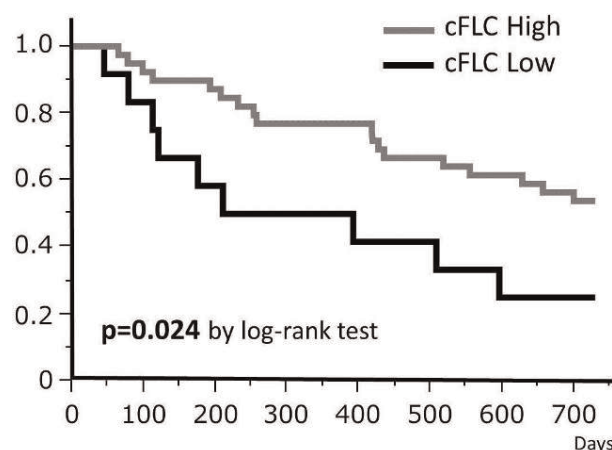
Background and Aims: It is needed to identify the patients at risk for exacerbations of chronic obstructive pulmonary disease (COPD). We previously reported that the lower IgG titre for periodontitis-related antibody associates with frequent exacerbations of COPD (Takahashi,

et al. PLOS One 2012). And recently, it is also revealed that lower serum IgA is associated with COPD exacerbation risk (Putcha, et al. PLOS One 2018). Immunoglobulin free light chains (FLC), produced during antibody synthesis, are thought to reflect B cells activation in various inflammatory disease. We hypothesized that the serum FLC might be a novel biomarker associated with exacerbation risk of COPD.

Methods: We enrolled stable male patients with COPD and prospectively observed for two years. We investigated the association between the serum combined FLC (cFLC; summing of kappa and lambda values) and exacerbations of COPD. The serum FLC analysis was performed by ELISA using commercially available measurement kit. Exacerbation was defined worsen of symptom according to the modified Anthonisen's criteria.

Results: Fifty-one patients with stable COPD were successfully evaluated ($71 \pm .2$ years old, GOLD A/B/C/D = 24/22/1/4). The patients with low cFLC ($<$ the lower quartile) was younger and have lower immunoglobulins than those with high cFLC. The patients with low cFLC showed significantly higher risk for exacerbation of COPD ($P = 0.024$ by log-rank test). Multivariate Cox proportional hazard model including mMRC, % FEV₁ and the number of prior exacerbation demonstrated that cFLC, serum IgA and %FEV₁ were independently and significantly correlated with the risk for exacerbation of COPD.

Conclusion: This study suggested that decreased antibody production may be associated with the risk for exacerbations of COPD and cFLC can be a novel biomarker identifying the exacerbation-prone patients with COPD.



AP413

INHALED STEROIDS AND RISK OF PNEUMONIA IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Treatment with inhaled corticosteroids (ICS) is well established for certain chronic obstructive pulmonary disease (COPD) patients. Despite this, treatment with ICS has been linked to an increased risk of pneumonia. However, results differed widely between studies (some trials reporting increased risk, others reported reduced risk). The magnitude of risk and how this compares with different ICS, dose regimen, and duration of use, remain unclear. Most trials are limited

by lack of pneumonia objective ascertainment. The objective of this study was to determine if the use of ICS is associated with an increased risk of pneumonia and to determine impact of different ICS regimen.

Methods: A retrospective, case-control study was conducted using secondary data (medical record) of COPD patient at RSUPN Dr. Ciptomangunkusumo and RS Dr. Ciptomangunkusumo Kencana Jakarta since January 1st 2012 until November 30th 2016. Sixty seven patients with radiographically confirmed pneumonia were matched to control subjects by age and comorbid. Cases were defined based on hospitalization for pneumonia (outpatient and inpatient). Exposure was prior use of ICS. Statistical analysis used to estimate the odds ratio (OR) of pneumonia associated with ICS use and impact of different ICS, different dose regimen, and different duration of ICS use with a risk of pneumonia.

Results: There are differences in ICS exposure between cases and controls. Treatment with ICS is linked to pneumonia (P 0.005; OR 0.31; 95%CI 0.13–0.71). Exposure to ICS in the case group was dominated by fluticasone propionate, while the control group was budesonide. There is no relationship between the types of ICS with pneumonia due to small sample size. Mostly ICS are used in low dose and short duration (median $\pm$ SD 32.5 $\pm$ 636.69). Treatment with lower dose is linked to a lower risk of pneumonia (P 0.019). There is no relationship between the duration of use with risk of pneumonia.

Conclusion: ICS has antiinflammation and immunosuppressant effect. ICS shows protective effect due to lower dose use.

AP414

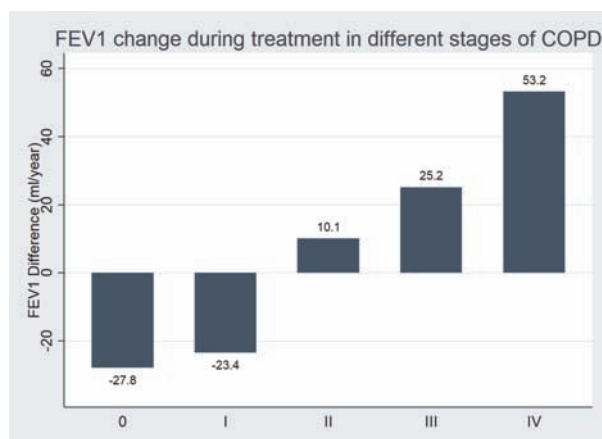
PATTERN OF PATIENTS DIAGNOSED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN A MEDICAL CENTER, TAIWAN, FROM 2006 TO 2017

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Background and Aims: GOLD (Global Initiative for Chronic Obstructive Lung Disease) was introduced in 1997 but the guideline adherence and large-scale patient outcome in this country is unknown. We designed a retrospective study to demonstrate the “real-world” of the clinical practice.

Methods: From the Integrated Medical Database of National Taiwan University Hospital, which was derived from the electronic medical record (EMR) system, de-identified data from patients with diagnosis of COPD were retrieved. Out-patient clinic records of patient demographics, pharmacy and spirometry data were analyzed.



Results: A total of 27,152 patients, with at least two visits for COPD, were retrieved from 2006 to 2017. The average age of initial COPD

diagnosis was 66.5 years. The smoking rate, including current and ex-smoking, was 39%. There were 44.6% patients with at least one spirometry, with or without bronchodilator test. Among those with spirometry, the proportion of patients with stages I to IV was 12.1%, 19.8%, 7.9% and 1.5%, respectively. Fifty-eight percent patients had normal spirometry. The mean follow-up duration within the study period was 3.7 years. Body mass index (BMI) declined inversely with the severity stages. For patients with multiple spirometry data during follow-up, the annual change in forced expiratory volume in one second (FEV1) was shown in figure. There were 17% and 12% patients changed to lesser and greater severity stages, respectively. Patients with more impairment of lung function had more improvement on FEV1 after treatments.

Conclusion: In patients with the diagnosis of COPD, the spirometry performance rate was low. The smoking condition was likely to be under-recognized or under-documented. For those with greater severity, the pulmonary function improved more with treatments.

AP415

CLINICAL USEFULNESS OF ONCE-DAILY TRIPLE THERAPY, CICLESONIDE AND TIOTROPIUM BROMIDE / OLODATEROL COMBINATION INHALER FOR COPD PATIENTS (2ND REPORT)

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Background and Aims: The triple therapy, ICS+LABA+LAMA could be used for GOLD group D, however, three drugs combination agents are not marketed in Japan at present, and still no findings which combination were the best choice. Ciclesonide Hydrate (CIC) and Tiotropium bromide/ Olodaterol Hydrochloride combination inhaler (CIC+TIO/OLO) are both once-daily fine mist preparations which could contribute to better adherence to treatment and distribution to more peripheral airways. Therefore, we conducted a clinical analysis to compare anti-inflammatory and bronchodilator effect especially on peripheral airway between CIC+TIO/OLO and other triple combination therapy.

Methods: COPD patients, classified as either group D or ACO have been treated with triplet more than 6 months were recruited. After obtaining informed consent, the current inhalers were switched to CIC 400 µg/day + TIO/OLO 5 µg/5 µg/day. Then COPD assessment test (CAT) score, Spirometry, fractional exhaled nitric oxide (FeNO), FOT (MostGraph-02) and exacerbation rate per year were examined before and after 6 months treatment with CIC+TIO/OLO.

Results: 17 patients are enrolled. GOLD group D were 6 cases, 11 cases were ACO classified by JRS definition. Triplet used before entry were SFC + TIO 8 cases, FP + GLY/IND 5 case. As a result, significant improvements were observed not only in CAT score (12. $\pm$.3 to 8. $\pm$.8) but also FeNO (40. $\pm$ 1.6 to 32. $\pm$ 5.9 ppb). Although no change are observed in FEV1 (1.5 $\pm$.6 to 1.6 $\pm$.7 L), MMF (0.8 $\pm$.6 to 1.0 $\pm$.7 L/s) improved significantly, which suggested bronchial dilatation might occur more peripheral airways.

Conclusion: CIC + TIO/OLO, the combination of once-daily fine mist preparations, could be a favourable option as a triple therapy for COPD and ACO patients.

AP416

THE IMPACT OF ATRIAL FIBRILLATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE DURING HOSPITALIZATION

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Background and Aims: Atrial fibrillation (AF) occurs frequently in patients with chronic obstructive pulmonary disease (COPD). There are limited data about the impact of AF in hospitalized COPD patients on other serious health outcomes, such as acute organ dysfunction, severe sepsis and respiratory failure. The aim of our study was to delineate the impact of AF in hospitalized COPD patients.

Methods: We defined COPD populations with and without AF from the National Health Insurance (NHI) database in Taiwan. The control subjects (patients with COPD without AF) were selected from the population of COPD patients who had no history of AF and were matched to the COPD patients with AF by age (± 1 year), gender, and the year of COPD diagnosis (± 1 year). The primary outcome was the time to any first event, which included acute organ dysfunction, severe sepsis and respiratory failure, during the hospitalization period. Secondary outcomes included a composite endpoint of acute organ dysfunction, severe sepsis and respiratory failure.

Results: The primary outcome probability was higher in COPD patients with AF than in COPD patients without AF, with an adjusted hazard ratio (aHR) of 1.170 (95% confidence interval (CI): 1.030–1.329), and higher risks of acute organ dysfunction and respiratory failure were also observed in the former group, with aHRs of 1.179 (95% CI: 1.0370–1.339) and 1.176 (95% CI: 1.006–1.374), respectively.

Conclusion: Compared with COPD patients without AF, COPD patients with AF had a higher risk of hepatic dysfunction and respiratory failure.

AP417

THE LONG-TERM EFFICACY OF DOMICILIARY NON-INVASIVE POSITIVE PRESSURE VENTILATION IN COPD: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background and Aims: Although non-invasive positive pressure ventilation (NIPPV) treatment for acute respiratory failure improves the outcome in COPD patients the results of studies in which COPD chronic respiratory distress was treated with NIPPV vary widely. We aimed to evaluate the long-term effect of domiciliary NIPPV.

Methods: We performed an extensive search of the MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials databases to identify randomized controlled trials (RCTs) pertaining to the long-term treatment of COPD with NIPPV ventilation over a period of more than 1 year.

Results: The eight trials included in this study comprised data from 913 patients. The mortality rates for the NIPPV and control groups, were 29% (118/414) and 36% (151/419). This difference was statistically significant (RR, 0.79; 95% CI, 0.65–0.95, $P = 0.01$). The mortality rates in the four trials that included stable COPD patients were reduced on application of NIPPV (RR 0.71, 95% CI 0.56–0.91, $P = 0.006$). In a further subgroup analysis, mortality was reduced when the mean baseline PaCO₂ level was high (RR 0.71, 95% CI 0.55–0.93, $P = 0.01$). The results of the subgroup analysis according to the mean IPAP level showed that the mortality rates in the NIPPV group in three trials were reduced (RR 0.72, 95% CI 0.54–0.96, $P = 0.03$). There was no difference in QOL between NIPPV and control groups (SMD –0.037, 95% CI –0.34–0.29, $P = 0.85$). There was no significant difference in the dropout rate between the two groups. (RR 0.99, 95% CI 0.72–1.36, $P = 0.94$).

Conclusion: Domiciliary NIPPV should be considered in COPD patients especially when used in patients with a stable status and relatively higher PaCO₂ level, and among those with a higher IPAP level.

THE INTERPRETATION OF RESPIRATORY SYSTEM IMPEDANCE IN THE EARLY EXPIRATORY PHASE MEASURED BY FORCED OSCILLATION TECHNIQUE

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Background and Aims: The Forced Oscillation Technique (FOT) can detect impairments of lung function by measuring the impedance of respiratory system (Zrs; respiratory resistance (Rrs) and respiratory reactance (Xrs)) during normal tidal breathing. Because the representative value of Zrs measured by FOT is the average value of total breathing/expiration/ inspiration period, there is little consideration on the dynamic change in Zrs during the respiratory cycle.

We assessed the change in Zrs during early expiratory phase.

Methods: 19 male subjects underwent the normal spirometry test (CHESTAC 55-V, CHEST MI. Inc., Tokyo, Japan) and Zrs measurement (MostGraph-01, Ver.1.70R, CHEST MI. Inc., Tokyo, Japan) on the same day.

We divided subjects into two groups by the result of the spirometry test; normal group ($n = 4$, mean age 55 years) and COPD group ($n = 15$, mean age 66 years). Furthermore we made three subgroups in COPD group; mild COPD ($\geq 80\%$ of %FEV1.0, $n = 6$), moderate COPD (50–80% of %FEV1.0, $n = 5$) and severe COPD ($< 50\%$ of %FEV1.0, $n = 4$).

We analyzed Zrs at the time of expiration started (Zrs(es)) and 0.5 sec after the start of expiration (Zrs(0.5)).

Results: There was no constant trend in Zrs during total breathing, exhalation, and inspiration period within all groups. Rrs of 5 Hz (R5) at 0.5 s (R5(0.5)) increased 2.70, 2.82, 3.74, 3.95 cmH₂O/L/s (normal, mild, moderate, severe group, respectively). Xrs of 5 Hz (X5) at 0.5 (X5(0.5)) was decreased 1.25, 1.14, 0.89, 0.53 cmH₂O/L/sec (normal, mild, moderate, severe group, respectively). $\Delta R5-20$, the difference of R5-20 between R5-20(0.5) and R5-20(es), was increased along with severity of COPD; 0.29, 0.47, 0.50, 0.88 cm H₂O/L/s (normal, mild, moderate, severe group, respectively). V25 showed a negative correlation tendency with R5(0.5) and $\Delta R5-20$.

Conclusion: It was suggested that Zrs in the early phase of resting expiration was related with the severity of COPD.

AP419

COULD PROBIOTICS USEFUL FOR COPD PATIENTS? AN EBM VIEW

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Background and Aims: Chronic obstructive pulmonary disease, COPD is characterized by an abnormal inflammatory response in the lungs and restricted airflow, which both result in difficulty doing the most vital thing in life — breathing. We would like to know whether the use of probiotics can improve the inflammation or the relief of symptoms in patients with COPD.

Methods: We performed a systematic literature search in PubMed, Embase, and Cochrane Library in any language from inception to May 2018 by using the key words- (copd[MeSH] OR Asthma[MeSH]) AND ("probiotic agent" OR probiotic#) NOT (atopic OR allerg*). We included 2 RCTs and 1 review to appraisal by casp tool.

Results: Panahi et al. 2017 include 65 subjects suffering from COPD of sulfur mustard (SM) were assigned to one probiotic capsule

(1×10^9 CFU containing seven strains of lactic acid-producing bacteria) every 12 h or placebo for six weeks. There were significant improvements in FEV1/FVC in the probiotic but not in placebo. CAT scores were decreased in both study groups. ($P < 0.001$)

Mortaz et al. 2013 Commonly used probiotics include lactic acid bacteria, particularly *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, and these are often used as dietary supplements to provide a health benefit in gastrointestinal diseases including infections, inflammatory bowel disease, and colon cancer. Probiotics also prevent and treat respiratory diseases.

Koning et al. 2010 include 30 COPD patients treated with antibiotics for a respiratory tract infection received 5 g of a multispecies probiotic or placebo twice daily for 2 weeks. Faecal samples was not affected by antibiotics in COPD, suggesting an existing imbalance of the microbiota, which may also have contributed to the lack of effect by probiotic intake.

Conclusion: There were not sufficient evidence to recommend probiotics for COPD symptom remission. We need further clinical and basic research to accurately define the role of probiotics in COPD improvement.

AP420

THE PREVALENCE OF VOIDING DYSFUNCTION AND THE EFFECT OF BRONCHODILATOR IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Most patients with chronic obstructive pulmonary disease (COPD) are elderly males. Recently, the use of long acting muscarinic receptor antagonist / long acting beta 2 receptor agonist (LAMA/LABA) combination inhaler therapy is increased in COPD patients. Muscarinic receptor antagonists have anticholinergic actions, which are known to cause or exacerbate dysuria. The aim of this study is that whether LAMA/LABA combination inhaler therapy is a risk factor for voiding dysfunction or not.

Methods: A cross sectional analysis was performed at a single medical center in South Korea. A total of 105 patients with COPD were enrolled and International Prostate Symptom Score (IPSS) were checked. If the IPSS score was 8 or more, it was defined that there was a meaningful voiding dysfunction.

Results: Mean age is $7 \pm$ years. Already known BPH was 28.6% ($n = 30$). There were 43 patients (41%) with an IPSS score of less than 8 and 62 patients (59%) with an IPSS score of 8 or more. In univariate logistic analysis, only shorter six minute walk test distance (Odds ratio 0.993, 95% CI 0.988–0.999, $P = 0.025$) was associated with voiding dysfunction. However, LAMA/LABA combination inhaler therapy ($P = 0.485$) and LAMA inhaler therapy ($P = 0.700$) were not a risk factor for voiding dysfunction.

Conclusion: Voiding dysfunction was relatively common in COPD patients. LAMA inhaler therapy did not seem to be associated with voiding dysfunction. Randomized control trials with larger population will be needed in near future.

AP421

LONG-TERM COURSE OF EMPHYSEMA WITHOUT AIRFLOW LIMITATION

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Background and Aims: It is not clear whether emphysema patients without airflow limitation would change to COPD in the later clinical

course. The aim of this study was to investigate the clinical features and long-term course of patients with emphysema but without airflow limitations.

Methods: We retrospectively analyzed the clinical records of patients who had emphysema on chest CT scans and underwent spirometry more than 2 times at the Shizuoka General Hospital since 2012. Patients were classified into 2 groups: emphysema without airflow limitation (non-COPD group) and emphysema with airflow limitation (COPD group), and the following parameters were compared: background, spirometry, forced oscillation technique, and the 5-year survival rate. In the non-COPD group, the rate of change to COPD was analyzed.

Results: Of the 74 patients who had emphysema on chest CT scans and underwent spirometry more than 2 times, 25 patients (32%) were classified into the non-COPD group and 49 patients (68%) into the COPD group. There was no significant difference in their background at the baseline (age, sex, BMI, Goddard score, and respiratory symptoms), spirometry (FVC, FEV1), diffusing capacity, and 5-year survival rate between the 2 groups. In the non-COPD group, respiratory resistance at baseline was significantly lower and the occurrence of pneumothorax in the 5 years' follow-up was higher than in the COPD group. Eight of 25 patients (32%) changed to COPD after 5 years. These 8 patients had a significantly lower FEV1/FVC at baseline compared to 17 patients who did not change to COPD. Twelve of 17 patients (71%) who did not change to COPD received bronchodilators because of respiratory symptoms.

Conclusion: In patients with emphysema, the background, spirometry, and 5-year survival rate were comparable regardless of the presence of airflow limitation. Thirty two percent patients of emphysema without airflow limitation had changed to COPD after 5 years.

AP422

PEDOMETER AS A TOOL FOR QUALITY OF LIFE IMPROVEMENT IN COPD PATIENTS

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a progressive disease which can lead to some systemic manifestations. Therapy to improve lung function is considered unresponsive to COPD. Assessing and treating COPD are not only based on airflow limitations but also other treatable clinical manifestations. The BODE (Body mass, Obstruction, Dyspnea, Exercise) index is composite marker of disease taking into consideration the systemic nature of COPD. It is one of multidimensional stratification systems which can be used to determine the risk of exacerbations and is also independent predictor of survival in COPD. Pedometer is an effective tool for monitoring and increasing the level of physical activity in healthy people but whether this tool is effective for improving the level of physical activity in COPD patients has not been known. This study aimed to analyze whether pedometer improved the BODE index.

Methods: Randomized controlled trial study in stable COPD outpatients in RS Dr. Moewardi Surakarta from November 1, 2016 to February 15, 2017. The effects of walking exercises using pedometer and control group pre- and post-intervention were analyzed with paired t test (alternative test Wilcoxon). The difference effects of walking exercise between pedometer and control were analyzed by unpaired t test (alternative test of mann whitney). All data were analyzed with SPSS 21 version, $P < 0.05$ was considered significant.

Results: The control group and pedometer group had significant result of BODE index improvement (2.65 ± 1.539) and (4.06 ± 2.076);

$P = 0.031$. Both groups had significant improvement of BODE index pre and post intervention, control group $P = 0.001$ (95% CI 0.865 to 1.959) and pedometer group $P = 0.034$ (95% CI 0.044 to 1.014).

Conclusion: Walking exercise improved quality of life in COPD patients.

Tabel 1. Research subject characteristic.

Variables ^a	Groups		P
	Treadmill (n = 18)	Pedometer (n = 18)	
Ages ^b	61,06 ± 6,82	68,12 ± 6,83	0,007
Gender			0,368
Male	13 (76,5%)	13 (76,5%)	
Female	4 (23,5%)	4 (23,5%)	
Education ^c			0,842
Elementary	11 (64,7%)	11 (64,7%)	
Junior High	3 (17,6%)	4 (23,5%)	
High School	3 (17,6%)	2 (11,8%)	
Works ^c			0,768
Farmer	3 (17,6%)	5 (29,5%)	
Services	5 (29,4%)	3 (17,6%)	
Workers	4 (23,3%)	3 (17,6%)	
Retired	5 (29,4%)	6 (35,3%)	
Smoking Status ^d			0,628
Smoker	15 (88,2%)	14 (82,4%)	
Passive Smoker	2 (11,8%)	3 (17,6%)	
Comorbid			0,500
Yes	3 (17,6%)	4 (23,5%)	
No	14 (82,4%)	13 (76,5%)	
Body Mass Index (BMI) ^a	22,28 ± 3,50	20,28 ± 4,63	0,167
Combined COPD assessment classification			0,538
Group B	11 (64,7%)	8 (47,1%)	
Group C	2 (11,8%)	2 (11,8%)	
Group D	5 (23,5%)	7 (41,2%)	
Airway obstruction classification based on VEPI			0,673
GOLD 1	2 (11,8%)	3 (17,6%)	
GOLD 2	8 (47,1%)	8 (47,1%)	
GOLD 3	4 (23,5%)	5 (29,4%)	
GOLD 4	3 (17,6%)	1 (5,9%)	

Information : ^a Numerical variable, described by mean ± SD, tested with t-test.

^b Numerical variable, described by mean ± SD, tested with Mann Whitney

^c Ordinal scale categorical variable, described by proportional frequent (%), tested with Chi Square.

^d Nominal scale categorical variable, described by proportional frequent (%), tested with Fisher's Exact Test

AP423

COMPARISON OF CLINICAL CHARACTERISTICS AND INCIDENCE OF ACUTE EXACERBATION IN PATIENTS WITH ASTHMA-COPD OVERLAP AND COPD

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Background and Aims: Asthma-COPD overlap (ACO) is characterized by persistent airflow limitation with several features usually associated with asthma and COPD. Acute exacerbation (AE) of ACO and COPD is an important event that worsens prognosis. The aim of this study was to investigate and compare clinical characteristics and incidence of AE between patients with ACO and COPD.

Methods: We examined 45 ACO patients and 171 COPD patients who visited our hospital from 2014 to 2016. AE was defined as an episode requiring treatment with oral corticosteroid and/or antibiotics, or a visit to the emergency room, or hospitalization.

Results: The frequency of use of inhaled corticosteroids and a long-acting beta2-agonist was significantly higher in the ACO patients vs the COPD patients (86.7 vs 30.4%, $P < 0.001$ and 88.9 vs 67.3%, $P = 0.005$, respectively). Patients with ACO had lower body mass index than those with COPD (21.2 vs 21.4 kg/m², $P = 0.031$). There was a significant difference between the COPD and ACO patients in exposure to tobacco smoke (52.0 vs 35.4 pack-years, $P = 0.011$). There were no significant differences in age, gender ratio, and pulmonary function test results.

During the follow-up period (median, 517 days), 26 patients with ACO and 65 patients with COPD suffered AE. Log-rank test showed that ACO patients had a higher incidence rate of AE than COPD patients ($P = 0.002$).

Conclusion: ACO patients had different clinical characteristics and a higher incidence rate of AE than COPD patients. Clinicians need to identify the characteristics of and prescribe more appropriate treatment for ACO patients.

AP424

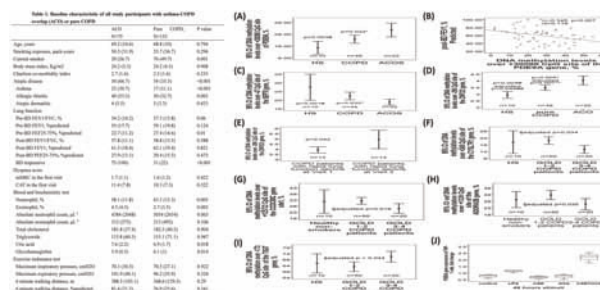
WHOLE GENOME DNA METHYLATION ANALYSIS OF ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE OVERLAP IDENTIFIES NOVEL EPIGENETIC SIGNATURES

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Background and Aims: We hypothesized that DNA methylation patterns may contribute to disease severity or frequent exacerbation in patients with asthma and chronic obstructive pulmonary disease (COPD) overlap (ACO).

Methods: Illumina's 450 K DNA methylation microarray was used to identify differentially methylated loci (DML) in a discovery cohort of 12 ACO patients and 6 healthy subjects. DNA methylation levels were validated by pyro-sequencing in a validation cohort of 22 ACO patients, 48 pure COPD patients, and 10 healthy non-smokers.



Results: Seventy-five of the 228 COPD patients were identified as ACO, which was independently associated with total number of exacerbations both in the past and following one year. Microarray analysis identified 404 DMLs in ACO patients vs healthy non-smokers. In the validation cohort, both +30088 CpG site of the PDE9A gene and -296 CpG site of the ZNF323 gene were hypermethylated, while -47 CpG site of the SEPT8 gene was hypomethylated in the ACO vs pure COPD or non-smokers. +348 CpG site of the CYSLTR1 gene, +125722 CpG site of the CCDC88C gene, and +1339 CpG site of the ADORA2B gene were all hypomethylated in COPD patients with severe airflow limitation, while -173 CpG site of the TIGIT gene were hypermethylated. -515 CpG site of the IFRD1 gene were hypomethylated in frequent exacerbators. DNA methylation levels over both -296 CpG site of the ZNF323 gene and +194 CpG site of the MPV17L gene were elevated after 1-year treatment in those with rapid lung function decline. Cigarette smoke extract and ovalbumin concurrent exposure result in over-expressions of the PDE9A, SEPT8, and IFRD1 genes.

Conclusion: PDE9A/ZNF323 hypermethylation and SEPT8 hypomethylation may constitute a determinant for ACO development, while CYSLTR1/CCDC88C/ADORA2B hypomethylation and IFRD1 hypermethylation may provide a biomarker for vulnerability to airflow limitation

and exacerbation in COPD, respectively. ZNF323/MPV17L hypermethylation may be involved in rapid lung function decline.

AP425

COPD ASSESSMENT TEST (CAT) SCORE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE BASED ON CLINICAL PHENOTYPES

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Background and Aims: Spanish chronic obstructive pulmonary disease (COPD) guideline classifies COPD into 4 clinical phenotypes: non-exacerbator (A), asthma-COPD overlap (B), exacerbator with emphysema (C) and exacerbator with bronchitis (D).

Methods: A cross-sectional observational study of quality of life (QOL) of COPD patients utilizing COPD Assessment Test (CAT), conducted in University of Malaya Medical Center from 1 June 2017 – 31 May 2018.

Results: Of 220 patients treated for COPD, 189 patients with post bronchodilator Force Expiratory Volume in 1 second (FEV1)/Force Vital Capacity (FVC) of <0.70 were recruited. Patients' demographic, clinical characteristics and CAT score are as shown in Table 1. Patients with COPD phenotype C and D had poorer modified medical research center (MMRC) functional status and global initiative of COPD (GOLD) class based on their FEV1.

Table 1. Demographic, clinical characteristics and CAT score according to clinical phenotypes.

Characteristics	COPD Phenotypes (n, %)				*p value
	A 54 (28.6)	B 25 (13.2)	C 35 (18.5)	D 75 (39.7)	
Age (years)	74.1±8.1	70.0±13.1	72.7±8.7	70.7±9.2	0.151
Gender (n, %)					
Male	50 (92.6)	23 (92.0)	32 (91.4)	70 (93.3%)	0.986
Female	4 (7.4)	2 (8.0)	3 (8.6)	5 (6.7%)	
Ethnic (n, %)					
Malay	19 (35.2)	10 (40.0)	12 (34.3)	32 (42.7)	0.734
Chinese	27 (50.0)	9 (36.0)	18 (51.4)	30 (40.0)	
Indian	8 (14.8)	6 (24.0)	5 (14.3)	13 (17.3)	
Smoking (n, %)					
Current	16 (29.6)	11 (44.0)	16 (45.7)	21 (28.0)	0.333
Previous	38 (70.4)	14 (56.0)	19 (54.3)	54 (72.0)	
MMRC (n, %)					
0-1	23 (42.6)	8 (32.0)	16 (45.7)	12 (16.0)	0.003
2-4	31 (57.4)	17 (68.0)	19 (54.3)	63 (84.0)	
GOLD class (n, %)					
1-2	33 (61.1)	15 (60.0)	16 (45.7)	29 (38.7)	0.001
3-4	21 (38.9)	10 (40.0)	19 (54.3)	46 (61.3)	
CAT score					
Total	18.0±8.0	18.3±10.1	15.8±8.0	23.6±8.0	<0.001
Cough	2.5±1.2	2.6±1.6	2.1±1.3	3.2±1.2	<0.001
Phlegm	2.6±1.8	2.4±1.9	1.6±1.6	3.3±7	<0.001
Tightness	1.4±1.7	2.2±1.7	1.7±1.5	2.6±1.6	<0.001
Breathlessness	3.4±1.7	3.0±1.7	3.2±1.5	4.0±1.3	0.012
Activity	2.5±1.8	2.3±1.9	2.0±1.7	3.0±1.6	0.033
Leaving home	1.7±1.9	1.9±1.9	1.6±1.8	2.4±1.6	0.038
Sleep	1.6±1.6	1.8±1.8	1.6±1.6	2.2±1.6	0.173
Energy	2.4±1.1	2.2±1.6	2.2±1.5	3.0±1.4	0.002

*Chi-square - categorical variables; ANOVA test - continuous variables.

Patients with phenotype D had significantly higher total CAT score than patients with other clinical phenotypes. Other than sleep quality, patients with phenotype D had significantly higher score in every other components, notably cough severity, phlegm volume, chest tightness, breathlessness upon walking uphill, activity limitation at home, ability to

leave home and energy. There was no different in terms of total and components CAT score of patients with phenotype A, B and C.

Conclusion: Patients with phenotype D had significant higher CAT score, thus poorer quality of life and higher tendency of exacerbation. This group of patients need better medical treatment and closer monitoring.

AP426

WHICH IS THE ADEQUATE TIMING? BLOOD EOSINOPHIL COUNT IN PATIENTS WITH COPD EXACERBATION

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Background and Aims: The blood eosinophil count in patients with COPD exacerbation is reported to be associated with response to therapy, and it is also reported that patients with a severe eosinophilic COPD exacerbation have a shorter length of hospitalization. However, there is no report about the change in blood eosinophil count during the course of COPD exacerbation and its significance. So we examined the utility of blood eosinophil count before and after COPD exacerbation in predicting future exacerbation risk.

Methods: We retrospectively investigated consecutive hospitalized patients due to COPD exacerbation at Iizuka Hospital between December 2012 and December 2017. Inclusion criteria were as follows: Patients who underwent the following blood eosinophil count tests: at stable state before and after the admission, and chest computed tomography (on admission); Patients who have continued visiting our institution after the discharge. The following data were extracted from medical records: age, sex, BMI, pulmonary function tests (FEV1%predicted), severity of emphysema (Goddard classification), blood eosinophil count [at stable states before and after the admission (Eo-b and Eo-a, respectively)], frequency of COPD exacerbation, length of stay, and clinical course during and after admission.

Results: 130 patients were included. During the follow-up period (mean, 2.6 years), 77 patients did not experience COPD exacerbation (non-Ex group) and 53 patients experienced it more than once (Ex group). There was a statistically significant difference between the two groups in Eo-a (median, 242.1/μl in non-Ex vs 150.0/μl in Ex group; $P = 0.002$), not in Eo-b (205.0/μl vs 176.6/μl, $P = 0.634$).

Conclusion: Low blood eosinophil count at a stable state after COPD exacerbation may be one of the risk factors of future COPD exacerbation.

AP427

ACCURACY OF PEAK EXPIRATORY FLOW RATE: HEIGHT RATIO (PEFR/HT2) MEASURED BY PORTABLE DEVICE IN PREDICTING LOW FEV1/FVC IN PATIENTS UNDERGOING SPIROMETRY AT SANTO TOMAS HOSPITAL

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Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disorder of significant public health importance. It is presently ranked as the third most important cause of death worldwide. A diagnosis of COPD is established by a post bronchodilator (BD) forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC) ratio of less than 0.7 or the lower limit of normal (LLN). It is largely under diagnosed in developing countries for various reasons including lack of affordable spirometers in primary care settings. The peak expiratory flow rate (PEFR) test measures how fast a person can exhale. A portable

inexpensive device can be used for this test. Recent reports suggest that peak flow measurements may be an inexpensive way of screening and initial identification of severe cases of COPD for subsequent confirmatory spirometry

Methods: A cross sectional analytical method of research in assessing the peak expiratory flow rate and its height ratio (PEFR/Ht2) measured by a portable device as the main tool in gathering the data.

Results: PEF measurements resulted in a sensitivity of 77–83% and 81–88% specificity with 85%, 86% and 91% accuracy in predicting FEV1/FVC <0.70, below the lower limit of normality and FEV1 percentage predicted of 50% and below respectively.

Conclusion: PEFR could be used as a simple tool in the primary health care setting to screen and identify severe cases of Chronic Obstructive Pulmonary Disease for subsequent spirometry.

AP428

R-VALUE COMPREHENSIVE EVALUATION METHOD FOR THE EFFECT AND LONG-TERM INFLUENCE OF TIAOBU FEI-SHEN THERAPIES ON CHRONIC OBSTRUCTIVE PULMONARY DISEASE RATS

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Background and Aims: This study aimed to evaluate the effect and long-term influence of Tiaobu Fei-Shen therapies (Bufei Jianpi, Bufei Yishen, Yiqi Zishen) on rats with chronic obstructive pulmonary disease (COPD) according to the established R-value comprehensive evaluation method.

Methods: 120 rats were randomly divided into control, model, Bufei Jianpi, Bufei Yishen, Yiqi Zishen and aminophylline groups. The COPD rat models were established by smoke inhalation and bacterial infection. Rats were gavaged with the corresponding treatments from week 9 to 20. Half of rats were left for another 12 weeks without treatment to observe the long-term effect. Indicators related to curative effect, including lung function, pathology of lung tissue and right ventricular hypertrophy index were observed. The effect was evaluated with R-value comprehensive evaluation method.

Results: From the 12th to 32nd week, three indicators related to lung function were significantly altered by Tiaobu Fei-Shen therapies and aminophylline, the relative improvement from high to low was Bufei Yishen, Yiqi Zishen, Bufei Jianpi, and aminophylline. Considering both the 20th and 32nd weeks, five indicators related to pathology of lung tissue were significantly improved in all treated groups ($P < 0.01$), the relative improvement from high to low was Bufei Yishen, Bufei Jianpi, Yiqi Zishen, and aminophylline. At the 20th, 32nd week, and both 20th and 32nd weeks, all eleven indicators related to curative effect were significantly improved in all treated groups ($P < 0.01$), especially Bufei Jianpi granule as compared with aminophylline at week 20 ($P < 0.05$), and Tiaobu Fei-Shen therapies as compared with aminophylline at both the 20th and 32nd weeks ($P < 0.01$, $P < 0.05$). The relative improvement from high to low was Yiqi Zishen, Bufei Jianpi, Bufei Yishen, and aminophylline.

Conclusion: R-value comprehensive evaluation method, established by mathematical theoretical analysis model, can reflect the individual characteristics of Tiaobu Fei-Shen therapies, which might provide new ideas for comprehensive evaluation of medicines.

COMPARISON OF THREE COMBINATIONS OF INHALED LONG-ACTING MUSCARINIC ANTAGONISTS WITH LONG-ACTING BETA AGONISTS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Background: Use of combinations of inhaled long-acting muscarinic antagonists with long-acting beta agonists (LAMA/LABA) is recommended for patients with chronic obstructive pulmonary disease (COPD). Three LAMA/LABA combinations are currently available, but there is a lack of reports that directly compare their effectiveness.

Objective: To compare the effectiveness of the three available inhaled LAMA/LABA combinations (glycopyrronium/indacaterol, tiotropium/olodaterol, and umeclidinium/vilanterol) in patients with COPD.

Methods: We conducted a retrospective review of electronic medical charts of 51 patients with stable-phase COPD receiving treatment with any LAMA/LABA combination for 1 year (April 1, 2017 to March 31, 2018). We compared changes after 12 weeks of treatment in the following clinical outcomes: various respiratory functions (FVC, FEV1, IC) modified Medical Research Council dyspnea score (mMRC), and number of exacerbations of COPD. We also compared adherence and frequency of side effects among patients receiving the three LAMA/LABA combinations.

Changes in mMRC (LAMA/LABA combinations)

		Tiotropium/Olo daterol	Umeclidinium/Vi lanterol	Glycopyrronium/ Indacaterol	Total
mMRC	pre	2.00	2.38	2.12	2.10
	after	1.23	2.13	1.12	1.33

Changes in PFT (LAMA/LABA combinations)

		Tiotropium/Olo daterol	Umeclidinium/Vi lanterol	Glycopyrronium/ Indacaterol	Total
FVC	pre	2.94	2.91	3.25	3.04
(L)	after	3.04	3.01	3.25	3.11
FEV1	pre	1.83	1.61	2.06	1.87
(L)	after	1.92	1.61	2.15	1.95
IC	pre	1.99	2.04	2.08	2.03
(L)	after	2.00	2.08	2.15	2.06

Results: All three LAMA/LABA combination agents showed similar improvement in respiratory function and mMRC score. See figure, there was no statistically significant difference in the improvement between the three groups. $P < 0.05$ Similarly, there were no differences in adherence, number of exacerbations of COPD, and frequency of side effects between the three groups.

Conclusion: The three currently available inhaled LAMA/LABA combination drugs showed similar improvement in respiratory function and mMRC score in patients with COPD.

AP430

COMPARING THE DIFFERENT DIAGNOSTIC CRITERIA OF ASTHMA-COPD OVERLAP

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Background and Aims: A unified diagnostic criteria for asthma and chronic obstructive pulmonary disease (COPD) overlap is not established. We aimed to investigate the prevalence, clinical characteristics, exacerbation risk, and agreement between the updated widely accepted different diagnostic criteria of asthma-COPD overlap (ACO).

Methods: This is a prospective, multicentre cohort study that analysed questionnaires for ACO, lung function, laboratory result, and exacerbation of 635 COPD patients in Korea.

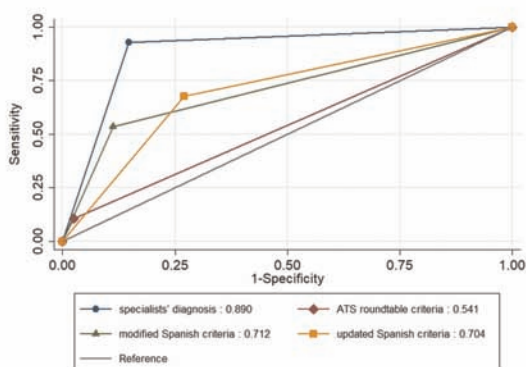
Table 1. The prevalence of ACO based on diagnostic criteria

Criteria	Number of patients, n (%)	
	meet the criteria	do not meet the criteria
ATS roundtable criteria		
Major		
Post-BD FEV ₁ /FVC < 0.7 and Age ≥40	635 (100)	-
Smoking ≥ 10 pack-year or exposure to air pollution ≥ 10year	523 (93.9)	34 (6.1)
History of Asthma before 40years or BDR > 400mL in FEV ₁	44 (7.8)	523 (92.2)
Minor		
History of atopy or allergic rhinitis	48 (8.6)	511 (91.4)
separate BDR ≥ 12% and 200mL	31 (4.9)	604 (95.1)
Blood eosinophil count ≥ 300cell/μL	141 (23.2)	468 (76.8)
ACO (all 3 major and at least 1 minor)	18 (3.6)	475 (96.4)
GINA/GOLD document ¹		
Component of asthmatic feature ≥3	106 (16.9)	522 (83.1)
Component of COPD feature ≥3	615 (97.9)	13 (2.1)
ACO (≥3 asthma and ≥3 COPD features)	98 (15.6)	530 (84.4)
modified Spanish COPD Guidelines		
Major criteria		
Previous history of asthma	34 (6.0)	533 (94.0)
BDR >15% and 400 mL	8 (1.3)	627 (98.7)
Minor criteria		
IgE >100 IU, or history of atopy	171 (52.8)	153 (47.2)
BDR >12% and 200 mL	27 (4.3)	608 (95.7)
Blood eosinophil >5%	104 (17.1)	505 (82.9)
ACO (At least 1 major or 2 minor)	86 (15.1)	484 (84.9)
updated Spanish COPD Guidelines		
1. Age ≥35, smoker ≥10 pack year and Post-BD FEV ₁ /FVC < 0.7	523 (93.9)	34 (6.1)
2. Current diagnosis of asthma ²	9 (2.0)	440 (98.0)
3. BDR ≥15% and 400 mL, and/or eosinophilia in blood ≥300 cell/μL	147 (24.1)	463 (75.9)
ACO (1 and 2 or 1 and 3)	135 (31.0)	300 (69.0)
specialists' diagnosis		
Answer yes to the question "Is this patient likely to be classified with ACO?"	168 (29.4)	403 (70.6)

¹GOLD/GINA criteria-based ACO was defined if the patients met at least 3 items in both the asthma and COPD categories.

²Current diagnosis of asthma must include (a) and (b): (a) respiratory symptoms of variable course with history and/or symptoms causing clinical suspicion; family asthma history or personal history of asthma in childhood, or personal history of atopy, or inflammation of the upper airway (e.g. rhinosinusitis), (b) post BD FEV₁ ≥ 12% and 200 mL, or diurnal variability of PEF ≥20%, or FENO ≥ 50 ppb

ACO, asthma-COPD overlap; ATS, American Thoracic Society; BDR, bronchodilator response; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; GINA, Global Initiative for Asthma; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FENO, fractional exhaled nitric oxide; IgE, immunoglobulin E; PEF, peak expiratory flow



Results: Among COPD patients, 18 (3.6%), 98 (15.6%), 86 (15.1%) and 135 (31.0%) met the ACO criteria for the American Thoracic Society (ATS) roundtable, global initiative for asthma/global initiative for chronic

obstructive lung disease (GINA/GOLD), modified Spanish COPD, and updated Spanish COPD guidelines, respectively (Table 1). ACO patients tended to be less male predominant, smoked less, had less airflow limitation, and were more frequently prescribed inhaled corticosteroids than non-ACO patients. Among 574 patients who were included in the exacerbation analysis, no significant differences were detected in the prevalence of exacerbation between ACO and non-ACO patients according to the used criteria during a 6-month follow-up period. When GINA/GOLD criteria were used as gold standard, the highest and lowest diagnostic agreement were shown in patients diagnosed by specialists and ATS roundtable criteria, respectively (area under the receiver operating characteristic curve, 0.89 vs 0.54; Figure 1).

Conclusion: For a more accurate ACO diagnosis, it is necessary to establish diagnostic criteria that can comprehensively evaluate asthmatic features.

AP431

DIFFUSING CAPACITY OF THE LUNGS FOR CARBON MONOXIDE IS A PREDICTOR FOR EXERTIONAL DESATURATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Table. Comparison of the characteristics between the ED and non-ED groups by univariate (P value) and multivariate (P* value) analyses

	ED group (N=34)	Non-ED group (N=79)	P	P*
Age	64.3±8.7	64.1±8.8	0.43	
Male (%)	97.1	97.5	0.90	
Smoking history (pack-yr)	18.9±13.3	17.7±13.1	0.32	
Current smoking status (%)	30.8	33.0	0.91	
BMI (kg/m ²)	23.3±3.9	23.7±3.6	0.79	
FVC (% of predicted)	63.7±18.3	74.3±18.9	0.03	0.31
FEV ₁ (%)	48.7±13.3	58.1±13.3	0.02	0.58
FEV ₁ (% of predicted)	43.7±15.8	57.2±15.7	0.02	0.43
HR (b/min)	101.8±15.8	78.4±15.4	<0.001	0.03
HR (b/min)	101.8±15.8	78.4±15.4	0.17	0.03
HR (b/min)	101.8±15.8	78.4±15.4	0.04	0.08
HR (b/min)	101.8±15.8	78.4±15.4	0.02	
HR (b/min)	101.8±15.8	78.4±15.4	0.11	
HR (b/min)	101.8±15.8	78.4±15.4	0.04	0.31
HR (b/min)	101.8±15.8	78.4±15.4	<0.001	<0.001
HR (b/min)	101.8±15.8	78.4±15.4	0.4	
HR (b/min)	101.8±15.8	78.4±15.4	0.07	0.79
HR (b/min)	101.8±15.8	78.4±15.4	0.79	0.019
HR (b/min)	101.8±15.8	78.4±15.4	0.79	
HR (b/min)	101.8±15.8	78.4±15.4	0.06	0.01
HR (b/min)	101.8±15.8	78.4±15.4	0.39	
HR (b/min)	101.8±15.8	78.4±15.4	0.00	
HR (b/min)	101.8±15.8	78.4±15.4	0.31	
HR (b/min)	101.8±15.8	78.4±15.4	0.31	
HR (b/min)	101.8±15.8	78.4±15.4	0.001	0.31
HR (b/min)	101.8±15.8	78.4±15.4	0.001	0.43
HR (b/min)	101.8±15.8	78.4±15.4	0.04	0.67
HR (b/min)	101.8±15.8	78.4±15.4	0.39	

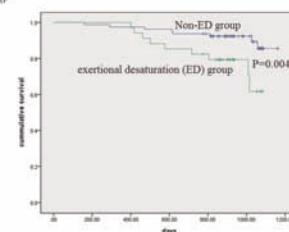
Abbreviations: ED, exertional desaturation; COPD, chronic obstructive pulmonary disease; FEV₁,

forced expiratory volume in 1 s; FVC, forced vital capacity; HR, heart rate; hCRP,

high-sensitivity C-reactive protein; MMRC, the modified medical research council; RR,

respiratory rate; SpO₂, oxygen saturation; 6MWT, 6-min walk distance

Initial means at the beginning of 6 MWT; *end* means at the end of 6 MWT



Background and Aims: Exertional desaturation (ED) is associated with a poor outcome in chronic obstructive pulmonary disease (COPD); however, it is uncertain which factors predict ED. The aims of this study were to investigate the impact of ED on mortality and the predictors of ED in stable COPD.

Methods: A total of 113 patients with clinically stable, widely severe COPD were enrolled into this cohort study from Kaohsiung Chang Gung Memorial Hospital, Taiwan ED was assessed using the 6-min walk test (6MWT), and defined as a post-exercise oxygen saturation (SpO₂) of <90% or a ≥4% decrease. Hazard ratios (HRs) for 3 years mortality were estimated using a Cox regression analysis.

Results: This study included the ED (N = 34) and non-ED (N = 79) groups. A multivariate analysis showed the diffusing capacity of the lungs for carbon monoxide (DLCO; [P = 0.03]), minimum oxygen saturation (P < 0.001), and maximum heart rate (P = 0.018) during a 6MWT were

significantly associated with ED (Table 1). The average survival duration was significantly different between ED and non-ED groups (856.4 vs 933.8 days, $P = 0.033$). After adjusting for age, sex, body mass index, 6MWD, forced expiratory volume in the first second, Modified Medical Research Council scale, GOLD stage, exacerbation, serum high-sensitivity C-reactive protein (hsCRP), and fibrinogen, the ED group had a significantly higher mortality than the non-ED group ($P = 0.012$; HR = 4.12; 95% CI: 1.37–12.39) (Figure 1).

Conclusion: ED is an independent factor associated with mortality in stable COPD and can be significantly predicted by DLCO.

AP432

This abstract has been withdrawn.

AP433

THE PROPORTION AND CLINICAL CHARACTERISTICS OF ASTHMA-COPD OVERLAP (ACO) IN TAIWAN: A CROSS-SECTIONAL STUDY

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Background and Aims: The Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines have given joint recommendations on the identification, diagnosis and treatment of asthma-COPD overlap (ACO). These recommendations have been adapted for clinical use in many Asian countries including Taiwan. However, their application to clinical practice has never been systematically evaluated. In addition, there are no prevalence data of ACO in Taiwan. The aim of this study was to determine the proportion and clinical characteristics of ACO among a cohort of COPD patients.

Methods: This observational cross-sectional study was conducted in 5 medical centres in Taiwan. From October 2016 through April 2017, consecutive COPD patients visiting outpatient clinics were interviewed and enrolled into a prospective cohort. Clinical characteristics, pulmonary function data, and laboratory data were collected and analyzed.

Results: Three hundred and forty COPD patients were enrolled into this study. The mean age was 71.7 years and 320 (94.1%) patients were male. Based on investigators' diagnosis, 103 (30.3%) patients were ACO cases. The major difference of clinical characteristics between patients with or without ACO were age, age of COPD diagnosis, duration of ACO/-COPD treatment, family history of asthma, reversible airflow limitation, medication for patients, and comorbidity rate. Our data suggests that the physician diagnosis of ACO in Taiwan is mostly in concordance with GINA/GOLD guidelines. In addition, the treatment for ACO in Taiwan was also consistent with the GINA/GOLD recommendations. LABA/ICS was the major medication used to control ACO.

Conclusion: In Taiwan, 30.3% COPD patients were diagnosed as having ACO. These COPD patients with asthma traits were younger, diagnosed with COPD earlier but treated with shorter duration. They also have higher percentages of comorbidities, family history of asthma, and reversible airflow limitation.

Table. Demographic and Clinical Characteristics of the Patients at Baseline

Characteristic	Total (N=340)	ACO (N=103)	Without ACO (N=237)	p-value
Age - yr (mean $\pm$ SD)	71.66 $\pm$ 10.38	69.01 $\pm$ 11.77	78.21 $\pm$ 9.51	0.004*
Male sex - no. (%)	320 (94.1)	96 (93.2)	224 (94.5)	0.62 ^{NS}
Weight - kg (mean $\pm$ SD)	64.26 $\pm$ 11.91	65.12 $\pm$ 12.52	63.59 $\pm$ 11.64	0.396 ^{NS}
Height - cm (mean $\pm$ SD)	164.18 $\pm$ 7.04	165.2 $\pm$ 8.00	163.73 $\pm$ 6.55	0.102 ^{NS}
Age at first COPD diagnosis or initial COPD treatment - yr (mean $\pm$ SD)	(N=330) 67.2 $\pm$ 10.44	(N=94) 65.01 $\pm$ 12.97	(N=236) 68.17 $\pm$ 9.12	0.031*
Age at symptom onset	N=336	N=101	N=235	
< 20 - no. (%)	3 (0.9)	2 (2.0)	1 (0.4)	
20-40 - no. (%)	5 (1.5)	4 (4.0)	1 (0.4)	0.01*
> 40 - no. (%)	328 (97.6)	95 (94.0)	233 (99.1)	

*statistically significant difference

SD, standard deviation; NS, non-significant; COPD, chronic obstructive pulmonary disease; ACO, asthma-COPD overlapping

AP434

This abstract has been withdrawn.

AP435

STUDY REGARDING THE CLINICAL EFFICACY OF AG NPP709 (SYNATURA®) IN PATIENTS WITH CHRONIC BRONCHITIS TYPE COPD

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Background and Aims: AG NPP709 (Synatura®) was developed by Korean pharmaceutical company (Ahn-Gook) and already proved to be superior in suppressing cough and sputum in patients with acute upper respiratory infection and chronic inflammatory bronchitis in previous phase III study. Thus, it can be assumed that AG NPP709 is effective in COPD patients with chronic bronchitis type, which is the main symptoms of cough and sputum.

Methods: Chronic bronchitis type COPD patients 1) with post-bronchodilator (BDR) FEV1/FVC ratio < 70, 2) over the age of 40 years with smoking history more than 10 pack years, and 3) with symptoms of chronic bronchitis including cough and sputum for more than 3 months were enrolled. This prospective open-label single-arm clinical trial examined clinical efficacy through pulmonary function test (PFT), COPD assessment test (CAT) scores and systemic inflammation state assessed by CRP, fibrinogen, IL-6, TNF- α and IL-33. A total of 30 patients enrolled and received a follow-up test after taking AG NPP709 for 3 months.

Results: Total 30 patients were included, all patients were male, mean age was 71.9 $\pm$.93. Of the total patients, 100% were ever smokers and mean smoking history was 46.8 $\pm$ 4.96 pack-years. The mean post-BDR FEV1/FVC ratio was 58.6 $\pm$ 1.4, FEV1 (%) was 75.9 $\pm$ 0.07. The mean total CAT score was 14.7 $\pm$.14. Of this patients, 26 were followed up after 3 months. In paired t test, significant improvement ($P < 0.05$) was observed in total CAT score ($P = 0.005$), fibrinogen ($P = 0.013$). Three patients experienced mild gastrointestinal side effects such as nausea. No serious adverse event was developed

Conclusion: AG NPP709 improved the symptoms, which is represented by the CAT score, in patients with chronic bronchitis type COPD, and improved systemic inflammation by significantly reducing fibrinogen levels. This study suggests that AG NPP709 can be used with efficacy and safety in chronic bronchitis type COPD patients.

AP436

EFFECTS OF Pedometer Intervention on Daily Physical Activity and QOL in Patients with COPD, Including Additional Analysis on ACO

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Background and Aims: Daily physical activity (DPA) interventions to induce behavioural changes are attracting special attention, especially, in relation to pedometer. To confirm the effects of pedometer intervention on the time course of DPA and COPD assessment test (CAT) in the patients with COPD and ACO (asthma and COPD overlap).

Methods: Male patients with stable COPD ($n = 38$, age $72. \pm .9$, % FEV = $7. \pm 0.8$, data expressed as Mean $\pm$ SD) who were regularly visiting to our out-patient clinics were retrospectively analyzed. Following the initial assessment and instructions, at each visit, CAT was scored by the patients, and medical professional stuffs which were composed of a physician, a physical therapist, and nurses advised the patients to put pedometer on and to record the daily counts every day.

Results: DPA significantly increased from the baseline (528 ± 427 , steps/day) to those at 3 month (667 ± 740 , $P < 0.01$), and it was well maintained over 1 year (6376 ± 3245 , $P < 0.01$). CAT scores significantly decreased from the baseline ($11. \pm .6$, points) to those at 3 month ($8. \pm .1$, $P < 0.05$). Two subgroups which were separated into COPD ($n = 23$) and ACO ($n = 15$) showed similar and significant increase in DPA at 3 month ($P < 0.01$). However, while DPA at 1 year tended to be better maintained in the subgroup COPD ($P < 0.01$), DPA in ACO significantly decreased from DPA at 3 month (651 ± 758) to DPA at 1 year (524 ± 311 , $P < 0.01$).

Conclusion: The pedometer education improved DPA and CAT maintained over 1 year. However, the long term effects in the subgroup ACO's seemed weaker.

AP437

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ASSOCIATED RISK FACTORS IN NORTH INDIA

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Background and Aims: COPD ranks among top five causes of premature death and years lived with disability in India. The lack of quality data and variation in the study characteristics underline the need for quality epidemiological studies at a national level to measure the prevalence of COPD in India.

The aim of this study was to assess the prevalence of COPD and associated risk factors in northern India.

Methods: We conducted a population based cross-sectional survey, as a part of a larger study to develop and pilot a community-based COPD management and control program in Sonipat district of India, among 2,355 participants aged ≥ 40 years residing in rural and urban areas of North (Haryana) India. Participants were selected using a multi-stage cluster random sampling technique. Data were obtained using a three-stage screening process that involved: interviewer administered questionnaire, pocket spirometry performed by community health workers. For individuals who screened positive, a diagnosis of COPD was confirmed with post-bronchodilation spirometry and defined according to the GOLD criteria (post-BD FEV1/FVC <0.70). Data was also collected on smoking history, exposure to environmental pollution, socioeconomic status, quality of life and symptom severity [measured using the COPD Assessment Test (CAT)]. We are presenting here our preliminary findings from the cross-sectional survey.

Results: The mean age of participants was 56.0 (SD $\pm$ 10.9 years) and 54% were women. The prevalence of COPD confirmed on spirometry was 4.42% ($n = 104$). Multivariate modelling demonstrated that a diagnosis of COPD in this cohort was associated with age, male sex, ever-

smoking status: RRR 3.10 (95% CI 1.46–6.58), history of pneumonia: RRR 3.20 (1.29–7.97), having a CAT score of >20 : RRR 29.4, (12.2–70.9).

Conclusion: The prevalence of COPD in Haryana province of northern India was approximately four percent, quality of life data demonstrates that individuals with COPD were experiencing a high symptom burden.

AP438

This abstract has been withdrawn.

AP439

SURVEY OF THE HEALTH-RELATED QUALITY-OF-LIFE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS AND DISEASE-RELATED INDIRECT BURDENS

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Background and Aims: Many COPD patients have physical limitations and they need caregiver. We assessed quality of life and the indirect burden of COPD patients, including the need for caregivers, home care, caregiver related burden, and time expenditures.

Methods: We recruited 355 COPD patients from 2 primary and 11 secondary/tertiary hospitals and graded the severity of airflow limitation: 10% of patients exhibited mild, 40% moderate, 30% severe, and 20% very severe limitations. The inclusion criteria were age ≥ 40 years and COPD ≥ 1 year in duration; all patients were recruited between June 2015 and October 2016. Participants in the survey, they were face to face interviewed with questionnaires for EQ-5D to investigate health related quality of life, caregiver accompanying rate and time requirement to visit clinic, loss of productivity of caregiver, and home care rate.

Results: The proportion of males was very high, particularly among those aged > 60 years. The quality of life tended to decline with age, from mild to very severe impairment, as revealed by the EuroQol five-dimensions five-level (EQ-5D-5L) scores and the EQ visual analogue scale (VAS). Family caregivers accompanied 22.6% of patients who visited outpatient clinics, and 25% of stage IV COPD patients. During emergency visits and hospitalization, this figure increased to $> 60\%$. In terms of home care, the rates were 28.5% for stage I patients, and 34.4, 31.8, and 52% for stage II–IV patients, respectively. The percentage of caregivers who stopped working was 13.6%. The EQ-5D index was strongly associated with the dyspnea scale ($r = -0.64$, $P < 0.001$). The average time required to see a doctor and visit the pharmacy (from door to door) was 154 minutes.

Conclusion: In patients with COPD, the EQ-5D index decreased, and disease-related home caregiving increased, with airflow limitation. The indirect burden must be targeted when managing COPD.

AP440

THE VALUE OF ALLERGY SCREENING IN CHINESE ADULT PATIENTS WITH CHRONIC RESPIRATORY DISEASES

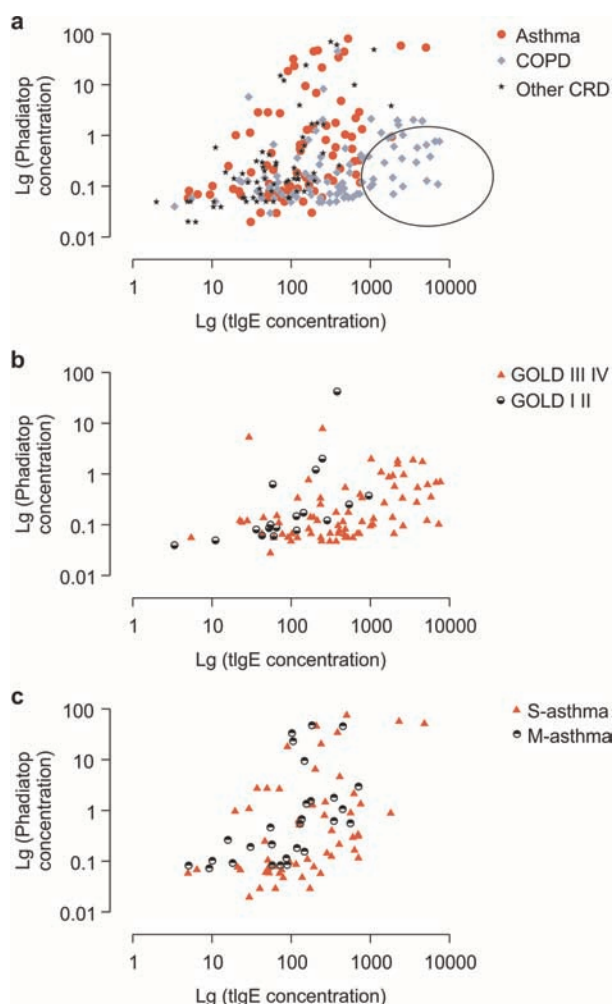
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Background and Aims: The prevalence of allergen-induced chronic respiratory disease (CRD) is increasing annually. This study aimed to

analyze sensitization characteristics of adult Chinese CRD patients and the value of allergy screening.

Methods: Serum immunoglobulin E (sIgE) was detected with an allergy screening test. Total immunoglobulin E (tIgE) levels were measured in 85 asthma patients, 98 chronic obstructive pulmonary disease (COPD) patients, and 69 patients with other CRDs. An sIgE concentration ≥ 0.35 kU/L indicated atopy.



Results: The total positive rate of allergy screening among CRD patients was 36.1%. Asthma had the highest rate (45.9%), followed by COPD (32.7%) and other CRDs (29.0%). The positive rate of allergy screening was significantly higher among urban asthma patients (56.1%) than among rural patients (25.0%, $P < 0.05$), and significantly higher among office staff (68.9%) than among outdoor workers (42.8%, $P < 0.05$). Patients with COPD (42.9%) and recurrent exacerbation were atopic. Atopy was a risk factor for dyspnea (OR = 1.22; 95% CI, 0.95–1.75, $P < 0.05$). Optimal scaling analysis revealed a correlation between tIgE levels and smoking index (Cronbach's $\alpha = 91.1\%$). In addition, the FVC levels in COPD patients with atopy were significantly lower than those without (2.06 L vs 2.63 L, $P < 0.05$). Up to 35.0% of patients who met the Global Initiative for Chronic Obstructive Lung Disease III (GOLD III) IV criteria and had a low Phadiatop level (≤ 10 kU/L), had a high tIgE level (≥ 1000 kU/L), compared to GOLD I II patients (5.5%).

Conclusion: Patients with CRD had high sensitization. Asthma patients who work indoors were more susceptible to allergies. Atopy was

associated with COPD pulmonary function, and we did not exclude COPD patients with more sensitization to uncommon allergens. It is necessary to initially screen the sensitization situation of CRD patients, which can guide the treatment, management, and prevention of CRD.

AP441

LIFE EXPECTANCY AND EXPECTED YEARS OF LIFE LOST IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: To determine the life expectancy (LE) and expected years of life lost (EYLL) in patients with severe chronic obstructive pulmonary disease (COPD).

Methods: 539 patients diagnosed with COPD and classified as severe according to the GOLD (Global Initiative for chronic obstructive lung disease) guideline at National Cheng Kung University Medical Center were recruited between January 2006 and December 2016. We recorded all patient's pulmonary function and severe acute exacerbation history in the preceding one year. We verify the study cohort's survival status and date of death by linkage with Taiwan National Mortality Registry from Health and Welfare Data Science Center. We estimated survival function by Kaplan-Meier method, and applied a rolling extrapolation algorithm to extrapolate the lifetime survival function and estimated their life expectancy. We also simulated age-, calendar year-, and sex-matched referents from national life tables to estimate the life expectancy, had the patients not developed COPD. We conducted a cross sectional survey of quality of life with the EuroQol five-dimension (EQ-5D) questionnaire among 291 patients, of which kernel smoothing mean is calculated and multiplied with lifetime survival function to obtain QALE (quality-adjusted life expectancy).

Results: There was no loss of LE for patients with mild COPD under GOLD definition. But those with moderate ($80\% > FEV_1 \geq 50\%$ of prediction) and severe and very severe ($FEV_1 < 50\%$ of prediction) COPD are associated with a shorter LE, or, 7.9 and 5.1 years, respectively, they also suffered from loss of life expectancy with EYLL of 7.6 and 10.7 years, respectively. The EYLL for those with severe acute exacerbation (AE) in the preceding one year is 10.0 years, which seems similar to those with severe and very severe stage.

Conclusion: Patients with COPD have an increased risk of mortality, especially for patients under very severe, severe and moderate stages and those with severe AE history in previous 1 year.

AP442

THE CORRELATION OF ABSOLUTE EOSINOPHIL COUNT IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN FILIPINO PATIENTS

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Background and Aims: Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases. Detection and measurement of airway eosinophilia in COPD

patients mostly require the assessment of induced sputum. Because of its limitations, several studies showed blood eosinophil count can potentially serve as respectable surrogate marker for sputum eosinophilic COPD.

Methods: This was a prospective cross sectional study at Philippine Heart Center. All patients >40 years old clinically diagnosed with COPD through spirometry done within six months were included. Demographic characteristics and absolute eosinophil count was recorded. Quantitative variables were summarized as mean and standard deviation, while qualitative variables were tabulated as frequency and percentage. Correlation between eosinophil level and degree of COPD was graphically presented in a scatterplot and analyzed using Pearson's product Correlation.

Results: We analysed 102 stable COPD patients. There were 59(57.84%) eosinophilic COPD and 43(42.16%) non-eosinophilic COPD patients. The mean age was 69 years old, mostly males, 81.37%. The mean ages of both groups were $65.7 \pm .9$ and $62.1 \pm .20$ on COPD eosinophilic and non-eosinophilic patients respectively, $P = 0.05$. Both study groups have more male subjects, 52(88.14%) and 31(72%); however, there were more females in the non-eosinophilic compared to the eosinophilic group 12(27.9%) vs 7(11.6%), $P = 0.04$. A high pack years smoked was reported in the eosinophilic group compared to the non-eosinophilic group ($54. \pm 2.0$ vs 43.4 ± 7.90 correspondingly, $P = 0.007$). Correlation between absolute eosinophil value and the degree of COPD was weak ($r = 0.3467$), but statistically significant with $P = 0.0004$.

Table 1. Baseline Demographic and clinical characteristics of COPD Patients with and without blood eosinophilia

Characteristics N=102	Eosinophilic COPD n=59	Non-Eosinophilic COPD n=43	P value
Age (in years)	65.74 $\pm$ 8.9	62.11 $\pm$ 9.20	0.05
Gender			0.04
Male	52 (88.14%)	31 (72%)	
Female	7 (11.6%)	12 (27.9%)	
BMI	21.2 $\pm$ 1.95	21.1 $\pm$ 2.11	0.80
Smoking history (pack-years smoked)	54.9 $\pm$ 22.0	43.47 $\pm$ 17.90	0.007
Co-Morbidities			
Type 2 DM	21 (35.59%)	12 (27.91%)	0.41
Hypertension	42 (71.19%)	23 (53.49%)	0.06
CAD	21 (35.59%)	17 (39.53%)	0.68
Dyslipidemia	7 (11.86%)	7 (16.28%)	0.57
Degree of COPD			0.025
COPD A	19 (32.20%)	21 (48.84%)	
COPD B	20 (33.90%)	18 (41.86%)	
COPD C	10 (16.95%)	3 (6.98%)	
COPD D	10 (16.95%)	1 (2.33%)	
Severity of airflow obstruction			0.373
GOLD I	34 (57.63%)	30 (69.77%)	
GOLD II	19 (32.20%)	11 (25.58%)	
GOLD III	6 (10.17%)	2 (4.65%)	
Medications			
ICS	0	0	0
ICS+LABA	24 (40.68%)	21 (48.84%)	0.41
LAMA+LABA	34 (57.63%)	22 (51.16%)	0.52

BMI: Body mass index; DM: Diabetes Mellitus; CAD: Coronary Artery Disease;

COPD: Chronic Obstructive Pulmonary Disease; ICS: Inhaled corticosteroid;

LABA: Long acting β_2 -agonist; LAMA: Long acting muscarinic antagonist

Conclusion: Absolute eosinophil levels above $\geq 0.40 \times 10^9/L$ showed the possibility of increased risk for exacerbation in stable COPD patients. This study was able to ascertain that as the degree of COPD elevates, the levels of the eosinophil count is also increased. However, there was no established relationship between severity of airflow limitation and the level of eosinophil count.

AP443

ENHANCING THE COMPETENCE OF NURSES IN COPD CARE CHI KEUNG LAM¹

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Background and Aims Introduction: Chronic obstructive pulmonary disease (COPD) is a major health problem worldwide and is likely

to increase during the next decades. However, nurses do not have sufficient updated knowledge to provide optimal care for patients with COPD. So, an updated COPD educational program was conducted. To improve COPD nursing care by enhancing nurse staff's knowledge in COPD. To standardized the nursing care provided for patients with COPD

Objectives Methods: Updated Guidelines of COPD management from Global Initiative For COPD (GOLD) was introduced. Workshop was held to introduce the indications and uses of inhalation medications for COPD

Re-demonstration of inhalation medications for COPD by nurses. COPD Bundles of Care were introduced

Chronic Disease management Model was introduced on caring patients with COPD. An educational program and workshop on COPD Care was held, the contents are as below:

Results: The participants indicated that knowledge and skill enhancement contributed to professional development and strengthened the nurses' confidence in caring patients with COPD.

Conclusion: The enhanced knowledge improved the nurses' confidence in performing nursing tasks and made the patients feel secure. Implementing COPD education programmes for nurses is of importance in securing safer patient care.

AP444

STUDY ON CHARACTERISTICS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH DIFFERENT PHENOTYPES YING FANG^{1*}, JINGPING ZHENG¹, WENHUA JIAN¹, DONGYING ZHANG¹

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Background and Aims: As for different clinical phenotypes in patients with Chronic Obstructive Pulmonary Disease (COPD), this study explored whether there're distinctive differences and their influencing factors in patients with different phenotypes of COPD.

Methods: Recruited patients who met the COPD diagnostic criteria in a respiratory clinic and collected patient-related clinical information. According to patient's clinical characteristics, radiological report signs are divided into Chronic **Bronchitis type** (continuous cough, sputum, shortness of breath, imaging suggest chronic bronchitis signs, with or without signs of emphysema); **Emphysema type** (no or occasional cough, sputum, shortness of breath, radiographic evidence of emphysema); **Asthma-COPD Overlap type** (clinical diagnosis Asthma-COPD Overlap, imaging suggestive of chronic bronchitis). To compare the three groups of respiratory symptoms, pulmonary function, imaging signs, acute exacerbations within 12 months whether it's a significant difference.

Results: In this study, 357 COPD patients were enrolled, including 157 patients in Chronic Bronchitis type, 78 patients in Emphysema type, and 122 patients in Asthma-COPD Overlap type. The degree of lung function impairment in patients with chronic bronchitis was more severe than other two types (POST-FEV1%_{PRED} $43.0 \pm 7.75\%$, $50.0 \pm 1.24\%$ vs $56.8 \pm 0.36\%$, $F = 17.345$, $P = 0.00$, POST-FEV1%_{FVC} $42.2 \pm 1.90\%$, $45.5 \pm 1.23\%$, $49.5 \pm 2.34\%$, $F = 12.880$, $P = 0.02$). Combined with the CAT score, the patients with Emphysema type subgroups were milder on the other two types ($10. \pm .4$, vs $12.8 \pm .0$, $13.4 \pm .4$, $F = 3.265$, $P = 0.03$). However, on the comparison of acute exacerbations within 12 months, the times of acute exacerbations in patients with Emphysematous type in the past 12 months was higher than that in patients with Chronic Bronchitis ($1.6 \pm .25$ vs $1.1 \pm .10$, $P = 0.04$).

Conclusion: The severity of lung function impairment and respiratory symptoms in patients with chronic bronchitis type were more severe than those other types. However, it was observed that patients in Emphysema type had higher rates of acute exacerbation than those with chronic bronchitis, which may be related to the absence or minimal respiratory symptoms.

This abstract has been withdrawn.

AP445

AP446

CARDIOPULMONARY EXERCISE TEST IN EVALUATION OF FUNCTIONAL CAPACITY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background and Aims: Assessment of severity in patients with Chronic Obstructive Pulmonary Disease (COPD) is usually done at rest by spirometry test. But cardiopulmonary exercise test (CPET) can be a measure to assess the functional capacity more accurately in patients with COPD.

Methods: Fifty eight patients with stable COPD were included in this study and categorised into four groups based on spirometric data following the GOLD guidelines 2018; GOLD 1 : mild COPD, GOLD 2: moderate COPD, GOLD 3: severe COPD and GOLD 4: very severe COPD. Symptom limited CPET was performed on treadmill using Bruce protocol through cardiopulmonary exercise machine in all fifty eight patients.

Results: Twenty one patients (36.20%) had moderate COPD; twenty six (44.82%) had severe COPD; eleven (18.96%) had very severe COPD and none were found to be categorised as mild COPD. All fifty eight patients attained anaerobic threshold (AT). Majority (34, 58.62%) of patients stopped exercise due to shortness of breath; decreased oxygen saturation was the cause of stopping exercise in eight (13.7%) patients; other causes of exercise limitation were increased heart rate, vertigo, leg fatigue, increased blood pressure, ventricular ectopic and chest tightness. Four patients were found to limit exercise due to combined shortness of breath and leg fatigue.

A significant correlation ($r = 0.47$, $P = 0.001$) between forced expiratory volume in first second (FEV₁, % predicted) and maximum oxygen uptake (Vo₂max, mL/kg/min) was observed.

Twenty seven (46.55%) patients with low (<40%) AT were identified among them seven were in GOLD 2 stage, twelve were in GOLD 3 stage and eight were in GOLD 4 stage.

Conclusion: Cardiopulmonary Exercise Test is useful to measure the functional capacity in COPD patients by assessing the maximum oxygen uptake. Thus it could be a good monitoring tool to see the outcome of pulmonary rehabilitation program for COPD patients.

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EOSINOPHILIC AIRWAY INFLAMMATION AND AIRWAY HYPERRESPONSIVENESS IN COPD

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Background and Aims: The differential diagnosis in patients with persistent airway limitation is sometimes not clear in older adults. Eosinophil inflammation in the airways may be observed in some cases with COPD, independent of asthma. However, little is known about airway eosinophilia in COPD in detail. This retrospective clinical study was designed to examine how airway eosinophilia develops in patients with COPD who have no symptom and no past history of asthma, and to

determine whether addition to inhaled glucocorticosteroid (ICS) on these cases is beneficial.

Methods: Sputum examination was carried out in the stable COPD (GOLD 2–3) with daily inhalation of long-acting bronchodilators (LABAs and LAMAs). When airway eosinophilia was diagnosed by qualitative (+) or quantitative assessment (>2%), ICS was added on these patients. COPD assessment test (CAT) and lung function test were followed up. In cases with FEV₁ >1.7 L or >70% of predicted values, acetylcholine provocation test was examined for assessment of airway hyperresponsiveness (AHR).

Results: Eosinophils in sputum were observed in 48 (43.2%) of 111 cases who have no clinical features of asthma. In 12 cases (48.0%) of 25 cases, the value of PC20 in the provocative test was less than 8000 mg/mL. After administration of ICS, CAT score were decreased from 8.8 to 5.1 points, and FEV₁ and IC were further increased by 151.0 and 239.6 mL, respectively (each $P < 0.05$). During observation for one year, exacerbation did not occur, in contrast dyspnea and wheezing occurred in four cases among patients who did not administrate ICS because of sputum eosinophil less than 2%.

Conclusion: Airway eosinophilia and AHR, which are characteristic features of asthma, develop in approximate 45% of COPD independent of asthma. Addition of ICS to bronchodilators is very effective on COPD with airway eosinophilia, which may be a novel phenotype of COPD, different from asthma-COPD overlap.

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THE APPLICATION OF INTELLIGENT WRISTBANDS IN THE ACUTE EXACERBATION OF COPD PATIENTS

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Background and Aims: To observe daily activities and night sleeping in patients with acute exacerbation of COPD by using intelligent wristbands.

Methods: We selected COPD patients for long-term follow-up since on June 2016. The subjects were required to fill out the related journal of the disease and wear a specific intelligent wristbands to recorded the daily activities and sleeping. To explore the change of the daily activities and night sleeping within the first 2 weeks, the acute exacerbation, and the 2 weeks after the acute exacerbation.

Results: Up to May 2018, 46 subjects were temporarily surveyed, with an average age of 65.96 ± 6.09 years, the average acute Aggravated 2.56 times / person, acute exacerbation: mild 11/25, moderate 28/25, severe 6/25, unable to judge the degree (taking Antibiotic drugs on oneself when some one feel poorly) 17/25. The degree of acute aggravation and step and mileage: mild (8456 ± 824.20 step, 5.67 ± 0.54 km), moderate (7332.82 ± 829 step, 4.77 ± 0.55 km), severe (4175.26 ± 839.60 , 2.7 ± 0.55 km), unable to judge the degree (10807.2 ± 49.58 step, $7.1 \pm .51$ km). The degree of acute exacerbation and total sleeping: mild 363.59 ± 26.02 minutes, moderate 334.15 ± 17.02 min, severe 327.45 ± 43.6 min, and unable to judge 401.89 ± 14.35 min. There was a significant difference between the step number and the mileage of the acute exacerbation 2 weeks before the acute exacerbation and the 2 weeks after the acute exacerbation ($P = 0.002-0.012$). Compared the reduction to the step number and mileage within before acute exacerbation and on

acute exacerbation indicated that the disease was worse. The increase of the number of steps and the mileage in the acute exacerbation indicated the improvement of the condition.

Conclusion: The acute exacerbation and recovery of COPD patients can be assessed according to the number of steps and sleep changes of patients wearing intelligent wristbands.

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IMPACT OF SMOKING ON COPD DEATH IN TAIWAN AND FORECASTING MORTALITY TO 2025

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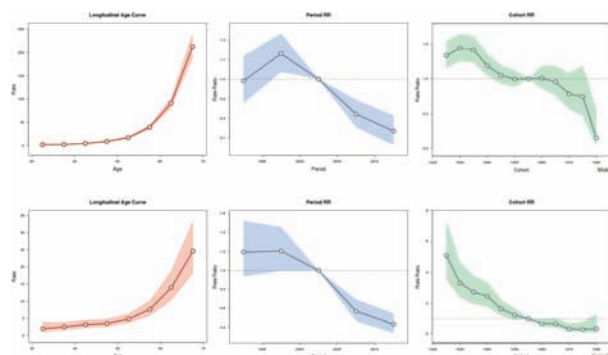
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Background and Aims: The aim of the WHO 25 by 25 goal is to reduce mortality from premature non-communicable diseases by 25% before 2025. Tobacco smoking is not only the leading preventable cause of death in the world but also leading cause of chronic obstructive pulmonary disease (COPD). The aim of this study is to estimate the 25 by 25 goal for premature mortality from COPD and the smoking attributable COPD death in Taiwan.

Methods: This is a National population-based study. Records of premature deaths due to COPD from 1990 to 2014 in Taiwan were abstracted from the database provided by the Ministry of Health and Welfare. Data for the age-specific prevalence of smoking were taken from the database, Taiwanese Adult Smoking Behaviour Surveillance System, provided by the Health Promotion Administration in Taiwan. We applied the age-period-cohort model to evaluate the trends and patterns of incidence and mortality of COPD and also to project the incidence of premature death from COPD from 2015 to 2024. We used the population attributable fraction to estimate the contribution of smoking in premature death from COPD.

Results: The age-period-cohort effect of smoking attributable COPD mortality in Taiwan was shown in the figure. Based on different case scenarios (no change, usual care and 30% reduction in smoking prevalence), the forecasting smoking attributable COPD mortality in Taiwan were 295×10^{-6} , 267×10^{-6} , 256×10^{-6} in men and 58.3×10^{-6} , 57.8×10^{-6} , 57×10^{-6} in women, respectively. Compared with the assumption of no change in smoking prevalence, an estimated of 326, 455 men and 6, 16 women would be saved under usual care and 30% reduction in smoking prevalence, respectively.

Conclusion: Strictly restriction on tobacco use, especially in men, is necessary for reduction of the forecasting smoking attributable COPD mortality in Taiwan.



DIRECT AND INDIRECT COSTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN KOREA

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Background and Aims: Understanding the burden of disease is important to establish cost-effective treatment strategies and to allocate healthcare resources appropriately. However, little reliable information is available regarding the overall economic burden imposed by chronic obstructive pulmonary disease (COPD) in Korea.

Methods: This study is a multicenter observational research on the COPD burden in Korea. Total COPD costs were comprised of three categories: direct medical, direct non-medical, and indirect costs. For direct medical costs, institutional investigation was performed at 13 medical facilities mainly based on the claims data. For direct non-medical and indirect costs, site-based surveys were administered to the COPD patients during routine visits. Total costs were estimated using the COPD population defined in the recent report.

Table. Total estimated costs of COPD in Korea

Category		Costs (million USD)	%
Direct medical	Formal	206.9	16.6
	Informal	44.2	3.5
Direct non-medical	Transportation	4.3	0.3
	Nursing	486.3	39.0
Indirect	Loss of productivity	407.8	32.7
	Premature deaths	96.2	7.7
Total		1,245.6	100

Results: The estimated total costs were more than 1,245 million US dollar (1,408 billion Korean won). Direct medical costs comprised approximately 20% of the total estimated costs. Of these, formal medical costs held more than 80% and tended to increase with increasing the severity of COPD. As direct non-medical costs, nursing costs made up the largest percentage (39%) of the total estimated costs. Costs for COPD-related loss of productivity formed four fifths of indirect costs, and accounted for up to 33% of the total costs.

Conclusion: The present study shows for the first time the direct and indirect costs of COPD in Korea. The results provide insight for an effective allocation of healthcare resources and to inform establishment of practical strategies to reduce burden of COPD in Korea.

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QT INTERVAL AS A PREDICTOR FOR THE SEVERITY AND PROGRESSION AMONG COPD PATIENTS

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APL011

Background and Aims: Chronic obstructive pulmonary disease (COPD) and cardiac arrhythmia are of high morbidity and mortality rate globally. In this study, we aim to explore the EKG parameters in patients with COPD, and their correlation with pulmonary function test.

Methods: This is a single center cross-sectional study. 272 patients with COPD was enrolled and admission EKG and pulmonary function tests were collected. Patients were separated into 3 groups based on FEV1% predicted. EKG parameters were compared between 3 groups. Regression analysis were performed to investigate the correlation between QT interval and FEV%, FEV1/FVC as well as residual volume/total lung capacity.

Results: Among the 3 groups based on FEV1% predicted, only QT interval was found to be of significant difference. Further regression analysis showed that the QT interval was significantly positively correlated to FEV% (R square = 0.032; 95% CI 0.010–0.546, $P < 0.05$) and FEV1/FVC (R square = 0.025; 95% CI 0.006–0.458, $P < 0.05$). No significant difference was found between QT interval and volume/total lung capacity.

Conclusion: QT interval from EKG is an important predictor for the severity and progression among COPD patients. Further studies are needed to determine whether QT interval could identify the prognosis and long term survival rate of COPD.

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FENO CONCENTRATION DISTRIBUTION IN COPD PATIENTS YU-IL KIM^{1*}, SUNG AHN², TAE-OK KIM³, MINSUK KIM³, HAYOUNG PARK³

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Background and Aims: The usefulness of fractional exhaled nitric oxide (FENO) test in asthmatic patients is well known. However, Studies on the usefulness of FENO test in patients with COPD are lacking. The FENO concentration distribution in COPD patients was analyzed and clinical characteristics of high FENO group in COPD patients were analyzed.

Methods: From December 2014 to June 2016, patients with COPD with FEV1/FVC <70% of those who underwent pulmonary function test and FENO test at Chonnam National University hospital in Korea were retrospectively evaluated for FENO concentration, history of asthma, peripheral blood eosinophil ratio and count, and bronchodilator response. The high FENO group was defined as FENO value greater than 25 ppb.

Results: A total of 190 COPD patients were included in the study. The mean age of the patients was $69. \pm 0.04$, the mean FEV1(%) was $65.9 \pm 24.2\%$ and the mean FENO value was slightly increased to $28. \pm 1.3$ (ppb). FENO values of less than 25 were 108, between 25 and less than 50 were 61, more than 50 were 21, and FENO value distribution was various. In univariate analysis, the blood eosinophil percent was higher ($2.62 \pm .653$ vs $3.71 \pm .001$, $P = 0.026$) and asthma history was frequent ($P = 0.002$, Odds ratio = 4.636) in the high FENO group. Asthma history was independent risk factor for increased FENO value (adjusted odds ratio = 5.231, $P = 0.006$) in multivariate analysis.

Conclusion: The distribution of FENO levels was various in patients with COPD. Asthma history in COPD patients was independent risk factor for increased FENO value.

PREVALENCE AND PREDICTOR FACTORS INFLUENCE OVERLAP SYNDROME AMONG COPD PATIENTS IN DR. CIPTO MANGUNKUSUMO HOSPITAL JAKARTA: A CROSS SECTIONAL STUDY

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Background and Aims: The occurrence of both chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) in an individual patient has been described as 'overlap syndrome'. Overlap syndrome present with obstruction that share several risk factors. This study aimed to evaluate the prevalence and possible predictor factors of the overlap syndrome and its association with comorbidities in COPD patients.

Methods: This study's design is a cross-sectional, consecutive sampling which involved patients in Dr. Cipto Mangunkusumo General Hospital Jakarta, Indonesia from August to December 2017. Subjects respond to Indonesian version of Berlin Questionnaire (INA-BQ) and additional information including smoking habit and history of hypertension. Data were analyzed with appropriate statistical methods using SPSS 20.

Results: Subjects with COPD (GOLD stages I-IV, risk groups A-D) were recruited from outpatient clinics. Information on age, gender, body mass index (BMI), smoking status, COPD assessment test, Indonesian version of Berlin Questionnaire (INA-BQ), comorbidities, medications and exacerbations in the past year was collected and a spirometry was performed. Of 88 subjects, 43 (48.8%) subjects were diagnosed with OSA-COPD Overlap Syndrome. Most of OSA-COPD Overlap Syndrome subjects 58.1% are elderly (≥ 60 years), 65.1% are male, 46.5% subjects have normal BMI ($BMI \leq 25$), 51.2% subjects have hypertension as comorbid, and 58.1% are smoker. This study showed that there is association between overlap syndrome and BMI with $P 0.002$. A significant relation was found between overlap syndrome and hypertension with $P 0.017$ and OR 2.95. However, overlap syndrome was not associated with age and smoking history.

Conclusion: Prevalence OSA-COPD overlap syndrome is 48.8%. Overlap Syndrome is highly prevalent in elderly (≥ 60 years) and high incidents in male population. Furthermore, overlap syndrome was associated with BMI and hypertension. Those results could be used by health workers to recognize more about the existence of overlap syndrome so that poor outcome from this disease could be prevented.

Critical Care Medicine 2

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MAJOR ADVERSE CARDIOVASCULAR EVENTS AND GASTROINTESTINAL BLEEDING DURING SEPSIS AND THEIR IMPACTS ON HOSPITALIZATION OUTCOMES

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Background and Aims: Sepsis patients were prone to gastrointestinal bleeding (GIB) and major adverse cardiovascular events (MACEs). Currently, there was limited data on the incidence of GIB and MACEs during the sepsis hospitalization, and these complications' impacts on the hospital outcomes remained unclear.

Methods: By using the specially applied sepsis cohort from the National Health Insurance Database of Taiwan, between 1999 and 2013, a total of 220,082 patients with the first episode of sepsis was retrieved. Logistic regression model with further joint effect analyses was conducted to examine the odds ratio (OR) of GIB and MACEs on hospital outcomes, including hospital mortality, ICU admission, and mechanical ventilation (MV) use.

Results: The mean age of enrolled patients was 70.15 (± 15.17) years. Septic shock developed in 50.78% of patients, MV use in 33.21%, and ICU admission in 54.49%. The complications of GIB developed in 3.80% of patients; MACEs of stroke in 1.54%, ICH in 0.92%, and AML in 1.59% of patients. In the joint effect analyses, the sepsis patients with only GIB had an increased risk of ICU admission (adjusted OR = 1.3, 95% CI 1.23–1.38) and MV use (aOR = 1.33, 95% CI 1.26–1.4) but without an increased risk of hospital mortality (aOR = 1.01, 95% CI 0.96–1.07). The patients with only stroke had an increased risk of ICU admission (aOR = 2.62, 95% CI 2.38–2.88) and MV use (aOR = 2.09, 95% CI 1.91–2.28) but decreased risk of hospital mortality (aOR = 0.89, 95% CI 0.82–0.97). Both ICH and AML markedly increased the risk of ICU admission and MV use; however, only slightly increased the risk of hospital mortality.

Conclusion: GIB and MACEs were associated with an obviously increased risk of ICU admission and MV use but not the hospital mortality. Prevention medications, such as anti-platelet drugs, statins, and PPIs, should be considered and balanced.

Table Joint effect analyses of association between "hospital mortality, ICU admission, receiving mechanical ventilation" and "GI bleeding, stroke, ICH, and AML"

Complications	N	Outcome ^a				Outcome ^a				Outcome ^a			
		Hospital mortality				ICU admission				Mechanical ventilation			
		Event	Event Rate	Adjusted OR ^b	(95% CI)	Event	Event Rate	Adjusted OR ^b	(95% CI)	Event	Event Rate	Adjusted OR ^b	(95% CI)
GIB	No	No	No	203522	77972	0.38	1[reference]	107413	0.53	1[reference]	64600	0.32	1[reference]
Stroke	No	No	No	7965	3720	0.47	1.01(0.96–1.07)	5285	0.66	1.31(1.23–1.38)***	3523	0.44	1.31(1.26–1.4)***
ICH	No	No	No	2990	1129	0.38	0.89(0.82–0.97)**	2162	0.72	2.62(2.38–2.88)***	1427	0.48	2.09(1.91–2.28)***
AML	No	No	No	1748	821	0.47	1.17(1.05–1.3)***	1571	0.90	8.18(6.84–9.8)***	1158	0.66	4.11(3.65–4.62)***
	No	No	No	3194	1738	0.54	1.15(1.06–1.24)**	2882	0.90	4.93(4.33–5.62)***	1856	0.61	2.03(1.87–2.21)***
	No	No	No	139	44	0.32	0.50(0.34–0.74)***	118	0.85	3.79(2.36–6.35)***	81	0.58	2.38(1.61–3.53)***
	No	No	No	106	33	0.31	0.53(0.34–0.83)***	96	0.91	8.12(4.16–16.5)***	74	0.70	4.84(2.96–7.93)***
	No	No	No	134	67	0.50	0.82(0.57–1.18)	119	0.89	3.07(1.69–5.55)***	92	0.69	2.61(1.74–3.93)***
	No	No	No	115	41	0.36	0.70(0.46–1.06)	106	0.92	12.41(5.99–25.71)***	72	0.63	3.42(2.18–5.36)***
	No	No	No	112	46	0.41	0.68(0.46–1.03)	106	0.95	12.28(5.1–29.56)***	77	0.69	3.48(2.18–5.57)***
	No	No	No	81	16	0.52	1.05(0.49–2.23)	79	0.94	7.37(1.59–34.13)***	22	0.71	3.29(1.37–7.91)**

Adjusted OR: adjusted for groups (GIB, stroke, ICH, and AML), age, gender, insurance premium, urbanization level, CCI score, drug use in Logistic regression model. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Abbreviation: AML, acute myocardial infarction; CI, confidence interval; GIB, gastrointestinal bleeding; ICH, intracranial hemorrhage; OR, odds ratio.

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ELECTRICAL IMPEDANCE TOMOGRAPHY AND RESPIRATORY MECHANICS CHANGE IN TWEEN LAVAGE INDUCED ACUTE LUNG INJURY PORCINE MODEL

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Background and Aims: A protective ventilation strategy using low tidal volume and high positive end expiratory pressure has been proposed to prevent ventilator-associated lung injury in patients with acute

respiratory distress syndrome (ARDS). Various mechanical ventilation modes for restoration of gas exchange have been investigated. This animal study was conducted to investigate the effects of different mechanical ventilation modes by means of advanced respiratory monitoring including gas exchange, respiratory mechanics, Alveolar fluid clearance, Cytokines change in BALF and electrical impedance tomography

Methods: 18 healthy pigs were anesthetized and mechanically ventilated. VCV or ASV group's animals with tween lavage lung injury were randomized to three h of ventilation with either control group. VCV group or ASV group at identical low tidal volume and minute ventilation over time. Breathing pattern, lung mechanics, hemodynamic variables, gas exchange, PICCO derived extravascular lung water (EVLW), and EIT image were determined hourly. Alveolar fluid clearance (AFC) and wet to dry lung weight ratio were determined postmortem.

Results: The preliminary findings showed that VT in the ASV group was 6.3–6.6 mL/kg, below to those in the VCV group ($P < 0.05$). There was no statistically significant difference in respiratory rate between the two groups. The peak airway pressure was decreased significantly in the ASV group compared with the VCV group ($P < 0.05$). Induction of lung injury resulted in significant deterioration of oxygenation ($\text{PaO}_2/\text{FiO}_2$) ($P < 0.05$). and elevated alveolar dead-space ratios in VCV groups ($P < 0.05$). Alveolar fluid clearance rate was increased significantly in the ASV groups compared with VCV groups ($P < 0.05$) and EIT image were change in different groups.

Conclusion: Our results suggest ASV may reduce ventilator-associated lung injury by lowering peak airway pressure and minimizing the decrease of AFC in a Tween lavage porcine lung injury model.

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PROPORTIONAL ASSIST VENTILATION AS A MODE OF WEANING IN ADULT PATIENTS REQUIRING MECHANICAL VENTILATION: A META-ANALYSIS

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Background and Aims: Proportional assist ventilation (PAV), is a form of synchronized partial ventilatory assistance that has shown benefit in weaning in terms of lessening asynchrony compared with commonly used modes such as pressure support ventilation (PSV). However, data for important clinical outcomes such as extubation failure, length of hospital and ICU stay and overall in-hospital mortality are lacking. Thus, this meta-analysis aims to determine the effectiveness of PAV as a mode of weaning in comparison to PSV in terms of extubation failure, length of in-hospital and ICU stay, overall mortality.

Methods: We reviewed articles in MEDLINE, Cochrane, Clinical-Trials.gov and other databases and included randomized controlled trials comparing PAV and PSV in terms of extubation failure or re-intubation, duration of ICU and hospital stay, and mortality. Data extraction and analysis utilized the standard methods proposed by the Cochrane Study Group. The authors independently assessed validity, eligibility for inclusion, and risk of bias, extracted data on the clinical outcomes of interest, and calculated relative risks and means with a 95% confidence interval using RevMan version 5.3

Results: We identified 3 studies which included an over-all total of 270 subjects. In terms of the clinical outcomes, PAV reduced extubation failure (Risk ratio 0.49 [0.26, 0.93]) and reduced duration of ICU (Mean difference -1.24 days [-2.01, -0.47]) and hospital stay (Mean difference -1.91 days [-2.92, -0.90]). No difference in terms of in-hospital mortality was seen (Risk ratio 0.97 [0.50, 1.87]). No heterogeneity was found in all of the comparisons done.

Conclusion: Using PAV as a mode of ventilation in weaning reduces extubation failure and lessens the duration of ICU and hospital stay. However, it will not decrease the overall mortality of patients.

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COMPARING INDIRECT CALORIMETRY AND ESTIMATING ENERGY EQUATIONS TO EXPLORE THE ENERGY EXPENDITURE IN BILATERAL LUNG TRANSPLANT PATIENTS

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Background and Aims: For the postoperative patients, the determination of energy expenditure (EE) to assess the energy requirement is very important. Little data was known regarding the EE in the patients who are receiving bilateral lung transplantation. Indirect Calorimetry (IC) is considered as a standard method for assessing EE, however the limitation were high cost, relatively complex and requirement for trained personnel.

The other methods to predict EE such as predictive equations were simple, fast and affordable. However, the accuracy was doubt especially in critical ill patients. The present study was to compare the methods for assessing EE between IC and predictive equations after bilateral lung transplantation.

Methods: Three patients receiving bilateral lung transplantation were measured Resting Energy Expenditure (REE) by using IC, M-COVXTM (Engstrom carestation, Datex-ohmeda Inc., Madison, WI, USA) after operation. At the same time, the predictive REE was calculated by using either the Harris and Benedict (HB) equation, or Ireton-Jones (IJ) equation for the mechanical ventilator patients. We compared the differences between these three methods in assessing EE.

Results: The estimated value of the HB equation is 1.1 times higher than the IC value. The value estimated by IJ equations is only 0.8 and 0.9 times of the IC value for the overweight and the normal weight patients respectively. For these patients without extracorporeal membrane oxygenation, the HB equation is close to the value measured by IC. The predictive value of the IJ equation is lower than the measured value of the IC, especially for the overweight patients.

Conclusion: In conclusion, the predictive equations to predict EE in lung transplantation patients is need to adjust by the body weight and it need further large scale study to confirm.

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THE COMPARISON OF SURGICAL AND MEDICAL PATIENTS EXPERIENCED UNPLANNED EXTUBATION

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Background and Aims: To compare the prognostic factors and outcomes of unplanned extubation (UE) among surgical and medical patients in 6 adult intensive care units (ICUs) in Chi Mei Medical Center.

Methods: We prospectively registered the UE patients and retrospectively reviewed the electrical medical records (EMR) in 96-beds ICUs between Jan 1, 2009 and July 31, 2017. Total 341 patients experienced UE, and 161 patients were in surgical group (47.2%).

Results: There were 112 female patients (32.8%), and the mean age was 65.1 years (range: 18–101 years). The mean Acute Physiology and Chronic Health Evaluation (APACHE) II score was 16.8 and mean Glasgow coma scale score was 10.1. One hundred thirty-seven patients (49.0%) were re-intubated within 48 h (failed UE), and sixty patients died (17.6%). Compared with medical group, the surgical patients had a similar mean value of ICU (14.3 vs 15.7 days), hospital stays (37.8 vs 37.5 days) and hospital costs (51.7 vs 46.3 × 10000 New Taiwan Dollars), but lower failed UE (40.4% vs 56.7%, $P = 0.002$) and hospital mortality (13.0% vs 21.7%, $P = 0.025$). Multivariate analyses were performed to evaluate those factors predicting failed UE and mortality, and it showed that higher APACHE II and positive end-expiratory pressure (PEEP) and not in weaning status before UE predicted failed UE, and uraemia, liver cirrhosis and cancer patients were independently associated with hospital mortality.

Conclusion: Among UE patients, surgical group had similar hospital stays and expenditures. After adjusting for confounding factors, surgical patients were not associated with hospital mortality nor failed UE. Those who had higher APACHE II and PEEP and not in weaning status were associated with failed UE. Uraemia, liver cirrhosis and cancer patients—were associated with higher mortality in patients who underwent UE.

AP458

USEFULNESS OF NON-INVASIVE POSITIVE-PRESSURE VENTILATION DELIVERED BY HELMET VS FACIAL MASK IN PATIENTS WITH POST-EXTUBATIONAL RESPIRATORY DISTRESS

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Background and Aims: Extubation failure is common in intensive care unit (ICU). Non-invasive positive-pressure ventilation (NIPPV) for post-extubational respiratory distress does not improve rates of intubation in heterogeneous groups of patients. Delivery of NIPPV with helmet would allow for higher pressure than facial mask without substantial air leak. We hypothesize the significant reduction of reintubation rates in the patients with NIPPV delivered by helmet would be expected.

Methods: Between March 1, 2017, and April 30, 2018, Thirty-nine consecutive patients with respiratory failure within 48 h after extubation and applied by NIPPV were retrospectively collected in a medical ICU in an academic, tertiary care hospital.

Results: Respiratory failure due to hypercapnia was sixteen patients, hypoxemia was nineteen patients, and post-extubational stridor was five patients. Comparing the NIPPV delivered facial mask with helmet, there was no difference in the rate of reintubation (53.8% vs 46.2%; OR, 1; 95% CI, 0.24–3.80) or ICU mortality (4.8% vs 11.1%; OR, 0.59; CI, 0.33–4.8), duration of NIPPV (2.6 vs 3.7 days, $P < 0.16$), and removal rate of carbon dioxide in blood. According to the cause of respiratory failure, comparing the difference in the rate of reintubation, ICU mortality, and removal of carbon dioxide, there were no differences between delivered by facial mask and helmet. Although there was no statistical significance, the severity was higher in the patients with delivered by helmet (sequential organ failure assessment, 2.23 vs 3.44; $P < 0.09$).

Conclusion: NIPPV delivered by helmet than facial mask significantly reduced the intubation rate among ARDS patients. However, in this study, the effect of NIPPV delivered by helmet was not significant in patients with post-extubation respiratory distress. The severity of the patients would be distorted by the small number of patients might influence our outcomes. Thus, we will collect more cases and analyze again each year.

AP459

DIFFERENT CHARACTERISTIC PATTERN IN ICU SEPTIC PATIENTS DUE TO PNEUMONIA OR NON-PNEUMONIA

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Background and Aims: To determine whether ICU patients with sepsis due to pneumonia or non-pneumonia were associated with different characteristics and outcomes.

Methods: This study evaluated adult medical ICU patients (18 y/o) with sepsis in Kaohsiung Chang Gung Memorial Hospital. 799 consecutive patients who met the criteria of sepsis-3 were included.

Results: According to infection source for sepsis, patients were divided into non-pneumonia group ($N = 276$), community-acquired pneumonia (CAP) group ($N = 387$) and hospital-acquired pneumonia (HAP) group ($N = 136$). With compatible age, APACH II score, and Charlson comorbidity index, the prevalence of COPD and TB were higher in CAP group, whereas DM, ESRD and CKD were remarkable in HAP group. Initial quick-SOFA was higher in HAP (1.5 ± 0.7 , 1.6 ± 0.6 and 1.7 ± 0.6 ($P = 0.027$)) and SOFA score was higher in non-pneumonia group (10.1 ± 3.8 , 8 ± 5 and $9 \pm .6$ ($P < 0.001$)), HAP group patients were elder with longer ICU and hospital length of stay. Besides, serum cytokines levels (GCSF (non-pneumonia: 1476 ± 3718 pg/uL, CAP: 99 ± 227 pg/uL and HAP: 63 ± 566 pg/uL, $P = 0.032$), TNF- α (78 ± 103 pg/uL, 6 ± 46 pg/uL and 5 ± 6 pg/uL, $P = 0.028$)) were different among 3 groups. However, there was no difference in survival (7-day, 14-day, 28-day ICU and hospital survival) among 3 groups.

Conclusion: ICU patients with sepsis due to pneumonia (CAP+HAP) or non-pneumonia were different regarding characteristics.

AP460

BODY MASS INDEX (BMI) CAN HELP PREDICT IMMUNE STATUS AND SHORT-TERM SURVIVAL IN PATIENTS WITH SEPSIS ADMITTED TO ICU

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Background and Aims: To determine whether patients with different BMI were associated with different immune profile and survival in patients with sepsis admitted to ICU.

Methods: This study evaluated adult medical ICU patients (18 y/o) with sepsis in Kaohsiung Chang Gung Memorial Hospital. 799 consecutive patients meeting the criteria of sepsis-3 were enrolled.

Results: Patients were defined as normal-weight group (BMI 18–25, $N = 491$), underweight group (BMI < 18, $N = 101$) and overweight group (BMI > 25, $N = 207$). With compatible age, APACH II score, and Charlson comorbidity index, the prevalence of COPD, TB, and CVA were higher in underweight group. DM and female gender were remarkable in overweight group. Comparing underweight and overweight group, underweight group had better 7-day (7% vs 14%), 14-day (13.9% vs 17.9%), 28-day (20.8% vs 27.1) survival tendency. Predicted hospital mortality among 3 subgroups were 45.6%, 33.7% and 38.6%, respectively ($P = 0.020$, Cox proportional hazards regression model). Segment/Monocyte ratio in blood (normal: $2 \pm 3\%$, under: 35.9 ± 37 , over: $2 \pm 1\%$, $P = 0.034$) and serum VEGF (17 ± 12 pg/uL, 37 ± 21 pg/uL, 11 ± 35 pg/uL, $P = 0.028$)

were also significantly different. In addition, the HLADR expression on monocyte at day 1 (85%, 81%, 89%, $P = 0.071$) and day 3 (88%, 81%, 91%, $P = 0.020$) were also different among 3 groups, suggesting slightly impaired immune response in underweight group.

Conclusion: Although with relatively impaired immune response, underweight group patients with sepsis were associated with better short-term survival after admission to ICU.

AP461

GENOTYPIC CHARACTERISTICS OF CARBAPENEM-RESISTANT ENTEROBACTERIACEAE IN PATIENTS WITH SEPSIS

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Background and Aims: *Enterobacteriaceae* are among the most common pathogens responsible for serious infections. The emergence and spread of carbapenem-resistant *Enterobacteriaceae* (CRE) have become an increasing concern for healthcare service worldwide. The rapid and accurate detection of CRE is important for infection control.

The aim of this study was to investigate the clinical characteristics of patient with sepsis and septic shock according to genotype features of CRE strains isolated in CRE surveillance of emergency department.

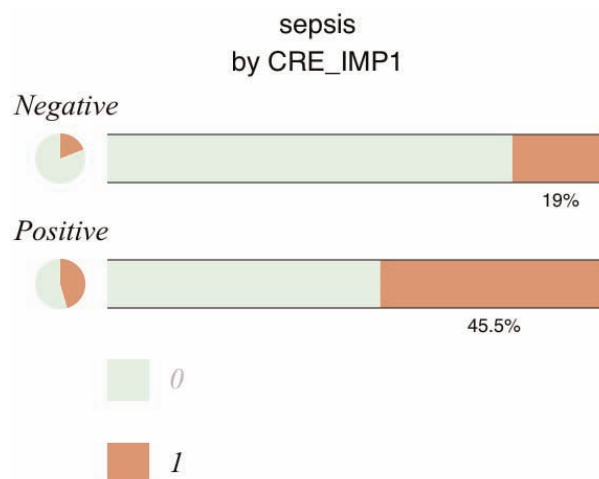
Methods: Patients from healthcare centres, other hospitals and with end stage renal disease (ESRD) screening CRE PCR (polymerase chain reaction) in emergency department were enrolled from NOV 21, 2016 to DEC 31, 2017, in one of the secondary referral hospital of South Korea.

A multiplex PCR was used for detection of carbapenems resistance gene (KPC, IMP, OXA-48, NDM, VIM). This study was reviewed and analyzed retrospectively.

Results: 244 patients who underwent CRE PCR surveillance in emergency department. CRE PCR positive patients were 64. The number of patients with KPC gene was 30, with IMP gene was 22, NDM gene was 14, OXA-48 gene was 5 and VIM gene was 6.

Patients with IMP gene associated with sepsis-3 was 45.5%, without IMP gene was 19% ($P = 0.026$) (Figure). Patients with IMP gene associated with septic shock was 36.4%, without IMP gene was 9.5% ($P = 0.009$). Patients with IMP gene associated with 90 day mortality was 40.9%, without IMP gene was 21.4% ($P = 0.100$).

Conclusion: IMP gene among CRE PCR positive patients was increasing in the patients with sepsis or septic shock in a city of South Korea.



AP462

CROSS-CULTURAL ADAPTATION AND PSYCHOMETRIC TESTING OF A CHINESE VERSION OF RESPIRATORY DISTRESS OBSERVATION SCALE

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Background and Aims: A reliable and valid dyspnea assessment scale for patients who are unable to express themselves is lacking in Taiwan. This study is conducted to develop a Chinese version of the Respiratory Distress Observation Scale (C-RDOS) and test its reliability and validity.

Methods: This study was conducted in two phases. The first phase entailed creating the C-RDOS in compliance with well-known guidelines. The second phase involved adopting a cross-sectional study design to test the internal consistency reliability, criterion and discriminant validity of the C-RDOS by using 80 intubated COPD patients, 80 orthopaedic surgery patients, and 80 healthy individuals. The 4-point verbal descriptor scale (VDS), peripheral oxygen saturation (SpO₂), and the 11-point numerical rating pain scale were used to assess subject's dyspnea and pain.

Results: C-RDOS was established with the good content validity (item-CVI of 1.0 and scale-CVI of 1.0). The inter-rater reliability among five evaluators was excellent (Kendall's W = 0.982, $P < .001$). The C-RDOS also displayed a good internal consistency reliability (Cronbach's α of 0.81). In testing the criterion validity, subject's C-RDOS scores and SpO₂ were negatively correlated ($r = 0.42$, $P < .001$), whereas their C-RDOS and VDS scores were positively correlated ($r = 0.89$, $P < .001$). The discriminant validity was presented by, after controlling for heart rate, subjects' pain scores were non-correlated with the C-RDOS scores ($r = 0.279$, $P = .205$).

Conclusion: The C-RDOS has been established with good reliability and validity. The C-RDOS can be used in clinics in Taiwan.

AP463

HYPERNATREMIA IN CRITICALLY ILL SEPSIS PATIENTS: A PROPENSITY SCORE ANALYSIS

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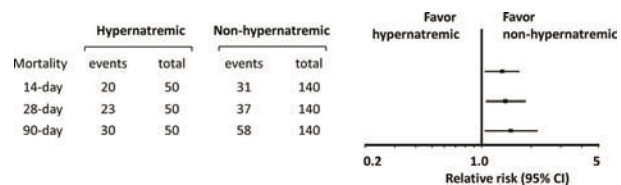
Background and Aims: Hypernatremia is common in patients admitted to the intensive care unit (ICU) and is associated with higher disease severity and mortality rates. We aimed to determine whether hypernatremia associated with higher mortality rate independent of disease severity using propensity score matching. We also tried to elucidate the impact of correctability of hypernatremia and acquired hypernatremia on mortality. Finally, association of hypernatremia with immune dysfunction was examined using 2 different methods.

Methods: Adult patients with severe sepsis or septic shock requiring ICU admission between August 2013 and June 2016 were included. Impaired immune responses were determined using monocyte surface protein expression of human leukocyte antigen DR and fold change of cytokine level after lipopolysaccharide (LPS) stimulation of peripheral blood mononuclear cells.

Results: Hypernatremia was noted in 9.8% (51 of 520) of patients at the day of ICU admission. Patients with hypernatremia are older (71.8 vs 66.0 y/o, $P = 0.010$) and had higher sequential organ failure assessment (SOFA) score (10.9 vs 9.2, $P = 0.040$). We used 1:3 propensity score matching to balance age and SOFA score between hypernatremia and

non-hypernatremia patients. A total of 190 patients (50 hypernatremic, 140 non-hypernatremic) were included into final analysis. Patients with hypernatremia had higher mortality rates than those without (14-day mortality, relative risk [RR]: 1.30, 95% CI: 1.02–1.65; 28-day mortality, RR: 1.36, 95% CI: 1.04–1.79; 90-day mortality, RR: 1.46, 95% CI: 1.02–2.11). Patients with persist hypernatremia at both day 1 and 3 had higher mortality rates than those without hypernatremia at both day 1 and 3 (log rank $P = 0.028$). Decreased immune responses after LPS stimulation were noted in patients with hypernatremia (Medium Fold change of granulocyte-colony stimulating factor: 0.99 vs 2.45, $P = 0.016$; tumor necrosis factor: 1.93 vs 2.81, $P = 0.031$).

Conclusion: Hypernatremia in critically ill sepsis patients are associated with impaired immune response and increased mortality risk.



AP464

TIME TO LUNG VOLUME RECOVERY AFTER SUCTIONING PREDICTS LUNG COLLAPSE AFTER PEEP DECREMENT IN RECOVERING ARDS PATIENTS

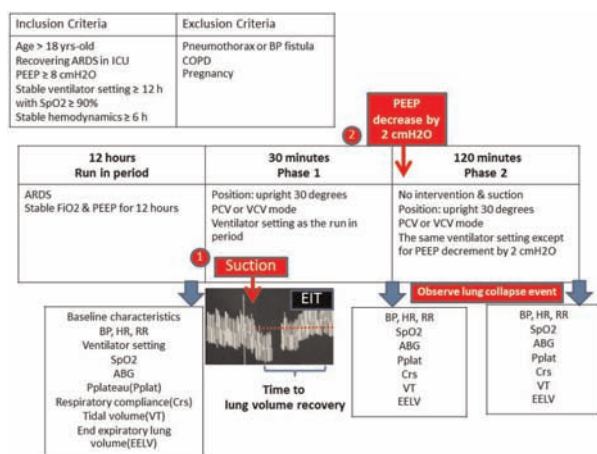
NAPPLIKA KONGPOLPROM¹¹Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross, Thailand

Background and Aims: In recovering ARDS patients, lung collapse frequently occurs, especially after PEEP reduction. However, factors predicting this event have not been established. Endotracheal suction commonly causes temporary oxygen desaturation and lung de-recruitment. We hypothesized that lung collapse after suction was possibly associated with lung collapse event after PEEP decrement. This study aimed to compare time to lung volume recovery after suction between ARDS patients with and without lung collapses after PEEP reduction.

Methods: We conducted a prospective observational study in recovering ARDS patients. We enrolled the patients who were assisted with either PCV or VCV mode, and using PEEP of ≥ 8 cmH₂O without ventilator adjustment for > 12 h. All patients had stable oxygenation and hemodynamic. We assessed time to lung volume recovery by using electrical impedance tomography. Time to lung volume recovery was defined as the duration from endotracheal suction to time that end expiratory lung volume returned to the baseline, and the lung collapse event was defined as the event that SpO₂ decreased by $\geq 3\%$ or PaO₂ decreased by $\geq 10\%$ after PEEP reduction. A study protocol showed in Figure 1.

Results: Totally, 15 endotracheal suction followed by decremental PEEP procedures were performed in 7 patients. The patients had median age of 69 [67, 81], median APACHE II of 15[13,20], median PEEP of 10 [8,12] cmH₂O and median respiratory system compliance of 24.5[9.9, 35.4] mL/cmH₂O. Three lung collapse events (20%) appeared after PEEP reduction. The median time to lung volume recovery after suction tended to be longer in the patients with lung collapse after PEEP reduction —180 [38, 800] milliseconds in lung collapse VS 29.5[10.75,159] milliseconds in non-collapse.

Conclusion: Time to lung volume recovery after endotracheal suction might predict the lung collapse event after PEEP reduction in recovering ARDS patients. Further studies should be conducted to confirm our results.



AP465

REVERSE TRIGGERING IN A PATIENT WITH CRYPTOCOCCAL MENINGITIS COMPLICATED WITH CEREBELLAR TONSILLAR HERNIATION NAPPLIKA KONGPOLPROM¹

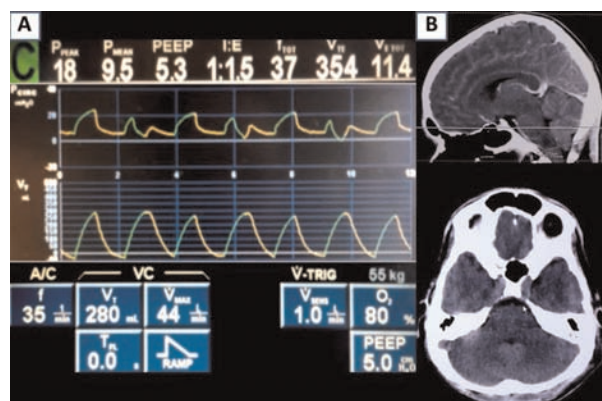
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Background and Aims: Reverse triggering is a type of patient-ventilator asynchrony characterized as the ventilator-triggered diaphragmatic contraction. This asynchrony was reported in ventilated patients who received heavy sedation or neuromuscular-blockade. Interestingly, reverse triggering also occurred in brain-dead patients after cardiac arrest.

Methods: We reported a case of reverse triggering which was a diagnostic clue of acute tonsillar herniation.

Results: A 19-year-old Thai man was admitted in our ICU due to HIV-infection with disseminated-cryptococcus. The patient presented with prolonged fever, dry cough and progressive dyspnea for 2 months. He developed meningeal-like headache 5 days before admission. On examination, he looked distress with hypoxemia. Besides headache, he had no neurological deficit. Chest X-ray showed diffused ground glass opacity in both lungs. CT-brain showed normal findings. Lumbar puncture(LP) revealed high open pressure(36 cmH₂O) with aseptic meningitis-CSF profile. Additionally, encapsulated yeasts were found in CSF. Anti HIV was positive. Amphotericin-B was administered for treatment of disseminated fungal infection, later confirmed as cryptococcosis. The patient became respiratory failure and was assisted with mechanical ventilation on the second day of admission. Then, he was transferred to ICU. Lung protective strategy with neuromuscular-blockade was provided and daily LP was performed to reduce intracranial pressure. Four days later, despite using high doses of sedatives and cisatracurium, the patient had cyclic-gasping (Figure 1A). Reverse triggering was considered. The patient's neurological signs showed E₁M₁V_T and sluggish pupil response, which possibly resulted from medications or brain dysfunction. Because reverse triggering was previously reported in patients with brain-death and our patient had a risk of increased intracranial pressure, emergency CT-brain was requested. The CT-brain showed diffused brain swelling with tonsillar herniation (Figure 1B). Subsequently, we withheld sedatives and reevaluated neurological signs. The patient still had spontaneous breaths and intact some brainstem-reflexes. Unfortunately, due to irreversible brain damage, he eventually passed away.

Conclusion: Reverse triggering appeared in the patient with brain herniation.



AP466

PROTECTIVE EFFECTS OF RAMELTEON ON ACUTE LUNG INJURY -INDUCED BY VENTILATOR IN A RAT MODEL

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Background and Aims: It is well-known that ventilation with high volume or pressure may be harmful, causing damage on previously healthy lungs or worsening it in already injured lungs. Up to now, there has been no pharmacological treatment that could prevent ventilator-induced lung injury (VILI). Melatonin has proven to be effective in acute lung injury. However, melatonin exerts its beneficial properties not only as a direct antioxidant substance but also via melatonin receptor activation. Ramelteon, a melatonin receptor agonist with highly selective agonist of the high-affinity MT1 and MT2 receptors, is reported to exert antioxidative and anti-inflammatory effects. Ramelteon attenuate VILI remains unclear. The purpose of this study was to determine the effect and mechanism of ramelteon therapy and the association of melatonin receptor on VILI in a rat model.

Methods: In this study, using a VILI rat model, the SD rats were randomly and equally allocated into 6 groups: group 1 (the control group); group 2 (the VILI group); group 3 (the VILI + melatonin pretreatment group); group 4 (the VILI + melatonin+ luzindole (melatonin receptor-antagonist) pretreatment group); group 5 (the VILI + ramelteon (melatonin receptor-agonist) pretreatment group) ; and Group 6 (the VIL + ramelteon + luzindole pretreatment group). The effects of ramelteon and melatonin receptor on VILI were investigated.

Results: We found the protective effect of melatonin in VILI was associated with melatonin receptor. Ramelteon pretreatment markedly reduced lung edema, malondialdehyde level, iNOS level, protein expressions of inflammatory factors (tumour necrosis factor- α , interleukin-1 β , interleukin-6, and NF- κ B) and apoptotic factors (caspase-3 and cleaved poly (ADP-ribose) polymerase). Additionally, ramelteon pretreatment significantly increased Hsp70 and interleukin-10 expression. However, the protective effect of melatonin or ramelteon was reduced by the luzindole treatment.

Conclusion: Our results suggest that melatonin receptors mediate the effects to attenuate VILI and ramelteon is a potential therapeutic drug for treating VILI.

AP467

FLUID BALANCE IS ASSOCIATED WITH MULTI-ORGAN DYSFUNCTION SYNDROME IN PATIENTS WITH SEPTIC SHOCK IN THE ICU

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Background and Aims: Positive fluid balance is an independent predictor for mortality in patients with septic shock. The role of fluid balance in sepsis-induced multi-organ dysfunction syndrome (MODS) has not been well addressed.

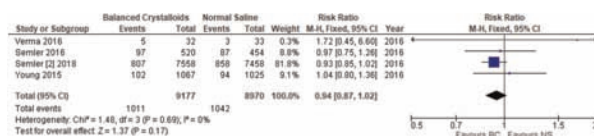
Methods: The study retrospectively recruited patients with septic shock in intensive care units of a tertiary hospital. Patient's baseline characteristics, cumulative intake, output and fluid balance in the first 24, 48, and 72 h since the onset of septic shock, presence of MODS, sequential organ failure assessment (SOFA) score, and clinical outcomes were analyzed.

Results: There were 22 patients enrolled in the study. Among them, 16 (72.7%) survived during their hospital stay and MODS developed in 18 (81.8%) patients. The fluid balances in the first 24, 48, and 72 h were increased in patients with MODS compared with those without MODS (148 ± 10 vs 91 ± 32 ; 160 ± 82 vs 125 ± 20 ; 208 ± 03 vs 65 ± 66 , mL; respectively). Patients with MODS had longer duration of ventilator ($17. \pm .2$ vs $\pm .6$, days; $P = 0.048$) and vasopressor use ($4. \pm .9$ vs $1. \pm .9$, days; $P = 0.031$) when compared with those without. In addition, the amount of fluid balance was correlated with the amount of intake (24 h; $r = 0.998$, $P < 0.001$. 72 h; $r = 0.621$, $P = 0.002$) rather than output (24 h; $r = 0.246$, $P = 0.258$. 72 h; $r = 0.281$, $P = 0.194$) in 24 and 72 h.

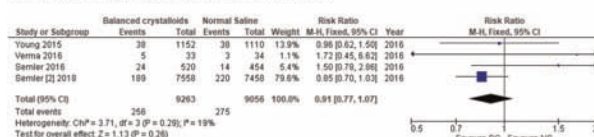
Conclusion: Positive fluid balance was associated with development of MODS in patients with septic shock. Excessive fluid intake is closely linked to the status of positive fluid balance.

Results: A total of 4 randomized controlled trials, which were all assessed to be good quality and low risk of bias, with 18,945 patients were included. Use of balanced crystalloids showed a trend towards lower incidence of AKI (RR 0.94, 95% CI [0.87–1.02], $P = 0.69$), RRT use (RR 0.91, 95% CI [0.77–1.07], $P = 0.29$) and ICU mortality (RR 0.91, 95% CI [0.82–1.01], $P = 0.95$). There is no significant heterogeneity identified.

Conclusion: Use of balanced crystalloids as intravenous fluid therapy among critically ill patients demonstrated a trend toward lower incidence of AKI, RRT and ICU mortality, compared to normal saline solution.



AKI rate (stage II or greater) among critically ill adult patients



Rate of RRT use among critically ill adult patients

AP469

RELATIONSHIP OF RETINOPATHY OF PREMATURITY WITH AEROSOL THERAPY IN MECHANICALLY VENTILATED PRETERM INFANTS

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Background and Aims: Aerosol administration is increasingly being used as a therapeutic intervention for mechanically ventilated preterm infants. However, the effects of inhalation therapy on retinopathy of prematurity (ROP) have not yet been explored.

Methods: A retrospective cohort study was conducted in a tertiary level neonatal intensive care unit (NICU) from 2011 to 2013. All preterm infants with a gestational age (GA) of 24–29 weeks receiving invasive intubation for more than 1 week in the NICU were included. Infants with severe congenital anomalies were excluded. ROP was defined as grade II or greater according to medical records by ophthalmologists. A multivariate logistic regression model was used to estimate the risk of ROP in relation to inhalation therapy after adjusting for confounders.

Results: In total, 205 infants were enrolled in this study, including 154 with inhalation therapy and 51 without inhalation therapy. Univariate analyses showed an association of inhalation with the following characteristics: sex ($P = 0.047$), GA ($P = 0.029$), sepsis ($P = 0.047$), bronchopulmonary dysplasia (BPD) ($P < 0.001$), and ROP ($P = 0.001$). Furthermore, logistic regression analysis indicated that inhalation therapy was an independent risk factor for ROP (odds ratio (OR) = 2.639; 95% confidence interval (CI) = 1.050–6.615). In addition, infants with a GA of 24–25 weeks (OR = 6.063; 95% CI = 2.482–14.81) and 26–27 weeks (OR = 3.825; 95% CI = 1.694–8.638) were at higher risk of ROP than those with a GA of 28–29 weeks. Other factors—including sex, sepsis, BPD, and delivery mode—did not carry significant risk.

Conclusion: The data suggest that aerosol therapy with pure oxygen delivery is associated with ROP. Respiratory therapists should exercise great caution when conducting inhalation therapy with excess oxygen in infants.

AP468

BALANCED CRYSTALLOIDS VS NORMAL SALINE SOLUTION AS INTRAVENOUS FLUID THERAPY AMONG CRITICALLY ILL PATIENTS: A META-ANALYSIS

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Background and Aims: Recent studies on critically ill adults had shown that use of normal saline with its supraphysiologic chloride content has been associated with an increased incidence of hyperchloremic metabolic acidosis, acute kidney injury (AKI), renal replacement therapy (RRT), hypotension and death. The objective of this meta-analysis was to assess the clinical outcomes associated with the use of balanced crystalloids vs normal saline solution.

Methods: We searched PubMed/MEDLINE, Embase and Cochrane Library (CENTRAL) databases in accordance with PRISMA guidelines. Our inclusion criteria were the following: randomized controlled trials, adult critically ill patients, comparisons between patients receiving either balanced crystalloids (Lactated Ringer's solution, Plasma-Lyte) or normal saline, and at least one endpoint that measure intensive care unit mortality, rate of AKI (defined as stage 2 or greater in the RIFLE criteria) and RRT use. Risk ratios (RRs) and confidence intervals were calculated via Review Manager Version 5.3 using the fixed-effect modelling.

AP470

DM SEPTIC PATIENTS ARE ASSOCIATED WITH IMPAIRED IMMUNE RESPONSE BUT NOT POOR SURVIVAL IN ICU
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¹*Kaohsiung Chang Gung Memorial Hospital, Taiwan*

Background and Aims: Diabetes mellitus (DM) is a widespread metabolic disorder. Without well control of blood glucose, numerous complications occurs in diabetic patients. Sepsis developed from various kinds of infections, complicated by multiple organ dysfunctions without effective management. DM grows the risk of developing infectious complications, including sepsis. DM is known to interface with numerous mechanisms of the immune system. The influence of DM on the results of sepsis is still disputed. We conducted a case-controlled study matched with propensity score to determine whether septic patients with DM associated with impaired immune response and poor clinical outcome ICU.

Methods: A combined retrospective and prospective observational study from a cohort of adult sepsis patients admitted to three medical ICUs at Kaohsiung Chang Gung Memorial Hospital (KCGMH) in Taiwan between August 2013 and June 2016. Cytokine expressions were measured with a MILLIPLEX MAP Human Cytokine/Chemokine Panel (Merck Millipore, Billerica, MA, USA) in 12 patients enrolled to biomarker study. Expression of cell surface TLR4 MFI and HLADR MFI on monocytes was measured by flow cytometry (Cytomics FC500; Beckman Coulter, Inc., Fullerton, CA, USA).

Results: This study evaluated adult medical ICU patients (18 y/o) with sepsis in KCGMH. Total 594 Patients with sepsis were identified and assessed for DM after adjustment of propensity score and there was no statistical significance change of Charson index, APACHE II score and comorbidity. DM patients had higher HbA1c, day 1, 3, 7 finger sugars ($P < 0.05$), lower Day (D)7 mortality ($P < 0.05$), lower D1 platelet count, higher systolic and pulse pressure, lower FiO₂ of ventilators, lower D7 respiratory rate ($P < 0.05$), compared with patients without DM. DM patients also had lower D1- IL10, lower D1 and 3 TLR4 expression and D7-VEGF.

Conclusion: DM septic patients are associated with impaired immune response but not poor survival in ICU.

AP471

CASE REPORT: BILATERAL PNEUMOTORAKS OF CATAMENIAL PNEUMOTHORAX WITH MULTIPLE BULLAE
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Background and Aims: Catamenial pneumothorax (CP) is a rare entity of spontaneous, recurring pneumothorax in women. We aim to discuss the aetiology clinical course, and surgical treatment of a 38-year-old women with CP. This patient had a right sided recurrent spontaneous pneumothorax within 72 h after onset of menstrual period. She had undergone thoracotomy and bullectomy bilateral.

Methods: case report

Results: Case report: A 38-year-old woman came to the emergency ward with dyspnea complaint after two days menstruation. Chest X-ray showed no vascular marking on the right and left lungs. We do chest tube insertion on the right lung to promote lung expansion. Chest CT scan revealed multiple bullae in the left lung. Pneumothorax occurs five times in the last one year for this patient. The biopsy of exploration thoracotomy found granulomatous inflammation,

Conclusion: Patients with CP after thoracotomy and bullectomy, the biopsy of exploration thoracotomy found granulomatous inflammation, after which the patient got anti-tuberculosis drug therapy.

Keywords: Catamenial pneumothorax, surgical treatment.

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CLINICAL OUTCOMES IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN VIETNAM ACCORDING TO SEVERITY OF THE BERLIN DEFINITION

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Background and Aims: The burden of clinical outcomes of ARDS according to the Berlin Definition has not ever been reported from Vietnam.

Methods: We conducted a retrospective chart review on patients who admitted and were diagnosed ARDS in a national tertiary care hospital, Hanoi, Vietnam between 2012 and 2016. The data on ventilator settings and conditions on gas exchange were collected at the time of 1st day and the 3rd day of admission. The primary outcome was hospital mortality. The secondary outcomes included comparisons of respiratory conditions among three groups of ARDS severity on the Berlin Definition.

Results: In 126 eligible patients, the median age was 53 (IQR, 39–63) years and 66% was male. 93% of direct risk for ARDS was pneumonia. Overall hospital mortality was 57.1%. In total patients, the period prevalence of severe ARDS on Day 1 was 53.0%; of moderate ARDS 37.3%; and of mild ARDS 9.5%. The ARDS severity changed on Day 3 due to improvement/deterioration of PaO₂/FiO₂ in each patient. Of the total patients on Day 3, severe ARDS was 27%; moderate ARDS, 35.7%; and mild ARDS, 12.7%. In addition, 6.3% of patients showed an improvement of over 300 of PaO₂/FiO₂. The hospital mortality did not differ significantly among three groups of ARDS severity on Day 1 ($P = 0.163$), but when compared among three groups of ARDS severity on Day 3, it was significant ($P = 0.017$). In the length of hospitalization using the Kaplan-Meier method, the survival time of severe ARDS was significantly shorter among three groups of ARDS severity on Day 3 ($P = 0.030$).

Conclusion: The present study demonstrated that the clinical outcomes of ARDS patients in Vietnam depends on the improved ARDS severity within three days from the hospital admission. In Vietnam, the mortality of ARDS can be verified by the Berlin definition.

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A STUDY ON THE PREDICTION OF DEATH IN ICU PATIENTS USING CRRT

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Background and Aims: Many patients with acute kidney injury or aggravation of chronic renal failure admit the intensive care unit for continuous renal replacement therapy (CRRT). This study aimed to identify predictors of in-ICU mortality in patients with CRRT for effective allocation of CRRT resources.

Methods: This study was a retrospective cohort study evaluating clinical data from the medical intensive care unit (ICU) of a 2000-bed university tertiary referral hospital in South Korea from July 2016 to February 2018. We used clinical information and laboratory results of patients before or at applying CRRT to investigate predictors of in-ICU mortality.

Results: Of the 783 patients, 194 patients had CRRT, of which 74 (38.1%) died. The mean age of the patients with CRRT was 65.9 years. In-ICU non-survivors ($n = 74$) showed higher mean SAPSII score (60.1 vs 45.6) and SOFA score (12.7 vs 9.9) than survivors ($n = 120$). Median ICU stay for in-ICU non-survivors was 3 days (1.0–12.5), and in-ICU survivors for 5 days (3.0–10.0). Among the various parameters, In-ICU non-survivors had higher levels of lactate (10.5 vs 3.9, $P < 0.001$) and delta neutrophil index (20.1 vs 9.9, $P < 0.001$). The area under the curve (AUC) of lactate on a receiver operating characteristic curve was 0.822 (95% confidence interval [CI], 0.762–0.882); the AUCs for the SAPSII score and SOFA score were 0.743 (95% CI, 0.671–0.814) and SOFA 0.729 (95% CI, 0.665–0.804), and increased to when SAPS II score or SOFA score and lactate were combined. When combined SAPS II score with lactate, the AUCs increased to 0.847 (0.792–0.902); for SOFA and lactate, the AUCs increased to 0.842 (0.786–0.897) to predict in-ICU mortality.

Conclusion: Adding lactate to severity scores or lactate alone can predict more accurately in-ICU mortality of patients with CRRT. Therefore, before CRRT apply, lactate may be used to enhance CRRT resource efficiency and family communications.

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ACUTE HYPERGLYCEMIA AGGRAVATES ACUTE LUNG INJURY VIA ACTIVATION OF SODIUM-POTASSIUM-CHLORIDE COTRANSPORTER 1

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Background and Aims: Acute lung injury (ALI) happens when administering supplemental supra-physiologic oxygen concentrations, sepsis, ischemia-reperfusion and etc. ALI leads high mortality and morbidities even under current modern medical treatment.

Alveolar fluid regulation is critical to the development of pulmonary edema in lung injury. Pulmonary ion transporters in the lung epithelium regulate water influx and out and should be important in ALI. Baso-lateral sodium-potassium-chloride co-transporter one (NKCC1) in the lungs mediates a net influx of ions into cells and regulates fluid balance in the lungs. Therefore NKCC1 should be important in lung injury.

Acute hyperglycaemia is known to be an established risk factor for many pathologic processes in lung injury and results in significant exacerbation of lung dysfunction, inflammation, and injury. Hyperglycaemia is shown to stimulate of NKCC expression. However, the relation between hyperglycaemia and NKCC1 in ALI is unknown.

Methods: Animals were divided to control, control with hyperglycaemia, ALI, ALI with hyperglycaemia, ALI+NKCC1 inhibitor, ALI+hyperglycaemia+NKCC1 inhibitor. Acute hyperglycaemia was established via intraperitoneal injection of 20% dextrose.

All of the animals were studied for NKCC1 levels, lung histopathology, lung wet/dry weight ratio (W/D), microvascular permeability (Kf), pro-inflammatory cytokines, and NF- κ B pathway.

Results: Acute hyperglycaemia resulted in higher expression of NKCC1 and aggravated lung injury with increased microvascular permeability, alveolar protein leakage, lung water, neutrophilic infiltration and pro-inflammation cytokines (IL-1 and TNF- α). Inhibition of NKCC1 resulted to less pulmonary edema and lung inflammation.

Conclusion: Acute hyperglycaemia aggravates lung injury via activation of NKCC1. NKCC1 inhibitor is effective to decrease lung injury.

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FACTORS AFFECTING FAMILIES' PERCEPTION ABOUT THE PROCESS OF DECISION TO FORGO LIFE-SUSTAINING TREATMENTS

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Background and Aims: The decision to forgo life-sustaining treatment remained most challenging for families of deceased patients in ICU end-of-life care. It is widely known that different attitude toward end-of-life care in ICU between Eastern and Western countries. The aim of this study is to better understand how Eastern families perceived a decision to forgo life-sustaining treatment.

Methods: We recruited families who had the experience of end-of-life family conference and decided to forgo life-sustaining treatment in ICU. Factors associated with families' perception about the process of decision to forgo life-sustaining treatment. The interview verbatim was analyzed using MAXQDA in five families. Five family members were interviewed. They had participated end-of-life family conference and acted as surrogate to forgo life-sustaining treatment.

Results: Three themes emerged: (1) Family readiness toward patients' acute, life-threatening illness is different. (2) Each of the family members all reach certain stressful turning point from looking for medical cure to settle with care. (3) After consensus about withdrawing life-sustaining treatments, families were longing for time spending together to get family connectedness and reassurance of patients' pain-free and comfort.

Conclusion: Our study revealed that families' experiences about end-of-life family conference and stressful decision making in end of life care. Families may have better preparedness in end-of-life decision if the information need can be met.

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HIGH PEAKED AIRWAY PRESSURES FROM A KINKED ENDOTRACHEAL TUBE

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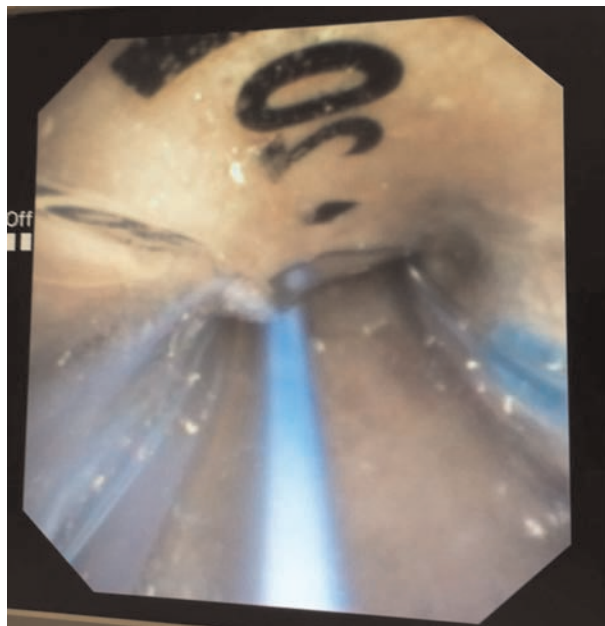
Background and Aims: Rapid deterioration of a mechanically ventilated patient is challenging, as trouble-shooting is time-sensitive, with a small margin for error. Problems relating to the endotracheal tube (ETT) should be considered and rectified if present.

Methods: We present a case of a middle-aged gentleman who was mechanically ventilated for severe community acquired pneumonia with hypoxic respiratory failure.

Results: Initial mechanical ventilation after intubation, where the patient was lightly sedated with intravenous propofol at Richmond Agitation-Sedation Scale (RASS) 0 to -1 was uneventful for the first 3 h. Thereafter, high peak airway pressures up to 64 mmHg manifested repeatedly. A series of rectification manoeuvres to check that the external circuitry and tubings were not kinked, and thorough physical examination to look for signs suggestive of pneumothorax or increased airway resistance were performed. Empirical administration of bronchodilators and increased sedation were trialed without success. An urgent chest radiography to confirm ETT placement and to look for development of pneumothorax was unyielding. Passage of an in-line suction catheter within the

ETT subsequently suggested a possible obstruction at the proximal ETT. We hence performed a direct laryngoscopy and flexible bronchoscopy, which revealed the cause to be a kinked ETT at the 20 cm marking (see image 1). We postulate that there could have been a manufacturing defect that resulted in the kinking of the ETT after endotracheal placement, as initial routine inspection prior to intubation had not revealed any obvious defects. An exchange of the defective tube with a new tube using a Bougie introducer was subsequently performed, and ventilation reinitiated successfully without further complications. Similar problems of kinked ETT tubes have also been described in previous case reports.

Conclusion: This case illustrates the need to consider a kinked ETT as a possible cause of difficulty in ventilation.



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THE MORTALITY RATE OF PRONE POSITION COMPARED WITH SUPINE POSITION FOR TREATING ARDS PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Prone position is regarded as an effective method for improving oxygenation in patients with acute respiratory distress syndrome (ARDS). It can also attenuate ventilation-associated lung injury by recruiting the atelectatic lungs and to increase arterial oxygenation. This analysis aimed to determine the effect on mortality in adults with ARDS in the prone position vs ventilation exclusively in the supine position.

Methods: We hypothesized that prone positioning reduces 60-day mortality from ARDS only when injurious high tidal volumes are avoided. We searched and collected the randomized controlled trials (RCTs) journals which reported the mortality rate of using prone position for treating ARDS from 2005 Jan. to 2018 Mar. in Cochrane Library, PubMed, and Medline. We used the keywords of prone position, supine position, adults, ARDS and mortality. According to risk level to evaluate the validity of studies and so as to Review Manager 5.3 to calculate for risk ratio, mean and standard deviation.

Results: There were 6 RCTs trials included in our study, and total 1046 patients were enrolled. In the treatment group, prone position group was associated with significantly decreasing the overall mortality rate: OR = 0.59 (95% CI = 0.39–0.87, Z = 2.62, P = 0.009, I² = 36%). PaO₂/FiO₂ ratio on Day 4 was significantly higher in the prone-positioning group compared with the supine position group (mean difference, 24.2; 95% CI, 8.66–39.1; I² = 28%).

Conclusion: In our systematic review of six randomized trials evaluating prone positioning compared with supine positioning for adults undergoing mechanical ventilation, we found a reduction in mortality when the prone position is used in patients with ARDS and PaO₂/FiO₂ ratio for all patients was significantly higher in the prone positioning group

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THE MORTALITY RATE OF LUNG RECRUITMENT MANEUVERS IN ARDS PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and Aims: Patients with acute respiratory distress syndrome (ARDS) exhibit significant lung dependent part atelectasis due to increased lung weight, interstitial and alveolar edema. High positive end-expiratory pressure (PEEP) and lung recruitment manoeuvres (LRMs) can decrease lung atelectasis and increase end-expiratory lung volume. LRMs are a common element of the “open lung” approach to lung-protective ventilation. However, the efficacy or mortality of recruitment strategy is uncertain.

Methods: We identified the randomized controlled trials (RCTs) which reported the using LRMs from 2008 Jan. to 2018 Jan. in Cochrane Library, PubMed and Embase database. We used the keywords of recruitment manoeuvres, open lung approach and ARDS. The meta-analyses and appraisals were conducted using RevMan 5.3 to calculate of risk ratio, mean and standard deviation. The results were pooled using fixed effects models weighted by inverse variance.

Results: We screened 421 citations from 4 trials eligible for inclusion. The type of LRMs varied widely between these trials and some involved a higher positive end-expiratory pressure (PEEP) ventilation strategy. The meta-analysis of all four trials also suggested a significant reduce 28 days mortality (RR: 0.83; 95% CI, 0.71–0.98; P = 0.42), and the use of a higher PEEP co-intervention did not significantly modify the mortality effect (P = 0.27 for heterogeneity). LRMs were also associated with improved oxygenation after 24 h (mean increase: 52 mm Hg; 95% CI, 23–81 mm Hg). The LRMs were not increased barotrauma (RR: 0.84; 95% CI, 0.46–1.55; P = 0.48).

Conclusion: The lung recruitment manoeuvres in ARDS patients can reduce 28 days mortality rate in hospital and improved oxygenation.

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DOES MECHANICAL VENTILATION HAVE ANY ROLE IN AFFECTING SLEEP ARCHITECTURE IN CRITICALLY ILL PATIENTS?

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Background and Aims: Sleep in ICU is not sound and restorative but disturbed and distorted. Survivors of critical illness reported their sleep to be of poor quality and a major stressor associated with their admission.

Among several factors, use of mechanical ventilation has been reported as an important cause of disturbed sleep in ICU.

Sleep parameters	IMV (n=15)		Spont Breathing (n=11)		U, P value
	Mean	SD	Mean	SD	
TRT	1336.5333	58.30691	1338.3818	77.57	62, 0.287
TST	536.2600	56.63021	498.4182	121.11827	71, 0.551
WASO	569.5200	91.80028	592.5273	187.31793	73, 0.646
N1	151.1133	52.12734	144.2273	27.64464	79, 0.856
N1%	27.9533	7.81015	29.9600	6.74736	65, 0.377
N2	333.7333	49.33801	291.2000	96.65563	68, 0.467
N2%	62.5400	8.46968	57.2455	8.29739	44, 0.048
N3	34.5420	13.38489	33.7273	11.85134	80, 0.917
N3%	6.5400	2.43305	6.8273	2.23074	72, 0.603
R	16.5793	21.12068	31.4773	18.45981	37, 0.018
R%	2.9600	3.53287	5.9000	3.32476	41, 0.032
A.I	27.0233	11.58720	16.7000	4.46122	36, 0.015
Sleep w/o wake	2.6993	1.36097	3.8373	1.09406	37, 0.018
D.sleep	258.4000	44.07179	253.4909	74.05331	79, 0.87
N.sleep	277.6800	56.49039	244.7000	80.22126	63, 0.33

Methods: 24 h polysomnography (PSG) study was done in two groups of patients who were recovering from their critical illness: Group 1 - IMV group and group 2- spontaneously breathing (SB) group. Frequency of nursing care activities were also recorded for both the groups. Quality of sleep in ICU was also assessed by using Richard Campbell sleep questionnaire (RCSQ) and sleep in ICU questionnaire (SICU).

Results: 26 patients completed the study (15 patients in group 1 and 11 patients in group 2). Pressure support ventilation was the mode in all group 1 patients. Mean REM stage duration in those who IMV and those who did not was 16.5 ± 1.12 mins and 31.4 ± 8.45 mins, respectively ($P = 0.018$). The difference in means of N2 stage between the two groups was also significant (62.5% vs 57.2% , $P = 0.048$). Mean arousal index (AI) in IMV and SB group were 27.0 ± 1.58 and 16 ± 46 respectively ($P = 0.015$). Mean sleep duration without wake was more in spontaneous group (2.69 ± 36 mins, $3.8 \pm .09$ mins : $P = 0.018$). Nursing care activities in patients who received IMV was more compared to SB patients (52.6 ± 6.78 , 48.5 ± 5 : $P = 0.14$) especially during day time (42 ± 75.38 , $\pm .5$: $P = 0.06$). Mean RCSQ score difference was significant (group 1- 54.6 ± 7.69 , group 2- $60.1 \pm .85$: $P = 0.04$).

Conclusion: Sleep in ICU is disturbed and fragmented. Mechanical ventilation is an important factor responsible for architectural distortion of sleep in ICU. Nursing care activities and noise are perceived as important factors for disturbed sleep in ICU

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EFFECTS OF DRIVING PRESSURE TO MORTALITY IN PATIENTS WITH SEVERE ARDS WHO RECEIVING PRONE POSITION

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Background and Aims: To date, four interventions have been demonstrated survival benefit in patients with ARDS, namely low tidal volume ventilation, early administration of neuromuscular blocking agent, extracorporeal membrane oxygenation, and prone positioning (PP). Recently data showed that ventilation with lower driving pressure (DP) also associated with a lower mortality. Therefore, we hypothesized that survival benefit from PP may link to decreasing of DP, and thus associated with decreased mortality in ARDS patients.

Methods: Prospective cross-sectional study in patients with severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150$ and received PP in intensive care unit of Phramongkutklao Hospital during October 2016 to December 2017. The primary outcome was difference in DP following PP compared between survivors vs non-survivors. Secondary outcomes were differences in oxygenation and respiratory compliance (Cr_s) following PP between two patient groups. Data were analyzed using SPSS v.23.0, and were presented as mean ($\pm$ SD).

Results: A total of seventeen patients with severe ARDS who received PP were analyzed. Average age was 60 years old. Baseline $\text{PaO}_2/\text{FiO}_2$ and C_{rs} were 115 and 21 mL/cm H₂O respectively. Average time to 1st session of PP was 12 h. Average duration of PP was 17.35 h. The most cause of ARDS was intrapulmonary cause. While the baseline DP before prone was not different between survivors (17.3 ± 2.7) vs non-survivors (17.9 ± 3.8 , $P = 0.70$), we found that survivors had significantly lower driving pressure (13.4 ± 2.6 cm H₂O) than non-survivors (16.2 ± 3.2 cm H₂O) at 2 h. following complete session of PP ($P = 0.047$). We also found that survivors had better oxygenation and C_{rs} than non-survivors but not significantly.

Conclusion: In patients with severe ARDS and received PP, compared to non-survivors, patients who survived had significantly less DP at 2 h. following complete of PP. Survival benefit of PP may exhibit through a reduction of DP. A further well-control trial with larger sample size is needed to confirm these findings.

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THE CIR-008885/MIR-30C/LRRC8D AXIS ENHANCES THE MACROPHAGE ACTIVATION INDUCED BY SILICA

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Background and Aims: Phagocytosis of SiO₂ into the lung causes an inflammatory cascade and irreversible pulmonary fibrosis. Circular RNAs (circ-RNAs), a new class of non-coding RNA, are ubiquitous in molecular biology since they may serve as transcription regulators or as sponges for small RNA regulators. Previous data from our laboratory using circular RNA microarray assay suggested that ciR-008885 expression in lung of mouse exposure to SiO₂ was increased, accompanied with up-regulation of LRRC8D. However, the mechanisms underlying ciR-008885/LRRC8D axis in pulmonary inflammation induced by SiO₂ remain unknown.

Methods: Mouse macrophage cell line (RAW264.7) was exposed to SiO₂ (50 µg/cm², 2–5 µm). ciR-008885 and miR-30C level were evaluated using quantitative real-time PCR (qRT-PCR) as well as FISH. LRRC8D protein level and the macrophage marker were detected by Western Blot and immunocytochemistry. siRNA was applied to specifically knock-down Lrrc8d in L929, combined with MTT and Flow cytometry to explore the functional change induced by SiO₂.

Results: After exposure to SiO₂, ciR-008885 expression was increased in a time-dependent manner, while LRRC8D protein level was up-regulated simultaneously, indicating a link between ciR-008885 and LRRC8D. Moreover, anti-miR-30C up-regulated LRRC8D protein, which was abolished by ciR-008885-siRNA, indicating that ciR-008885 regulated LRRC8D via ceRNA mechanism. Moreover, SiO₂ exposure induced decrease of the migration and cell apoptosis, which were reversed by knock-down of LRRC8D, confirming the role of LRRC8D in functional change induced by SiO₂.

Conclusion: Our data suggested a link between ciR-008885/miR-30C/LRRC8D axis and macrophage activation in silicosis, thereby providing new insight into the potential use of LRRC8D in the development of novel therapeutic avenues for silicosis.

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ASSESSMENT OF THE PATHOPHYSIOLOGICAL SIZE RANGES OF AIR MICROSUSPENSIONS CAUSING DEVELOPMENT AND PROGRESSION OF RESPIRATORY DISEASES

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Background and Aims: Worldwide millions deaths occur each year due to air pollution, of which 25% are caused by respiratory diseases. Air pollution contributes to an increase in morbidity and the number of exacerbations in patients with respiratory pathology. Suspended particulate matter (SPM) is one of the main criteria of air pollution. The relationship between micro-sized SPM and a high risk of development and progression of respiratory diseases, including asthma, chronic obstructive pulmonary disease, fibrosis and lung cancer, has been established. The aim of the study was to reveal the features of the fractional composition of SPM of the atmospheric surface layer in two districts of Vladivostok with different levels of technogenic pollution.

Methods: Air samples were collected in two districts of Vladivostok with high (unfavorable area, UA) and insignificant (favourable area, FA) technogenic pollution. The collection was carried out into the liquid absorption medium using an electric aspirator and simultaneously on the filter. The analysis of dispersion was conducted by laser granulometry and the calculation of SPM mass concentration. SPM was divided into the size ranges (0–0.1 µm, 0.1–1 µm, 1–2.5 µm and 2.5–10 µm) according to the mechanisms of pathophysiological effect.

Results: The ultrafine particles are found in the air of UA. Levels of SPM with aerodynamic diameter of 0.1–1 µm and 1–2.5 µm in the air of UA was 5 times ($P = 0.04$) and 2.7 times ($P = 0.003$) higher respectively than in FA. These particles reach bronchioles and settle in the lung alveoli. The concentration of SPM with aerodynamic diameter of 2.5–10 µm in the air of UA was 3.3 times ($P = 0.00004$) higher than FA. These particles settle on the trachea and bronchi epithelium resulting in mucous membrane irritation.

Conclusion: The air of UA is characterized by the presence of the ultrafine particles and a higher concentration of particles of respirable and tracheobronchial fractions.

PULMONARY TOXICITY OF CROSS-LINKED SOLUBLE POLYACRYLATE FOLLOWING INTRATRACHEAL INSTILLATION

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Background and Aims: It was reported on April 2017 that six employees in Japan used cross-linked soluble polyacrylate, one of polymeric materials, were affected with severe pulmonary disease by the Ministry of Health, Labour and Welfare. The relation between the material and the disease have not been unclear. The material is often used in all over the world, therefore, immediate investigation in relation to this problem is mandatory.

Methods: By permission of the authorities, we conducted intratracheal instillation studies of cross-linked soluble polyacrylate which employees used in order to examine its pulmonary toxicity. F344 rats were received intratracheal instillation at 0.2 or 1 mg of cross-linked soluble polyacrylate with respirable size in aqueous solution. Cell analysis, chemokines in bronchoalveolar lavage fluid (BALF) and histology of lung tissue were analyzed at three days, one week, one month, three months and six months after the instillation.

Results: Both the 0.2 and the 1.0 mg cross-linked soluble polyacrylate groups showed a transient increase in the total cell and neutrophil counts in the BALF and in the expression of cytokine-induced neutrophil chemoattractant (CINC)-1, CINC-2, chemokine for neutrophil, and heme oxygenase-1 (HO-1) as an oxidative stress marker, in the BALF. Histology of lung tissue showed pulmonary fibrosis following persistent remarkable inflammation.

Conclusion: According to our results suggest that cross-linked soluble polyacrylate has high pulmonary toxicity through pulmonary inflammation as an endpoint of toxic endpoints.

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EFFICACY AND SAFETY OF VERNONIA CINEREA PASTILLES FOR SMOKING CESSATION

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Background and Aims: Vernonia cinerea (VC) is a Thai traditional medicine which studies have been conducted in regards to its various forms including infusion tea, lozenges, and capsules where findings have indicated higher efficacy than placebo. Findings however, have not shown any statistical significance. This study therefore prepared VC pastilles via extraction, with the period of drug use for 12 weeks. Aim: The aim of this study was to compare the efficacy and safety of VC pastilles with placebo. The primary end points was continuous abstinence rate (CAR) at Week 12, and the secondary end points were the 7-day point prevalence abstinence rate (PAR) and adverse events.

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Methods: A 12 weeks, randomized, double-blind, placebo-controlled, parallel trial was conducted at community pharmacy. Volunteer aged 18 to 60 years old who were low to moderate nicotine dependence. Smoking status was established by self-reports and confirmed by end-expiratory carbon monoxide, ≤ 6 ppm showed cessation success.

Results: 54 volunteers in VC pastilles group and 57 volunteers in placebo group. At the end of week 12, CAR of the VC pastilles group was 35.19%, whereas the placebo group was 17.54% ($P = 0.034$, $RR = 2.01$ 95% CI: 1.03–3.92). The VC pastille group's PAR was 46.30%, whereas the placebo group was 31.58% ($P = 0.112$, $RR = 1.47$, 95% CI: 0.91–2.36). The adverse events of the two groups did not differ.

Conclusion: CAR of VC pastilles at week 12 is more efficacy than placebo for smoking cessation in low to moderate nicotine dependence smoker and no severe adverse events were found.

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SURVEY ON RESPIRATORY DISORDERS IN PRESCHOOL CHILDREN PRE AND POST ADMISSION TO PRESCHOOLS IN KANDY, CENTRAL SRI LANKA

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Background and Aims: Respiratory symptoms are a common complaint among preschool children, particularly following admission to preschools. Air pollution, which has lately become a serious problem in Kandy may also contribute to ill health among these children. The objective is to compare the prevalence of respiratory symptoms in preschool children pre and post admission to preschools.

Methods: A cross sectional descriptive study where randomly selected preschool children in urban and rural areas were enrolled for the study. Information regarding demographics, family history of illness and clinical information was obtained from parents of children using an interviewer administered questionnaire. Data were analysed with Microsoft Excel.

Results: 146 preschool children were enrolled out of which 69 were urban. There were 36 and 44 male children in the urban and rural groups respectively.

The following table gives details about the number of children from urban and rural preschools who had respiratory symptoms pre and post admission to preschool. Fisher's exact test was used and both urban and rural groups had a P value of 0.00 indicating a significant increase in respiratory symptoms post admission to preschool.

Conclusion: Preschool children have a significantly higher number of respiratory symptoms following admission to preschool. This was present in both groups of children, both urban and rural. Modern preschools are highly congested with poor attention to ventilation. Many children with infections are sent back to school prior to complete resolution of symptoms particularly in families where both parents are employed. All these factors may contribute to the above finding.

			Respiratory symptoms post admission	
			yes	no
Urban	Respiratory symptoms prior to admission	yes	36	0
		no	4	29
Rural	Respiratory symptoms prior to admission	yes	24	2
		no	12	39

SURVEY OF RESPIRATORY SYMPTOMS AMONG PRESCHOOL CHILDREN IN RESPONSE TO DOMESTIC TRIGGERS IN KANDY, CENTRAL SRI LANKA

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Background and Aims: Indoor air pollution in the form of biomass fuel combustion or burning incense sticks and other triggers such as animal fur, are known to adversely affect respiratory health. Respiratory symptoms are seen more often in preschool children due to a variety of reasons. In the urban community of Kandy, the recent surge of air pollution may also be a contributing factor. The aim is to assess the correlation of respiratory symptoms with domestic triggers.

Methods: A cross sectional descriptive study where randomly selected preschool children in urban and rural areas were enrolled for the study. Information regarding demographics, family history of illness and clinical information was obtained from parents of children using an interviewer administered questionnaire. Data were analysed with Microsoft Excel.

Results: 146 preschool children were enrolled out of which 69 were urban. There were 36 and 44 male children in the urban and rural groups respectively.

The presence of domestic environmental triggers in urban and rural areas is shown in the table below. Among these children respiratory symptoms were present in 40 (57.97%) of urban preschoolers and 24 (31.17%) of rural preschoolers. Therefore, although a much larger percentage of rural preschoolers (94.81%) were exposed to domestic environmental triggers than urban preschoolers 18 (26.09%), urban children suffer more respiratory symptoms.

Conclusion: The presence of domestic environmental triggers show no correlation with the presence of respiratory symptoms among preschoolers. Therefore, the influence of the environment of the preschool towards respiratory health needs to be studied thoroughly. However the long term consequences of these domestic triggers is not assessed in this study and needs further evaluation.

	Urban	Rural
Biomass fuel	0	59 (76.62)
Passive smoking	0	6 (7.79%)
Incense sticks	5 (7.25%)	55 (71.43%)
Animal fur	8 (11.59%)	33 (42.86%)
Poultry	5 (7.25%)	2 (2.60%)
At least one trigger	18 (26.09%)	73 (94.81%)

AP487

OCCUPATIONAL LUNG CANCER: EXPERIENCE IN A MEDICAL CENTER IN SOUTHERN TAIWAN

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Background and Aims: Asbestos is a well known carcinogen inducing mesothelioma specifically. For public health in labours, identifying all occupational lung cancers not only induced by asbestos but also by other substances is important. We try to investigate different categories of work and offer workers better information for personal protection.

Methods: A hospital based case series survey was conducted to identify occupational lung cancer in a medical center in southern Taiwan

from 2009 to 2017. All recently diagnosed lung cancer patients were initially involved and detail occupational history including material exposed at the work place were screened. Patients who had suspicious occupational exposure were referred to the doctor of occupational and environmental medicine and further investigation was done to clarify if they contacted class 1 carcinogens defined by the International Agency for Research on Cancer (IARC). To clarify uncertain contents at the work place, sampling and laboratory analysis were performed. Information including personal protective devices, environmental ventilation and work operation were also collected in this study.

Results: A total of six occupational lung cancer patients (2 methothelioma, 2 adenocarcinoma and 2 squamous cell carcinoma) were finally enrolled. Five of them exposed to asbestos and the other one was related to chromium. Categories of work included paint manufacturer, insulation pads processing, shipbreaking, air cooling tower assembly, automotive wires processing and metal polishing.

Conclusion: Not only mesothelioma but also other lung cancers were found in patients with exposure of asbestos. Air cooling tower, which was not recognized as a dangerous material before, was incidentally found to contain lining of asbestos. We shall pay much attention to the occupational exposures in lung cancer cases because carcinogens can be hidden in some career which we might not be familiar with before. The more information we find will help labours take necessary protective devices and prevent occupational lung cancers.

AP488

EFFECTS OF TUNGSTEN OXIDE ON LUNGS FOLLOWING INHALATION

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Background and Aims: Little is known about effects of tungsten oxide on lungs. We exposed tungsten oxide nanoparticles to rats for 1 month to evaluate the pulmonary toxicity of tungsten oxide.

Methods: Male 10-week-old Fischer 344 rats were classified into 3 groups; control (15 rats), low-dose (15 rats), and high-dose (15 rats) exposed groups. The rats of low-dose, and high-dose groups were exposed to tungsten oxide at low dose ($2 \pm 2 \text{ mg/m}^3$) and high dose ($10 \pm 1 \text{ mg/m}^3$) for 4 weeks, respectively. The rats of 3 groups were dissected after 3 days, 4 weeks, and 12 weeks from the ends of exposures. Bronchoalveolar lavage fluid (BALF) was collected from right lungs of the rats in the dissections using saline, then the cell counts, the concentrations of HO-1, CINC-1, and CINC-2, and the activity of LDH in the BALF were analyzed. Formalin fixations of the left lungs were performed as histopathological examinations.

Results: The total and neutrophil cell counts in the BALF did not show significant differences between control, low-dose, and high-dose exposed groups dissected after 3 days, 4 weeks, and 12 weeks from the ends of exposures. The percentage of neutrophils in the BALF of high-dose group at only 3 days significantly increased compared to that of the control group. The concentration of CINC-1 in the BALF of high-dose group dissected after 3 days significantly increased compared to that of the control group, although this response was a transient one. In the

analyses of concentrations of CINC-2 and HO-1, and the activity of LDH in the BALF, there were no significant differences between these groups.

Conclusion: In this study, inhalation exposure of tungsten oxide nanoparticles caused transient inflammation in rats, suggesting that the tungsten oxide may not have high inflammogenic effect in lung.

AP489

ANALYSIS OF CLINICAL FEATURES IN PATIENTS WITH PNEUMOCONIOSIS COMPLICATED WITH PULMONARY EMPHYSEMA

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Background and Aims: To investigate the clinical features of pneumoconiosis complicated with pulmonary emphysema.

Methods: selected 868 patients with pneumoconiosis were selected from December 2015 to December 2016 in Hunan occupational disease prevention and treatment hospital. Collected the results of high-resolution spiral CT, arterial blood gas, ECG, pulmonary function and MRC score. The subjects were divided into pneumoconiosis complicated with pulmonary emphysema group and simple pneumoconiosis group according to the results of HRCT. The smoking, MRC score, pulmonary function, blood gas and complications were compared.

Results: A total of 868 patients were enrolled in the study. Emphysema 232 people, accounting for 26.73%. The incidence of emphysema in the first phase of pneumoconiosis was 12.69%, and the incidence rate of emphysema in pneumoconiosis was 17.03%. The incidence of three Stage pneumoconiosis was highest, up to 60.76%, the incidence of emphysema increased with the increase of stages of pneumoconiosis ($P = 0.000$). The smoking index of pneumoconiosis combined with emphysema group was significantly higher than that of simple pneumoconiosis group ($P = 0.000$). The MRC score of pneumoconiosis complicated with pulmonary emphysema group was higher than that of simple pneumoconiosis group ($P = 0.000$). In pneumoconiosis complicated with pulmonary emphysema group the FEV1%, FVC%, FEV1/FVC, DLCO%, oxygen partial pressure were significantly lower than that of simple pneumoconiosis group ($P \leq 0.05$). The combined rate of Bullae of lung in pneumoconiosis complicated with pulmonary emphysema group was higher than that of simple pneumoconiosis group ($P = 0.000$).

Conclusion: The risk factors of pneumoconiosis complicated with emphysema are advanced age, pneumoconiosis stage and smoking. Patients with pneumoconiosis complicated with pulmonary emphysema had heavier breathing difficulties, more serious pulmonary function and active endurance, the degree of hypoxia is more serious, and had a higher incidence of complications. The pulmonary function of pneumoconiosis complicated with pulmonary emphysema is not consistent with the typical CPFE.

AP490

THE LEVEL AND DYNAMICS OF RESPIRATORY DISEASES MORBIDITY IN RUSSIA

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Background and Aims: The specific weight of respiratory diseases (RD) in the structure of general and primary morbidity in the Russian Federation (RF) in 2017 was 24.7 and 44.7%, respectively. The analysis of the dynamics of RD prevalence allows to make management decisions in

the healthcare. We aimed to study the dynamics of RD morbidity on the territory of RF.

Methods: The materials of the state statistical monitoring of RD on the territory of RF since 2005 till 2017 were used. Index methods of assessment, relative and extensive values of indices and methods of statistical series were used.

Results: The analysis of statistical series showed the growth of the primary RD morbidity from 2015 till 2006 in all regions of RF. The highest growth was observed on the territories of North-Western and Far-Eastern federal districts (29.5 and 23.3%, respectively). In general, the growth of the primary RD morbidity for the period was 18.1%, and of the general disease incidence 10.7%, against the annual average growth rate of 1.48% and 0.98%, respectively. In comparison with 2005 the level of the primary disease morbidity among adults in RF increased by 9.4%, and among children by 13.9% and was 162.8‰ and 1187.0‰, respectively (2016). The highest rates of morbidity growth are observed for COPD (20.3%) and asthma (16.1%). The growth of morbidity of chronic diseases of lower airways (asthma, COPD, chronic bronchitis) was 21.05% against annual average growth rate of 1.75%, and it reached the level of total registered morbidity of 2774.1‰. At the same time pneumonia incidence have a stable tendency to decrease from 2010.

Conclusion: On the territory of RF there is an expressed regional differentiation of the level and dynamics of RD caused by the influence of factors of the environment and a high growth of chronic pathologies incidence unlike pneumonias and respiratory infections.

AP491

COMPARISON OF OCCUPATIONAL EXPOSURE LIMITS OF CHEMICAL SUBSTANCES IN WORKPLACE BETWEEN CHINA GBZ 2.1 AND GERMAN MAK

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Background and Aims: to systematically compare the difference between the current standard GBZ2.1-2007 of occupational exposure limits (OELs) in China and the German maximum workplace concentration MAK in the aspects of definition, formulation principle, specific values of OELs, etc., and provide the suggestions and basis for the revision of GBZ2.1

Methods: According different type to build the database for OELs of GBZ2.1 and MAK Values (2015), compare the databases and analyze the difference between them.

Results: the results showed that the formulation principles of OELs, the sources of legal OELs, the quantity and mark of OELs between China and Germany were different. So the study and application on OELs of pregnancy toxicity for chemical hazardous agents to formulate the OELs, the OELs of heavy metals, such as cobalt, molybdenum, beryllium, thallium, and so on, formulated in China did not exist in German MAK and American ACGIH, and the OELs were no longer formulated for cancerogenic substance in Germany.

Conclusion: There were great difference in values of OELs for the chemical hazardous agents both in China and Germany, and the partial OELs in China were higher than those in German MAK and American ACGIH simultaneously. The updating frequency of OELs in China was slower, so the updating cycle should be shortened. When revising the current GBZ2.1, the OELs in the advanced countries can be taken as a reference. The management and assessment on cancerogenic substance in the German risk classification and assessment method deserves the further discussion and research.

SURVEY ON RESPIRATORY SYMPTOMS OF URBAN VS RURAL PRESCHOOL CHILDREN IN KANDY, CENTRAL SRI LANKA

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Background and Aims: A surge in the degree of air pollution has been noticed recently in Kandy, located in central Sri Lanka due to a variety of reasons including demographic transition with more people moving into cities, increased use of personal vehicles, and changes in the natural environment. Air pollution has been linked to poor respiratory health. Respiratory symptoms are very common among preschool children. The number of preschools has also increased in the recent past, particularly in urban areas. The aim is to compare respiratory symptoms in preschool children of urban vs rural areas.

Methods: A cross sectional descriptive study where randomly selected preschool children in urban and rural areas were enrolled. Information regarding demographics, family history of illness and clinical information was obtained from parents of children using an interviewer administered questionnaire. Data were analysed with Microsoft Excel.

Results: 146 preschool children were enrolled out of which 69 were urban. There were 36 and 44 male children in the urban and rural groups respectively.

Respiratory symptoms among these two groups are tabulated below. When comparing the prevalence of respiratory symptoms among urban and rural preschoolers the Chi square estimate was 8.213 with a P value of 0.004.

Conclusion: Preschoolers in urban preschools have a higher prevalence of respiratory symptoms compared to their rural counterparts. Cough, wheezing and respiratory tract infections are particularly high in the urban group. These symptoms may be directly related to air pollution either by increasing infections or asthma and warrants further study.

Symptom	Urban	Rural
Cough	23 (33.33%)	9 (11.69%)
Wheezing	12 (17.39%)	8 (10.39%)
Shortness of breath	0	5 (6.49%)
Respiratory tract infections	14 (20.29%)	9 (11.69%)
Allergic rhinitis	1 (1.45%)	6 (7.79%)
Multiple symptoms	8 (11.59%)	12 (15.58%)
Total number of children with symptoms	40 (57.97%)	24 (31.17%)

AP493

A THERAPEUTIC METHOD FOR PM2.5-INDUCED LUNG INJURY BASED ON EXOSOME IN RATS

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Background and Aims: PM2.5-induced lung injury (ALI) is a common environmental injury characterized by severe oxidative stress and excessive inflammatory responses. But the current therapeutic methods are largely supportive. We promote a new treatment based on exosome derived from BMSCs.

Methods: The bone marrows of 4-week-old, male Sprague Dawley rats were used to obtain BMSCs, rats were euthanized via cervical dislocation. After 72 h, the medium was replaced and fresh medium was provided every 3 days. BMSCs were identified via flow cytometry, multi-directional differentiation capacity, and morphology. The exosome was

extracted and purified from BMSCs by differential centrifugation and identified by morphology and exosomal markers. 15 male rats of 6-week-old with ALI induced by PM2.5 were randomly divided into 3 groups, which were termed as group 1 to group 3. Group 1 was a control group. After exposing with PM2.5, the rats were treated with PBS through tail veins. The rats in group 2 were treated with carnosine (15 mg/kg). The rats in group 3 were treated with exosome (1 mg/kg). 6 h later, all the rats were executed under anaesthesia. The expression level of TNF- α , SOD1 and ROS in lung tissue were determined. The lung tissue injury level was evaluated by immunohistochemistry.

Results: The level of ROS (H2O2 and MDA activity) and TNF- α of group 3 was similar with group 2, which was lower than that of group 1. And the level of antioxidant kinase (SOD1) of group 3 was higher than that of group 1 and group 2. The immunohistochemistry results indicated that there was alleviation in the lung tissue of group 2 and group 3.

Conclusion: The exosome equipped therapeutic effect for PM2.5-induced lung injury through anti-oxidant and anti-inflammatory effect.

AP494

OBSTRUCTIVE AIRWAY DISEASE IN TRIBAL AND NON-TRIBAL POPULATIONS IN RURAL BENGAL, INDIA

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Background and Aims: Studies regarding the respiratory diseases suffered by the people of both tribal and non-tribal population of rural Bengal, India are lacking. It is important to look into their respiratory status to find out the prevalence of respiratory diseases in them.

Methods: We screened 1082 subjects ($n = 546$ tribes and $n = 536$ non-tribes) of Rajnagar block of Birbhum district, West Bengal, India for the presence of respiratory ailments using chest X-ray, spirometry, and clinical evaluations. The status of the obstructive lung disease (OLD) was analyzed in them.

Results: The frequency of OLD was 39(7.14%) and 66 (12.31%) among the tribal and non-tribal population. The mean age of the OLD patients was 45.3 ± 6.19 and 55.6 ± 2.23 with the male and female ratio being 21:18 and 48:18 for the tribal and non-tribal population respectively. The severity of OLD (GOLD III and IV) was higher in nontribal population (36%) compared to the tribal population (10%). The predicted percentage of FEF25-75 was significantly low in non-tribal population (68.74 ± 28.43) compared to the tribal population (81.7 ± 8.74).

Conclusion: The tribal population appears to have lesser frequency and severity of OLD compared to the non-tribal population in the same geographic area of West Bengal, India. The reason behind this may be related to the differences in their smoking habits and use of fuels by them. Further researches are being conducted to elucidate the proper reason for such differences.

FEV ₁	Tribal population N=39	Non Tribal population N=66
≥ 80 mild	7 (17.9%)	2 (3.0%)
50-79 moderate	20 (66.0%)	27 (40.9%)
30-49 severe	10(25.6%)	30(45.4%)
<30 v. severe	0(0%)	6(9.09%)

Table 1: The predicted percentage of forced expiratory volume in one second (FEV₁) which determines the OLD severity for both populations are shown.

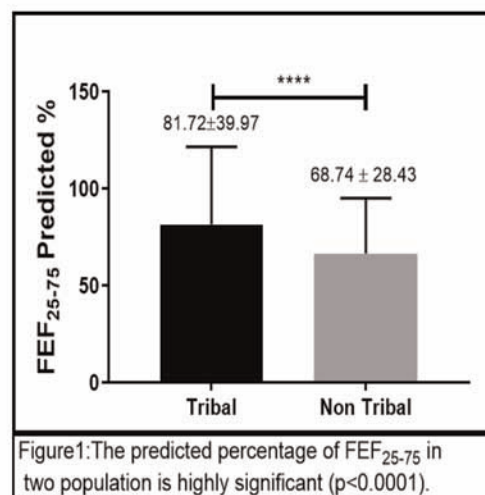


Figure1: The predicted percentage of FEF₂₅₋₇₅ in two population is highly significant ($p < 0.0001$).

Interstitial Lung Disease 2

AP495

THE USE OF KETOCONAZOLE FOR THE TREATMENT OF REFRACTORY HYPERCALCAEMIA IN SARCOIDOSIS

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Background and Aims: Hypercalcaemia is a well-described complication of granulomatous diseases, including sarcoidosis. The primary mechanism for this is increased production of calcitriol by activated mononuclear cells working independently of physiologic parathyroid hormone (PTH) control. We present a case of refractory hypercalcaemic sarcoidosis in which the addition of ketoconazole, a synthetic imidazole antifungal, was required to restore normocalcaemia.

Methods: A 54-year-old man with a history of poorly-controlled type 2 diabetes, hypertension, and peripheral vascular disease was referred for work-up of severe hypercalcaemia detected on routine blood tests. A computed tomography (CT) scan of the chest revealed scattered pulmonary nodules and bilateral hilar lymphadenopathy suggestive of sarcoidosis. Confirmatory histopathology revealing non-caseating granulomas was obtained via endobronchial biopsies of the inferior lingular segment of the left upper lobe. Sequential treatment of hypercalcaemia with empiric pamidronate (60 mg), intravenous fluids and diuretics as well as immunosuppressive therapy with prednisolone (0.5 mg/kg daily) and methotrexate (10 mg weekly) was used. Despite this, no biochemical improvement was observed after almost two months of therapy.

Results: Ketoconazole was added to the patient's treatment due to its purported ability to inhibit macrophage 1- α -hydroxylation of calcidiol. Normalisation of the patient's calcium level was finally achieved after

one week of ketoconazole therapy (400 mg daily) taken in conjunction with Diet Coke®, an acidic beverage.

Conclusion: Ketoconazole appears to be a safe and effective treatment for patients with hypercalcaemic sarcoidosis that is refractory to conventional and immunosuppressive therapy.

AP496

SYMPTOMS OF INTERSTITIAL LUNG DISEASE THAT AFFECT QUALITY OF LIFE

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Background and Aims: Interstitial lung disease is progressive, but there are few studies on the changes in quality of life and affecting symptoms over time. Therefore, we examined the time course of the chronic obstructive pulmonary disease assessment test (CAT) score to clarify the symptoms using the eight items in the CAT.

Methods: Sixty-three patients with interstitial lung disease were evaluated by the CAT repeatedly with an interval of 20 months on average, excluding the period of acute exacerbation. The hospital records for the pulmonary function test were also collected for analysis.

Results: The CAT score improved or stayed the same in 31 patients and deteriorated in the others. The duration from disease onset to the first evaluation in the improved group was shorter than that in the deteriorated group, and logistic analysis demonstrated that five years from onset was the cut-off point for deterioration (AUC = 0.75, $P = 0.01$). Symptoms in the improved group were all ameliorated except for chest tightness and confidence in leaving home. In the deteriorated group, chest tightness, breathlessness, activity limitation at home, less confidence in leaving home, and less energy were more frequently observed. The most common item in the CAT was breathlessness in all patients. Forced vital capacity and diffusion capacity of the lung for carbon monoxide at the first evaluation were more impaired in patients of the deteriorated group ($P = 0.04$ and $= 0.008$, respectively). Moreover, pulmonary function declined on repeated evaluations in patients of both groups.

Conclusion: Breathlessness may be the main symptom in interstitial lung disease, but quality of life can be improved in patients with a short duration from disease onset regardless of progressive impairment in pulmonary function. Improvement in quality of life becomes difficult over time due to poorer pulmonary function.

AP497

CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES COMPARED TO CONNECTIVE TISSUE DISEASE RELATED-INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: Patients with interstitial lung disease (ILD) may show evidence of autoimmunity without meeting criteria for a defined connective tissue disease. A recent European Respiratory Society/American Thoracic Society statement proposed criteria for patients with interstitial pneumonia with autoimmune features (IPAF).

To compare clinical characteristics and clinical outcomes of patients with IPAF to patients with connective tissue disease related-interstitial lung disease (CTD-ILD) and patients with idiopathic pulmonary fibrosis (IPF).

Methods: ILD patients who were consecutively enrolled in a single institution ILD cohort between 2008 and 2015 were evaluated for the study. Clinical data had been prospectively collected, while radiologic imaging and pathologic findings were re-reviewed for present study.

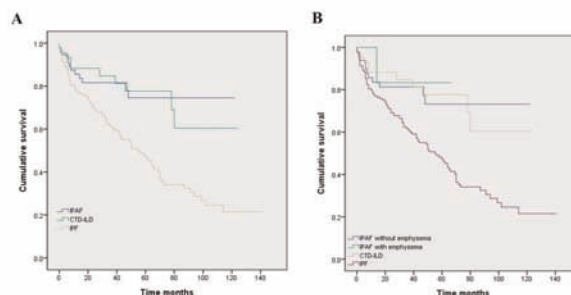
Results: Out of 409 patients with ILD, 56 (13.7%) patients met the classification of IPAF and 148 (36.2%) patients had idiopathic pulmonary fibrosis (IPF). Forty-four (10.8%) patients were diagnosed of CTD-ILD. The proportion of males (25.0%) in the IPAF group was low when compared to the CTD-ILD (38.6%) and IPF (63.1%) groups. Mean age and the proportion of ever smokers were significantly different between the three groups ($P < 0.001$ and $P < 0.001$, respectively). The IPAF group had the lowest proportion of patients with emphysema on high resolution CT (HRCT) ($P = 0.004$). There were no significant differences in pulmonary function test parameters between 3 groups (Table 1). Among 56 IPAF patients, 36 (64.3%) patients showed nonspecific interstitial pneumonia (NSIP) pattern on HRCT. Among 12 IPAF patients who underwent surgical biopsy, organizing pneumonia was the most frequent histopathologic pattern (50%). Overall survival (OS) of IPAF was significantly better than the IPF groups ($P = 0.005$) (Figure 1A). After stratification by presence of emphysema, no significant difference in OS exists between the IPAF patients without emphysema and with emphysema ($P = 0.713$) (Figure 1B).

Conclusion: Compared to CTD-ILD and IPF groups, IPAF group showed differences in clinical characteristics and in outcome.

Table 1. Comparison of clinical characteristics between IPAF, CTD-ILD and IPF

	IPAF (n=56)	CTD-ILD (n=44)	IPF (n=149)	p-value
Sex (male) (n,%)	14 (25.0)	17 (38.6)	94 (63.1)	<0.001
Mean age (SD)	65.9±13.0	62.5±14.0	71.5±9.6	<0.001
Ever smoker (n,%)	11 (19.6)	18 (40.9)	84 (56.4)	<0.001
Emphysema from CT (n,%)	7 (12.5)	13 (41.9)	43 (33.6)	0.004
FVC (% of predicted)	83.6±18.6	84.0±14.5	80.1±18.7	0.348
FEV1 (% of predicted)	96.9±20.6	92.3±20.5	95.2±24.7	0.665
TLC (% of predicted)	90.1±18.9	93.6±24.2	91.7±24.5	0.805

Abbreviations: CT: computed tomography; CTD-ILD: connective tissue disease-related interstitial lung disease; DLCO: Diffusing capacity of the lungs for carbon monoxide; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; IPAF: interstitial pneumonia with autoimmune features; IPF: interstitial pulmonary fibrosis; SD: standard deviation; TLC: total lung capacity.



AP498

CLINICAL ANALYSIS OF THE CASES OF INTERSTITIAL PNEUMONIA COMBINED WITH MALIGNANT TUMOR ASSOCIATED WITH POLYMYOSITIS AND DERMATOMYOSITIS IN OUR HOSPITAL

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Background and Aims: Various autoantibodies have been identified in polymyositis (PM) and dermatomyositis (DM) in recent years, and the clinical course of PM/DM was different according to complicated autoantibodies. PM/DM often complicated interstitial pneumonia (IP) and malignant tumor. However, it has not been concluded whether to treat first IP or malignant tumor in general. Therefore, we investigated the clinical course in PM/DM patients with IP combined with malignant tumor experienced in our hospital retrospectively.

Methods: We retrospectively investigated the clinical course of the patients with a diagnosis of PM/DM with IP and malignant tumor from April 2014 to March 2018 in Gunma University School of Medicine.

Results: We were involved in 6 cases of PM/DM with interstitial pneumonia and malignant tumor. PM/DM-related autoantibodies were confirmed in 5 cases. Two cases have anti-transcriptional intermediary factor 1- γ (TIF1- γ) antibody, 2 cases have anti-melanoma differentiation-associated gene 5 (MDA5) antibody, and 1 case has anti-aminoacyl t ribonucleic acid synthetase (ARS) antibody, respectively.

Two cases preceded treatment for malignant tumor, and 4 cases preceded treatment for IP or DM. The reasons that preceded the treatment of IP and DM were subacute exacerbation of IP or severe myositis with early stage of malignant tumor. At the present time, 4 cases are treating malignant tumor, but all cases become exacerbated the symptoms of IP or dermatitis and myositis after malignant tumor treatment. One case died due to IP.

Conclusion: There is no prescription which treatment should be prioritized for IP or malignant tumor in PM/DM patients. However, there are cases in which the patient dies due to progress of IP even after treatment of the malignant tumor. We should make a decision as a priority to treat in individual case.

AP499

PREVALENCE OF ANXIETY AND DEPRESSION AS WELL AS ITS IMPACT ON QUALITY OF LIFE IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Background and Aims: To study the prevalence of anxiety and depression in patients with Interstitial Lung Disease (ILD) using validated questionnaire.

Methods: This was a prospective, observational study comprising 112 newly diagnosed patients with ILD as per the ATS/ERS statement 2013. These patients were screened for the presence of anxiety and/or depression using the Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Rating Scale for Depression scores (HRSD) respectively. Based on the presence of anxiety and/or depression, these patients were grouped into: Group 1 (Anxiety alone), Group 2 (Depression alone), Group 3 (Anxiety & Depression both) and Group 4 (Neither Anxiety nor Depression). In addition, in these patients, Health Related Quality of Life (HRQoL) was assessed using Short Form-36 (SF-36) questionnaire.

Results: Anxiety was seen in 67/112 (59.8%) and depression in 64/112 (57.1%) patients. The mean HAM-A and HRSD scores were

10.17 $\pm$ 10.39 and 9.17 $\pm$ 6.11 respectively. The patients were categorised as follows: Group 1 with 21 (18.75%), Group 2 with 18 (16.07%), Group 3 with 46 (41.07%) and Group 4 with 27 (24.11%). There was a statistically significant difference in HRQoL between the groups ($P = 0.000$) with the physical component as well as mental component score of SF-36 being worse in Group 3.

Conclusion: Chronic lung diseases such as ILD continue to cause significant morbidity and mortality. The findings in our study indicate that anxiety and depression have higher prevalence in Indian patients with ILD. A number of parameters affect the overall HRQoL in patients with ILD. Recently, both anxiety and depression have been seen to have an impact on HRQoL in ILD. The presence of anxiety/depression significantly influenced patient HRQoL in our study, highlighting the need for improved detection and treatment of such conditions in this patient population.

AP500

CLINICAL PROGNOSIS OF ACUTE EXACERBATION OF COMBINED PULMONARY FIBROSIS AND EMPHYSEMA

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Background and Aims: Combined pulmonary fibrosis and emphysema (CPFE) has been recognized as a unique entity that is characterized by upper lung emphysema and lower lung fibrosis. It was reported that CPFE patients also were in risk to have acute exacerbation, being similar to idiopathic pulmonary fibrosis (IPF) patients. However, there are few reports on the prognosis of acute exacerbation of CPFE (AE-CPFE). The aim of this study is to investigate the clinical prognosis of AE-CPFE.

Methods: We retrospectively reviewed the medical records of patients in Shinshu University Hospital in Matsumoto, Japan from 2003 to 2017 and identified 23 patients with AE-CPFE and 41 patients with acute exacerbation of IPF (AE-IPF). CPFE were diagnosed with the findings of fibrosis concomitant with usual interstitial pneumonia and more than 7 points of low attenuation area score by high resolution computed tomography.

Results: The mean age of the AE-CPFE was 73.4 years, which was statistically similar to mean age of AE-IPF (71.0 years, $P = 0.16$). There were no significant differences of the treatments contents and respiratory management for both of before and after exacerbation between the AE-CPFE and AE-IPF. However, the mean serum KL-6 and white blood cell (WBC) counts were significantly lower in the AE-CPFE (KL-6: 1069 U/ μ L; WBC: 9357/ μ L) than in the AE-IPF (KL-6: 2130 U/ μ L, $P < 0.001$; WBC: 10809/ μ L, $P = 0.029$). There was no significant difference of the base line of Gender-Age-Physiology score between the two groups (AE-CPFE: 4.5, AE-IPF: 4.7, $P = 0.58$). The median survival time was 117.3 days in the AE-CPFE and 68.4 days in the AE-IPF. The Kaplan-Meier curves showed that the survival time was longer in the patients with AE-CPFE than the patients with AE-IPF by log rank test ($P = 0.0053$).

Conclusion: The prognosis of AE-CPFE is significantly better than that of AE-IPF.

AP501

PATTERN OF INTERSTITIAL LUNG DISEASES IN A SINGLE CENTER OF SRI LANKA

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Background and Aims: Interstitial lung diseases are a diverse group of entities, either idiopathic or secondary to many different

aetiologies. Pattern of interstitial lung diseases widely varies geographically. Data on epidemiology and pattern of ILDs are limited in Sri Lanka.

We aimed to describe the epidemiology and pattern of ILDs in single center of Sri Lanka

Methods: A descriptive cross sectional study conducted in a single tertiary care center of Sri Lanka. A random sample of patients who were diagnosed with ILDs according to standard criteria was selected. Demographic and clinical data were collected using medical records. Data were analyzed using Microsoft excel.

Results: Total of 58 subjects were included, of which 36 (62.0%) were females. Mean age was 60.78 years (range 13–77). Twenty (34.4%) had idiopathic interstitial pneumonias (IIP), in which 12 (60%) were non-specific interstitial pneumonias, 2 (10 %) idiopathic pulmonary fibrosis, 2 (10%) desquamative interstitial pneumonias and 4 (20%) cryptogenic organizing pneumonias. 14 (24.1%) had ILDs secondary to well defined autoimmune diseases, of which there were 5 (35.7%) rheumatoid arthritis, 4 (28.5%) diffuse systemic sclerosis, 2 (14.2%) limited systemic sclerosis, 1 (7.1%) overlap syndrome, 1 (7.1%) mixed connective tissue disease and 1 (7.1 %) polymyositis. Furthermore, 7 (12.0%) were classified as interstitial pneumonia with autoimmune features (IPAF). There was one case of ILD secondary to amiodarone toxicity. Fourteen (24.1%) of total cohort were diagnosed with hypersensitivity pneumonitis and 1 (1.7%) had sarcoidosis.

Conclusion: Secondary ILDs were more prevalent than idiopathic cases in the study population. Nonspecific interstitial pneumonia was the commonest type of IIP. Hypersensitivity pneumonitis, which accounted for nearly 1/4th of ILDs in study group, should be an important differential diagnosis for IIPs. IPAF, a newly described entity, was found in 12% of all ILDs. This should encourage further studies on this group.

AP502

THE SERUM KL-6 LEVELS IN UNTREATED IDIOPATHIC PULMONARY FIBROSIS CAN NATURALLY DECLINE IN ASSOCIATION WITH DISEASE PROGRESSION

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Background and Aims: Serum KL-6 is known to be a useful biomarker for the diagnosis and assessment of the disease activity in idiopathic pulmonary fibrosis (IPF). However, some patients with untreated IPF present with a serial decline in their serum KL-6 levels, despite showing clinical progression. The aim of the present study was to evaluate the association between the time course of the serum KL-6 levels and the clinical course of patients with untreated IPF.

Methods: We conducted a retrospective study of 59 patients who met the diagnostic criteria for IPF, who regularly underwent laboratory tests including the measurement of KL-6 and pulmonary function tests, and who were untreated during the follow-up period.

Results: The baseline forced vital capacity (FVC) %predicted among non-survivors ($n = 29$) was lower than that among survivors ($n = 30$, $P = 0.02$). The baseline levels of serum KL-6 among non-survivors were higher than those among survivors ($P = 0.024$). The rates of decline in comparison to the baseline FVC values were comparable between survivors and non-survivors; however, the rates of change in comparison to the baseline KL-6 levels were heterogeneous in both survivors and non-survivors, and the KL-6 levels of the non-survivors were observed to decline significantly more frequently in comparison to the survivors ($P = 0.001$).

Conclusion: A decline in the serum KL-6 levels of patients with untreated IPF does not mean that the disease activity has subsided.

Serum KL-6 levels can naturally decline in association with disease progression.

AP503

EFFICACY AND SAFETY ANALYSIS OF THE WHOLE LUNG LAVAGE IN TREATMENT OF PULMONARY ALVEOLAR PROTEINOSIS

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Background and Aims: Pulmonary Alveolar Proteinosis (PAP) is a rare interstitial lung disease and the whole lung lavage (WLL) is still the most effective treatment in the management. The aims of this study is to evaluate the efficacy and safety of the WLL in the treatment of PAP.

Methods: The cases with PAP received treatment of WLL were recruited, during the period December in 2001 to December in 2017 in the inpatient department of Pulmonary and Critical Care Medicine, The First Affiliated Hospital, Sun Yet-Sen University. The changes of chest image, lung function, arterial blood gas, modified medical research council (mMRC) dyspnea scale and 6-min walk test (6MWT) were compared before and after WLL. Meanwhile, review the complication before and after this treatment to evaluate the safety.

Results: 25 patients with PAP undergoing WLL were included in this study. There were 13 males and 12 females with an average age of 42.5 years (22–63 years). 20 patients completed MMRC scores before and after WLL and improved significantly after WLL ($1.1 \pm .64$ vs $2.1 \pm .37$, $P < 0.05$). The SaO_2 , PaO_2 , and oxygenation index at 1 h after extubation were not significantly improved, but were significantly improved at 1 day after WLL. After WLL, lung function testing items such as FEV1%, FVC, and DLCO% were significantly improved. Transient hypoxemia occasionally occurs in WLL treatment. All patients had cough and sputum with varying degrees after operation. Among them, 3 cases had low fever after operation and were cured after antibiotic therapy. No serious incident occurred.

Conclusion: WLL is an effective and safe treatment for PAP.

TABLE1. MMRC scores and 6MWT

Parameter	Before WLL	After WLL	α -value
MMRC	2.14 ± 0.37	1.19 ± 0.64	<0.05
6MWT	325.35 ± 6.88	395.01 ± 2.19	0.17

TABLE2. ABG results

Parameter	Before WLL	1h After WLL	α -value	1d After WLL	α -value
$\text{SaO}_2(\%)$	85.35 ± 6.88	90.01 ± 2.19	0.11	95.01 ± 2.19	<0.01
$\text{PaO}_2(\text{mmHg})$	61.87 ± 16.58	81.73 ± 7.58	0.03	81.73 ± 7.58	<0.01
OI	302 ± 26.15	322 ± 23.79	0.19	362 ± 35.19	<0.01

TABLE3. Lung function tests

Parameter	Before WLL	After WLL	α -value
DLCO(%预计值)	45.79 ± 12.15	59.64 ± 20.13	0.002
DLCO/VA(%预计值)	62.74 ± 21.12	77.49 ± 20.01	<0.01
FEV1% pred	71.45 ± 22.62	83.75 ± 21.02	<0.01
FVC	76.54 ± 13.09	83.81 ± 16.28	<0.01
FEV1/ FVC	89.08 ± 23.63	99.12 ± 12.13	<0.01

AP504

B CELL ACTIVATING FACTORS IN PATIENTS WITH AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS

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Background and Aims: We have reported that the elevation of B cell activating factors, such as B cell activating factor belonging to the tumor necrosis factor family (BAFF) and a proliferation-inducing ligand (APRIL) in serum and in bronchoalveolar lavage fluid (BALF) in the patients with autoimmune pulmonary alveolar proteinosis (APAP). From these results, an increase in B-lymphocytes in peripheral blood and BALF is suspected. Therefore, we confirmed the BAFF and APRIL producing cells by immunohistochemically in PAP region and analyzed the ratio of B-lymphocytes in peripheral blood.

Methods: Ten patients with APAP (Male: 7, Female: 3, Age: 5 ± 7 years), 20 healthy controls (Male: 11, Female: 9, Age: 4 ± 2 years) and 10 lung disease controls (Male: 8, Female: 2, Age: 5 ± 8 years) were enrolled in this study. Lung disease controls involved idiopathic pulmonary fibrosis ($n = 4$), asbestosis, COP, CVD-IP, LC, LIP, sarcoidosis ($n = 1$, respectively). Immunohistochemical staining was performed by Avidin-Biotin Complex method. CD19 and CD20 positive cells were measured by flow cytometry in the peripheral blood and BAL samples. B cell activating factor (BAFF and APRIL) levels in serum and in BALF were measured by ELISA using commercially available kit (R&D systems and eBioscience).

Results: Expression of BAFF and APRIL were confirmed on alveolar macrophages. The CD19 expressed B cells were significantly increased in the patients with APAP compared to healthy control in peripheral blood ($P = 0.006$). However, there was no differences in CD20-expressing B cells in peripheral blood between APAP and healthy control. And we also confirmed no differences in CD19- and CD20-expressing B cells between APAP and disease controls in BALF.

Conclusion: Overproduction of autoantibody against GM-CSF may allow an abnormality of humoral immunity in the pathogenesis of APAP by B cell activating factors.

AP505

THE CHRONOLOGY OF PULMONARY AND CUTANEOUS MANIFESTATIONS IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE PATIENTS: A CASE SERIES

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Background and Aims: More than 80% of systemic sclerosis patients have pulmonary involvement, and the interstitial lung disease is the most common form. However, the time sequence of interstitial lung disease (ILD) development in Systemic sclerosis (SSc) is not well defined, and we try to evaluate the chronology of these two manifestations.

Methods: We describe 3 cases of SSc related ILD patients with different presentation of symptoms.

Results: The first case is a 58-year-old male who has SSc with initial presentation as bilateral hands sclerodactyly and positive anti-nuclear antibody (ANA) and anti-Scl70. However, he suffered from progressive dyspnea on exertion about 4 years later, and the image revealed bilateral interstitial infiltration. His pulmonary function deteriorated quickly even under medication treatment and he received lung transplantation 5 years later. The second case is a 62-year-old male initially presented with both bilateral hands sclerodactyly and dyspnea on exertion for 1 month. He is treated with oral prednisolone with stable condition. The third case is a

59-year-old male who had dyspnea on exertion for years. Initially autoantibody screen only showed ANA 1:160 homogeneous. He had received nintedanib for more than 1 year and the sclerodactyly was noted with positive anti-Scl70 later. The patient's pulmonary function seemed stationary during this period.

Conclusion: We report three SSc patients with different chronology of pulmonary and cutaneous manifestations. The regular physical examination and autoimmune examination are crucial in early detection of different presentation in SSc patients.

AP506

MULTIPLE CYSTS FORMATION IN PULMONARY LUNG CHAIN DEPOSITION DISEASE (LCDD). A CASE REPORT

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Background and Aims: To review the clinical features of the patient with cystic pulmonary light chain deposition disease (LCDD) and record high-resolution CT and histopathological findings.

Methods: A 60-year-old woman who diagnosed multiple myeloma was admitted. There were diffuse proliferation of plasma cells by the bone marrow puncture that she received. And multiple cystic pulmonary tumours found in CT. We analyze the method and result of the diagnosis.

Results: CT showed multiple cystic pulmonary tumours with thin wall ranged 5–30 mm in the both lung. There were no abnormality in the heart, kidney and liver. Right upper lobe wedge resection was performed via video-assisted thoracic surgery to establish a definitive diagnosis. Thoracoscopic findings revealed multiple white oval formed tumours in the visceral pleura. Operation time was 126 min, there was not the intraoperative complications. Histological HE staining findings of the surgical specimen revealed amyloid-like acidophilic material, and the immunohistochemical congo red staining revealed monoclonal IgG with a kappa component. According to the above results these tumours had a diagnosis of pulmonary LCDD.

Conclusion: Video-assisted thoracic surgery was effective to diagnose pulmonary LCDD in multiple cysts formation.

AP507

PULMONARY ALVEOLAR PROTEINOSIS WITH UPPER-LOBE PREDOMINANCE IN A NON-SMOKING YOUNG FEMALE

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Background and Aims: Pulmonary alveolar proteinosis (PAP) is a very rare interstitial lung disease. Most of the previously reported cases occurred in male smokers and radiographically exhibited either diffuse or mid-to-basal-predominant involvement of the lung parenchyma. In this thematic poster, we aim to report the clinical, radiographical, and functional findings of a non-smoking young female who developed PAP that predominantly involved her upper lung lobes.

Methods: The relevant histories, laboratory data, serial thoracic images, histological findings, and serial pulmonary function measurements of the patient were reviewed and will be coherently and graphically presented in this thematic poster.

Results: The patient was a never-smoking female and aged 43 years when she developed PAP. She had type 2 diabetes mellitus, but her occupational and exposure history was unremarkable. Screening tests for underlying HIV infection and connective tissue disease all reported negative. Examination of her peripheral blood smear did not detect leukemic cells. Her chest radiograph showed patchy and linear infiltrates mainly in the perihilar and upper fields, while her chest CT scan revealed multiple well-delineated "crazy-paving" opacities predominantly involving the apical and upper lung zones. Due to an undiagnostic bronchoalveolar lavage, peripheral wedge-biopsy of her left upper lung via video-assisted thoracoscopy was performed, and the diagnosis of PAP was established histologically. Serial pulmonary function tests showed a declining trend in her forced vital capacity, and a mild but persistent impairment in her diffusion capacity for carbon monoxide.

Conclusion: PAP needs to be considered in the differential diagnosis for an upper-lobe predominant interstitial lung disease.



AP508

IMPACT OF PHYSICAL ACTIVITY PRIOR TO AND AFTER ANTIFIBROSIS THERAPY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: Forced vital capacity (FVC) is used for the evaluation of antifibrosis therapy; however, repeating a respiratory function test in patients with advanced idiopathic pulmonary fibrosis (IPF) is challenging. On the contrary, physical activity – a predictive indicator of prognosis in patients with IPF – is easily measurable. This study examined changes in physical activity prior to and after antifibrosis therapy in patients with IPF and their impact on the clinical course.

Methods: Physical activity was measured using a pedometer with accelerometer (Lifecorder GS; Suzuken Co. Ltd) prior to and 6 months after antifibrosis therapy. The relationship between changes in physical

activity and clinical parameters (quality of life and respiratory function), number of hospitalizations, and survival were assessed.

Results: The study included 16 patients with IPF (males: 12 patients/females: 4 patients), aged $6 \pm .4$ years. The background of patients prior to treatment initiation included the following: (1) treatment with nintedanib (11 patients) and pirfenidone (5 patients); (2) FVC percentage: $70. \pm 6.9\%$; KL-6 levels: 107 ± 52 U/mL, 6-min walk distance: 39 ± 6.9 m, and steps/day: $6,42 \pm ,217$. Six months after initiation of therapy, Group A (8 patients) demonstrated a decrease in the rate of steps by $<30\%$, whereas Group B (8 patients) showed a decrease by $>30\%$. The chronic obstructive pulmonary disease assessment test and St. George's respiratory questionnaire score showed a strong tendency in Group B. Among the 7 patients (Group A: 3 patients; Group B: 4 patients) who expired during the course of treatment, the number of hospitalizations were 0.54 and 1.26 times per year in Groups A and B, respectively; survival after initiation of treatment was 22.3 and 14.3 months, respectively.

Conclusion: Decreased physical activity prior to initiation of antifibrosis therapy is associated with low quality of life and a poor clinical course of patients with IPF.

AP509

HISTONE DEACETYLASE 3 INDUCES ALVEOLAR EPITHELIAL-MESENCHYMAL TRANSITION UNDER HYPOXIC CONDITION

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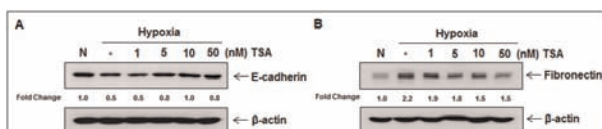
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Background and Aims: Epithelial-mesenchymal transition (EMT), a process by which epithelial cells undergo a phenotypic conversion that gives rise to myofibroblasts, plays a pivotal process in the development of lung diseases such as pulmonary fibrosis. In lung diseases, alveolar epithelial cells are exposed to hypoxic condition. From recent studies that hypoxia induces EMT of alveolar epithelial cells, and histone deacetylases (HDACs) are aberrantly overexpressed in basal cells of idiopathic pulmonary fibrosis (IPF) lungs, we aimed to elucidate whether hypoxia promotes mesenchymal transition of alveolar epithelial cell through activating HDACs.

Methods: To evaluate the effect of HDACs in alveolar EMT, we performed quantitative real-time PCR, Western blot analysis, immunocytochemistry using siRNA transfection in human and rat alveolar epithelial cells, and immunohistochemistry using a bleomycin-induced fibrosis mouse model.

Results: Hypoxia induced expression of alveolar EMT markers in A549 and RLE-6TN cells. Specifically, exposure to hypoxia decreased an epithelial marker, E-cadherin, and reversely increased expression of mesenchymal markers, Fibronectin and α -SMA in both cell lines. Additionally, a HDAC inhibitor, TSA was able to repress hypoxic effect such as loss of E-cadherin and gain of Fibronectin in alveolar epithelial cell (Fig A,B). Among HDAC family, inhibition of HDAC3 using siRNA increased E-cadherin, and decreased Fibronectin, Snail, α -SMA in hypoxic conditions, and this process is dependent on Akt pathway.

Conclusion: Histone deacetylase 3 induces mesenchymal transition of alveolar epithelial cell via repressing Akt pathway in hypoxic conditions.



AP510

CLINICAL SIGNIFICANCE OF FERRITIN LEVELS IN BRONCHOALVEOLAR LAVAGE FLUID FROM PATIENTS WITH ANTI-AMINOACYL-TRNA SYNTHETASE ANTIBODY-POSITIVE INTERSTITIAL LUNG DISEASE

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Background and Aims: Serum ferritin measurements are known as useful prognostic marker in rapidly progressive interstitial lung disease (ILD) with dermatomyositis; however, little is known about the ferritin levels in serum and bronchoalveolar lavage fluid (BALF) and their clinical significance from patients with anti-aminoacyl-tRNA synthetase antibody-positive ILD (ARS-ILD). The aim of this study was to examine the ferritin levels in serum and BALF in relation to clinical manifestations in patients with ARS-ILD.

Methods: This retrospective study included ARS-ILD patients admitted to our hospital from April 2005 to March 2018. The patients were divided into refractory group and non-refractory group. The refractory cases were defined as those who underwent recurrence or acute exacerbation under corticosteroid therapy. Serum and BALF ferritin concentrations were measured at the initial admission and were compared between two groups. We also examined the relationship between ferritin measurements and clinical manifestations or laboratory data which were obtained from medical records.

Results: A total of 29 patients with ARS-ILD were enrolled in this study. Sixteen out of 29 cases (55.1 %) were divided into refractory group. There was no significant difference in serum ferritin levels between two groups (median; refractory, 202 ng/mL, and non-refractory, 123.0 ng/mL; $P = 0.309$). The BALF ferritin levels in refractory group were significantly higher than those of non-refractory group (median: 154.7 ng/mL and 108 ng/mL, respectively; $P = 0.004$). The values of %DLco in refractory group were statistically lower than those of non-refractory group (median; 75.3% and 64.7%, respectively; $P = 0.023$). In the refractory group, the ferritin levels in BALF significantly correlated with PaO₂ ($r = -0.596$, $P = 0.049$) and %DLco ($r = -0.607$, $P = 0.036$), respectively.

Conclusion: We conclude that BALF ferritin levels could predict the therapeutic responsiveness in ARS-ILD. Moreover, BALF ferritin levels could reflect disease severity in refractory cases.

AP511

AN EXPERT QUESTIONNAIRE ANALYSIS FOR DEVELOPING IDIOPATHIC PULMONARY FIBROSIS PATIENT-REPORTED OUTCOME SCALE

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Background and Aims: Patient reported outcome (PRO) instrument is an important component of idiopathic pulmonary fibrosis (IPF) clinical effect evaluation. However, there lack IPF-PRO based on China's cultural background and elements at present. The Delphi method is to develop a consensus opinion on a specific subject within an expert group in a structured way and widely applied in developing the PRO. The goal for this study was screen good items for IPF-PRO by expert consultation.

Methods: Delphi method was applied to this research, a multidisciplinary panel of 20 experts including quality of life research, respiratory

medicine, psychometrics and statistician were invited to contribute to the Delphi survey by using the "Expert consultation questionnaire on IPF-PRO" (Internet version) formulated by the Item Management Team. The consultation questionnaire contains 5 domains 159 items, including 92 physical items, 17 psychological items, 11 environmental items, 25 social items and 14 satisfaction items. Detailed recommendations were developed to evaluate the importance, familiarity, judgment basis and influence of the items through the statistical analysis in positive degree, concentrative degree, coordination degree and authority degree of obtained data by using SPSS version 23.0.

Results: 15 valid questionnaires were recovered from A total of 20 expert questionnaires. The recovery rate was 75%, that is, the positive coefficient was 75%. The range of mean important scores was from 2.47 to 4.87, range of full mark ratio was from 7% to 87%, and range of rank sum was from 409 to 1782.5. The range of variation coefficient was from 0.07 to 0.85 and the coordination coefficient was 0.26 ($\chi^2 = 158$, $P < 0.05$). The authority coefficient was 0.903.

Conclusion: The positive degree and authority degree were both high. However, the concentrative degree and coordination degree remained to be improved, and some items should be optimized.

AP512

IDIOPATHIC PULMONARY FIBROSIS IS A POSSIBLE RISK FACTOR FOR OSTEOPOROSIS

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Background and Aims: Idiopathic pulmonary fibrosis (IPF) is a devastating chronic fibrosing lung disease of unknown aetiology with the mean survival time of 2–3 years from diagnosis. Because the use of anti-fibrotic drugs such as pirfenidone and nintedanib would prolong the survival of patients with IPF, comorbidities should be focused for the management. Some comorbidities such as lung cancer, coronary arterial diseases and gastro-oesophageal reflux have been recognized. Osteoporosis is now recognized to be a major comorbidity in COPD. However, it has not been clarified the clinical significance of osteoporosis in IPF. The goal of this study was to determine whether osteoporosis is one of the comorbidities in IPF.

Methods: Review patients with interstitial pneumonia admitted to our hospital, and retrospective analysis was performed. Bone mineral density was measured by a dual-energy X-ray absorptiometry scan of the lumbar spine and the thigh bone. Urinary N-telopeptide of type I collagen and deoxypyridinoline were also measured. Interstitial pneumonia was divided into three subtypes, IPF, non-IPF and interstitial pneumonia associated with connective tissue disease (IP-CTD).

Results: Among 151 patients with IIP, twelve (15%) and 30 (20%) patients had osteoporosis and decrease in bone mineral density, respectively. The prevalence of osteoporosis was not different among IPF, non-IPF and IP-CTD. A multivariate analysis revealed increase in age, female gender, increase in LDH, and IPF diagnosis as the risk factors for osteoporosis.

Conclusion: IPF is a possible risk factor for osteoporosis.

AP513

AN EXPERIENCE OF PULMONARY REHABILITATION IN A PATIENT WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA: A CASE REPORT

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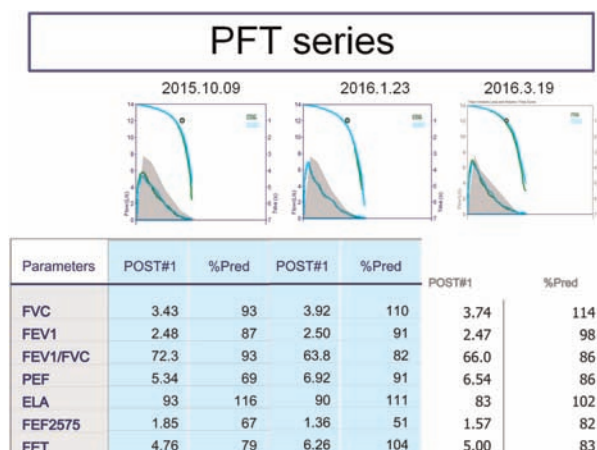
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Background and Aims: The term combined pulmonary fibrosis and emphysema (CPFE) was established in 2005. The common presentation of pulmonary fibrosis and emphysema was dyspnea. Pulmonary rehabilitation was certificated with efficacy in idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease, of which emphysema is part. Here, we propose a case of combined pulmonary fibrosis and emphysema, and pulmonary rehabilitation was performed meanwhile. To show the outcome after pulmonary rehabilitation.

Methods: We retrospectively recruited an 83-year-old patient who was diagnosed as combined pulmonary fibrosis and emphysema. The patient received weekly pulmonary rehabilitation and had regularly followed in outpatient department. We would show the patient's outcome with pulmonary rehabilitation.

Results: The patient subjectively had less sensation of dyspnea. Modified Medical Research Council (mMRC) dyspnea scale was around two to three. The level of FEV1 did not deteriorate very soon.

Conclusion: Pulmonary rehabilitation may be beneficial for the patient with combined pulmonary fibrosis and emphysema. More clinical study was needed to test the view of point.



AP514

ANALYSIS OF CLINICAL FEATURES AND COUGH CHARACTERISTICS OF PATIENTS WITH INTERSTITIAL LUNG DISEASE

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Background and Aims: Cough is normal feature in interstitial lung disease (ILD). Compared with non-UIP, patients with UIP are less likely to respond to treatments and have poorer outcomes. What is the relationship among cough, pathology and clinical features? Our study gave a preliminary analysis.

Methods: 107 ILD inpatients were enrolled in our hospital from October 2016 to October 2017, divided into UIP and non-UIP group

according to the results of lung biopsy and/or high resolution computed tomography. While all patients were also divided by cough frequency into group A (patients with frequent coughs) or group B (patients with infrequent coughs and no cough), and divided by visual analogue scale (VAS) score to either high-VAS-score group (at least 5 points) or low-VAS-score group (less than 5 points). their Basic characteristics, clinical symptoms, pulmonary function tests and serum indicators were compared between different groups. Patients were followed up in March 2018 according to worsening or death as the endpoint.

Results: Cough is very common in both UIP and non-UIP group (92% vs 81.7%). Single cough was more occurred in UIP patients than non-UIP patients ($P = 0.019$). No significant differences were observed for the course, time, character and day cough score, night cough score or VAS. Worsening was shown in 20 (55.56%) patients of group A and 11 (22.1%) patients of group B ($P < 0.01$). However, no significant differences were observed between high-VAS-score group and low-VAS-score group (9 vs 22, $P = 0.79$). Patients with frequent coughs have poorer exercise tolerance and significantly higher CA199 level and KL6 level and lower FVC% and TLC%, indicating the progression of ILD.

Conclusion: Frequent cough may be a clinical indicator of disease progression. It is crucial to shorten the assessment period and give active intervening measures.

AP515

ACUTE EXACERBATION OF PLEUROPARENCHYMAL FIBROELASTOSIS IN PATIENT STATUS POST HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE REPORT

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Background and Aims: Pleuroparenchymal fibroelastosis (PPFE) is a rare subtype of diffuse parenchymal lung disorder, which has been increasingly recognized. Recent studies imply its association with pre-existing medical conditions, including hematopoietic stem cell transplantation (HSCT). To date, detailed behaviour of the disease remains unclear.

Methods: We hereby report a case suspected to be compromised with fatal acute exacerbation of the disease. Autopsy study exhibited unique pathologic changes.

Results: A 58-year old man admitted to our facility with the complaint of acute worsening of dyspnea. His past medical history was remarkable with aplastic anaemia, which was successfully treated and induced complete remission for 10 years. At annual follow-ups, gradual progression of upper lobe-predominant subpleural thickening had been pointed out by chest X-rays. Lung function test also exhibited gradual decline in forced vital capacity.

At his presentation, physical exam was remarkable with extensive hypoxia with tachypnea and bilateral fine crackles. Radiologic studies revealed newly developed ground glass opacities on his bilateral lungs. The patient was empirically treated with broad-spectrum antibiotics, but his respiratory failure deteriorated. He was subsequently treated with steroid pulse therapy, which transiently improved his respiratory status and radiological findings. Gradual tapering of steroid induced recurrent exacerbation of the disease. In order to stabilize his condition, intravenous cyclophosphamide and tacrolimus were introduced, but his condition continued to deteriorate. The patient died at day 136 of admission. Post-mortem examination demonstrated subpleural fibrosis with massive elastin fibre deposition in lungs, which was consistent with pathologic pattern of PPFE. We also found that extensive exudates with enormous macrophage infiltration filled alveolar space in the non-fibrotic area, which we speculated to be the culprit of his acute respiratory decline.

Conclusion: We experienced a case of PPFE who developed fatal acute deterioration of the disease. Postmortem histologic exam suggested possible novel pathophysiology in acute exacerbation of the disease.

AP516

CLINICAL ANALYSIS OF 45 DIABETIC PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Background and Aims: To explore the clinical features, treatment and prognosis of diabetic patients with idiopathic pulmonary fibrosis (IPF).

Methods: Retrospective analysis the clinical data of 45 diabetic patients with IPF, to explore the characters of clinical manifestation, pulmonary function, chest radiology, laboratory examination and pathological examination and to summarize the prognosis.

Results: Patients showed progressive dyspnea and cough, and some (75.6%) had hypoxemia. The lung function of the patients present with the restricted ventilation 75.6% (34/45), diffuse function 64.4% (29/45) and small airway obstruction 60.0% (27/45). The lung CT of these patients showed lung multiple grid and strip shape. 22 routine bronchoscopic lung biopsy showed more neutrophils infiltrating in pathological examination. 40 patients received oral hypoglycaemic drugs or hypodermic injection of insulin to control blood sugar. Glucocorticoids were used in 36 patients. The 40 patients (88.9%) improved, and 5 patients (11.1%) died of respiratory failure.

Conclusion: For diabetic patients, lung function and chest radiography should be checked regularly to find IPF early. For diabetic patients with IPF, it is recommended that intravenous use or inhalation of small doses of glucocorticoid to improve prognosis on the basis of controlling blood sugar.

AP517

INTERVAL OF PREVIOUS X-RAY EXAMINATION IN ADVANCED LUNG CANCER WITH INTERSTITIAL PNEUMONIA

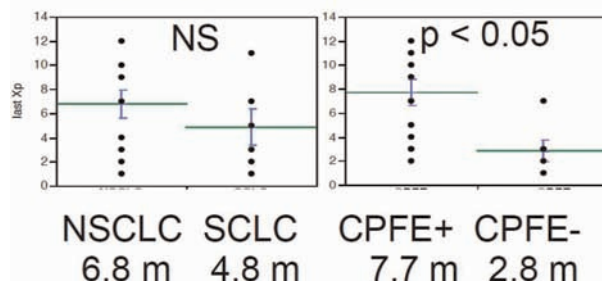
AYAKA ITO^{1*}, KONOMI KOBAYASHI¹, HIKARU TOYOTA¹, FUMINORI TOMYO¹, SHOKI MIYOSHI¹, YUTA KOIZUMI¹, MASAO YAMAGUCHI¹, NOBUHIKO SEKI¹, KEN OHTA², HIROYUKI NAGASE¹

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Background and Aims: Interstitial pneumonia (IP) is frequently complicated by lung cancer. Despite the regular chest X-ray follow up, lung cancer is often diagnosed at progressive stage in IP patients. We carried out this study to investigate the previous history of chest imaging in advanced lung cancer with IP patients and tried to identify the optimal interval of examination.

Methods: Four hundred and twenty-one patients were diagnosed with advanced lung cancer during 2012 to 2014 in Teikyo University Hospital. Among those patients, 22 patients with IP were eligible for current study (lung cancer stage III: $n = 7$, IV: $n = 15$) and we retrospectively investigated the previous chest X-ray histories. Patients without previous imaging history were excluded.

Duration between last X-ray and lung cancer diagnosis



Results: Median duration from last chest-X ray examination to diagnosis of lung cancer was 7 months (3 months in stage III ($n = 7$), 10 m in stage IV). Although the median duration in NSCLC group was 6.8 m, the duration tended to be shorter in SCLC group (4.8 m). The median duration in non-CPFE group was significantly shorter than CPFE group (2.8 vs 7.7 m). In half of cases, tumor shadow could not be identified in last chest X-ray examination.

Conclusion: This study suggests that chest imaging for IP patients should be performed in at least 4 to 6 months interval to detect lung cancer in early stage.

AP518

THE EXPRESSION AND SIGNIFICANCE OF P-ERK1/2, FGF2, FGFR2 IN IDIOPATHIC PULMONARY FIBROSIS AND NON-SMALL CELL LUNG CANCER

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Background and Aims: The IPF and NSCLC have an obvious correlation in gene mutation, epigenetics and the of activation specific signalling pathways. The tyrosine kinase pathway which is the important signalling pathway is strongly activated not only in many cancers but also in IPF. The pathway once activated will regulate many important physiological processes, which are associated with the initiation or progression of cancer. In this study, we focused our research on the expression of FGF2/FGFR2, and the downstream ERK1/2/p-ERK1/2 in NSCLC patients, IPF patients and other non-malignant diseases patients to verify the common pathogenesis between the IPF and NSCLC.

Methods: Quantitative reverse transcription-polymerase chain reaction (RT-q PCR) and western blot were used to detect the expression of FGF2, FGFR2, ERK1/2 and p-ERK1/2 in carcinoma tissue and para-carcinoma tissue in NSCLC patients, bronchoalveolar lavage fluid in the IPF patients and the normal control group. The normal control group refers to the patients with the main symptom of cough and confirmed healthy by the bronchoalveolar lavage.

Results: Compared with the para-carcinoma tissue, the ERK1/2 mRNA expression is significantly increased ($P < 0.001$) in lung carcinoma tissue. Compared with the para-carcinoma tissue, the p-ERK1/2 protein expression in lung carcinoma tissue is significantly increased ($P < 0.001$).

Compared with the para-carcinoma tissue, the FGF2 mRNA and protein expression in lung carcinoma tissue are significantly increased ($P < 0.001$). Compared with the control group, the FGF2 protein expression in IPF patients' bronchoalveolar lavage fluid is increased ($P = 0.010$).

Compared with the para-carcinoma tissue, the FGFR2b mRNA is significantly decreased ($P < 0.001$) and the FGFR2c mRNA and protein

expression is significantly increased ($P < 0.001$) in lung carcinoma tissue. Compared with the control group, the expression of FGFR2 protein in IPF-patients' bronchoalveolar lavage fluid is increased ($P = 0.027$).

Conclusion: The expression of p-ERK1/2, FGF2 and FGFR2 protein in NSCLC patients and IPF patients is increased than the control group. The increased expression of FGF2/FGFR2/p-ERK1/2 suggests that the signalling pathway may contribute to the pathogenesis of lung fibrosis in IPF patients and tumorigenesis in NSCLC patients.

AP519

HUMIDIFIER LUNG: CHARACTERIZATION OF FEATURES AND COMPARISON TO OTHER HYPERSENSITIVITY PNEUMONITIS PHENOTYPES

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Background and Aims: Humidifier lung (HL) is a relatively rare form of hypersensitivity pneumonitis (HPs) associated with the inhalation of moisture from humidifiers contaminated by various organisms. Because many of the past studies were case reports, clinical characteristics of HL have not been well described. The aim of this study is to characterize HL and compare this phenotype with other forms of HPs.

Methods: We collected the clinical data of patients with any form of HPs, from April 1990 to March 2018, via chart review. Additionally, published case reports of HL were identified via PubMed and Ichushi-Web searches and included in the analysis. The clinical characteristics of HL were compared with the other forms of HPs, including summer-type HPs, bird fancier's lung, farmer's lung, and various exposures to fungi.

Results: A total of 42 patients with HL (10 cases from the chart review and 32 from the published case reports) and 48 patients with other forms of HPs were analyzed. In the HL group, the patients were more likely to have fever compared to other HPs patients (90.4% vs 45.8%, $P < 0.001$). There was also a significant increase in WBC count (HL vs other HPs; median 13,780/uL vs 8,755/uL, $P < 0.001$) and C-reactive protein (median 5.30 mg/dl vs 1.51 mg/dL, $P < 0.001$) in the HL patients. Conversely, the serum KL-6 level was significantly lower in HL patients than in patients with other HPs (median 543 U/mL vs 1,827 U/mL, $P < 0.001$). The ratio of CD4+ to CD8 cells of bronchoalveolar lavage fluid in HL patients was within the normal range but was higher than that of patients with other HPs (median 1.5 vs 0.3, $P < 0.001$).

Conclusion: These data indicate that the mechanisms of HL may differ from the other forms of HPs. These findings could help to differentiate HL among HPs cases.

A RARE CASE OF SARCOIDOSIS-TUBERCULOSIS MASQUERADING AS MALIGNANCY WITH GALAXY SIGN AND HYPERCALCAEMIA

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Background and Aims: Incidence of tuberculosis is increasing in our region. Sarcoidosis on the other hand is a rare but there is an increase report of cases of sarcoidosis in our region. Both diseases share remarkable similarities in their clinical and radiological presentations but has different treatment strategies. To make matter more complicated, both sarcoidosis and tuberculosis can exist in the same patient and the exact incidence of tuberculosis-sarcoidosis is unknown.

Methods: We present a rare case of a 73-year-old Chinese gentleman who was diagnosis with sarcoidosis and tuberculosis.

Results: This patient is an ex-smoker with underlying chronic kidney disease, type 2 diabetes mellitus, hypertension and dyslipidaemia. He presented with facial numbness and was noted to have hypercalcaemia (corrected Calcium 3.07 mmol/L) with suppressed iPTH. His erythrocyte sedimentation rate was >120 mm/h. There were no respiratory or constitutional symptoms. Chest radiograph showed right upper lobe mass. CT done showed multiple irregular lung nodules of varying sizes, with presence of mediastinal, hilar and abdominal lymph nodes. Endobronchial ultrasound showed a large lymph node at station 4R but did not yield any cytology. Subsequently a CT guided biopsy revealed non-necrotizing granulomatous inflammation. The case was discussed in MDT meeting and the diagnosis of sarcoidosis was made based on hypercalcaemia, histopathology of non-necrotizing granuloma and presence of galaxy sign on CT scan. Patient was started on Prednisolone 20 mg OD. His corrected calcium was 3.45 mmol/L then. However, 2 weeks later, he presented with confusion and recurrent fall with corrected calcium was 3.12 mmol/L. Sputum acid fast bacilli was positive and he was subsequently started on Akurit-4 on top of the prednisolone.

Conclusion: This case illustrates a rare case of tuberculosis-sarcoidosis coexistence masquerading as lung malignancy with rare presentation of hypercalcaemia and galaxy sign on CT scan.

AP521

COMBINED MARKER ASSAY, NOT THE VALUE OF A SINGLE KL-6 IN EARLY DIAGNOSIS OF IPF

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Background and Aims: explore the clinical value of serum markers in the early diagnosis of pulmonary fibrosis by analyzing the clinical data and the level of serum markers in patients with pulmonary fibrosis.

Combined Marker Assay, Not the Value of a Single KL-6 in Early

Diagnosis of IPF

Abstract: Objective: To explore the clinical value of serum markers in the early diagnosis of pulmonary fibrosis by analyzing the clinical data and the level of serum markers in patients with pulmonary fibrosis. **Methods:** From June 2015 to June 2017, 20 patients with idiopathic pulmonary fibrosis were identified in the Department of Respiratory and Internal Medicine, the Second Hospital of Jilin University, 10 in the healthy control group, 6 in the bronchial asthma group, and chronic obstructive pulmonary disease. 6 cases of the disease group, the clinical data of the above groups were retrospectively analyzed. Serum 5ml of fasting venous blood was collected from the above groups of patients and the serum was separated. The expression of CXCL-13, VEGF, CCL-18, EGF, SP-A, SP-D and KL-6 in serum was detected by ELISA. The differences of serum markers in each group were analyzed, and the sensitivity and specificity of each serum markers were compared. **Results:** Compared with the healthy control group, the levels of serum KL-6, SP-A, SP-D, EGF, VEGF, CCL18, and CXCL13 in the IPF group were significantly higher than those in the healthy control group. Compared with the IPF group, there were differences in the expression levels of serum markers in the Asthma group, the COPD group, and the remaining serum markers were lower than the IPF group except CCL18. According to the ROC curve, the sensitivity of EGF>CXCL-13>KL-6>SP-D>SP-A>VEGF>CCL18 was evaluated in each of the biological parameters of IPF patients. The AUC value of the combined index was significantly greater than the AUC value of a single serum marker. When the seven markers were combined, the AUC value measured was largest, and the AUC value between the combined marker and each single marker was statistically significant ($P < 0.05$). **Conclusions:** the 7 serum markers are of certain significance for the early diagnosis of IPF. The combined serum markers are more sensitive and specific than the single markers for the diagnosis of IPF, and have higher cost benefit for the management of IPF patients.

Key words: idiopathic pulmonary fibrosis, serum markers, combination, diagnosis.

Methods: 20 patients with idiopathic pulmonary fibrosis were identified in the Department of Respiratory and Internal Medicine, the Second Hospital of Jilin University, 10 in the healthy control group, 6 in the bronchial asthma group, and chronic obstructive pulmonary disease. 6 cases of the disease group, the clinical data of the above groups were retrospectively analyzed. Serum 5 mL of fasting venous blood was collected from the above groups of patients and the serum was separated. The expression of CXCL-13, VEGF, CCL-18, EGF, SP-A, SP-D and KL-6 in serum was detected by ELISA. The differences of serum markers in each group were analyzed, and the sensitivity and specificity of each serum markers were compared.

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When the seven markers were combined, the AUC value measured was largest, and the AUC value between the combined marker and each single marker was statistically significant.

Conclusion: the 7 serum markers are of certain significance for the early diagnosis of IPF. The combined serum markers are more sensitive and specific than the single markers for the diagnosis of IPF, and have higher cost benefit for the management of IPF patients.

AP522

DRUG-INDUCED LUNG INJURY DUE TO BEPRIDIL WITH POSITIVE DLST AFTER SPONTANEOUS IMPROVEMENT IN CLINICAL FEATURES

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Background and Aims: Bepridil is an antiarrhythmic drug with few reports of drug-induced lung injury.

Methods: We report the case of a 73-year-old woman who had commenced treatment with oral bepridil 4 months earlier and subsequently developed cough and difficulty in breathing more than 1 month prior to presentation.

Results: Initial evaluation at our department revealed infiltrative shadows in both lung fields on chest-computed tomography. Serum KL-6 levels were 10,570 U/mL. A drug-induced lymphocyte stimulation test (DLST) was negative. Bronchoscopy and bronchoalveolar lavage fluid analysis revealed 41% lymphocyte cell subpopulations. Based on a high index of suspicion of drug-induced lung injury due to bepridil oral administration was stopped immediately, resulting in spontaneous resolution of symptoms. A repeat DLST performed 1 year after drug discontinuation was positive.

Conclusion: We report this as a rare case of spontaneous resolution of symptoms in which DLST became positive after discontinuation of the drug.

Lung Cancer 2

AP523

THERAPEUTIC OUTCOMES IN PATIENTS WITH CT1MI-CN0M0 LUNG CANCER DOMINANT WITH GROUND GLASS OPACITY TREATED BY CARBON ION RADIOTHERAPY

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Background and Aims: Carbon ion radiotherapy (CIRT) has been expected to be an alternative for surgery for early-stage non-small-cell lung cancer (NSCLC) and adopted as the second-best choice even in operable patients. Recently, NSCLC with ground glass opacity (GGO) dominant image has been reported as a less invasive. The purpose of this study was to investigate the demographic data, perioperative courses and therapeutic outcomes of patients who underwent CIRT for patients with early-stage NSCLC showing GGO dominant shadow.

Methods: From November 1994 to February 2012, CIRT was applied for 602 c-T1/T2/T3N0M0 NSCLC lesions of 599 patients at the National Institute of Radiological Science. A total of 14 (2.3%) patients suffered NSCLC with GGO dominant image. The medical records were retrospectively reviewed.

Results: There were 13 men and 1 women, whose mean age was 75 (60–85) years old at the time of hospitalization for CIRT. The average major axis of the tumor was 25 (16–44) mm; on the other hand, the mean solid part was 4.7 (0–22) mm. All the tumours were pathologically diagnosed as adenocarcinoma. The clinical stages before CIRT with NSCLC were as follows: 2 TisN0M0, 6 TmiN0M0, 5 T1aN0M0 and 1 T1cN0M0. Three of the 14 patients were inoperable because of poor respiratory function ($n = 2$) or chronic heart failure ($n = 1$), or the other patients were operable, but refused surgery and selected CIRT. The average CIRT

dose was 43 (32–48) Gray equivalents (GyE) and no severe complication (>grade II) was recorded. After the median follow-up period after CIRT was 77 months (range, 29–130 months), the Kaplan-Meier estimate of overall survival or disease-specific survival after the CIRT showed that the 5-year survival rate was 78.6% or 92.9%, respectively.

Conclusion: Our data demonstrated that CIRT was effective and feasible in treating patients with early-stage NSCLC showing GGO dominant shadow.

AP524

THE ROLE OF PATIENT'S SELF-REPORTED HEALTH-RELATED QUALITY OF LIFE AS A PREDICTOR OF OVERALL SURVIVAL IN ADVANCED NON-SMALL CELL LUNG CANCER WITH AGE OVER 75

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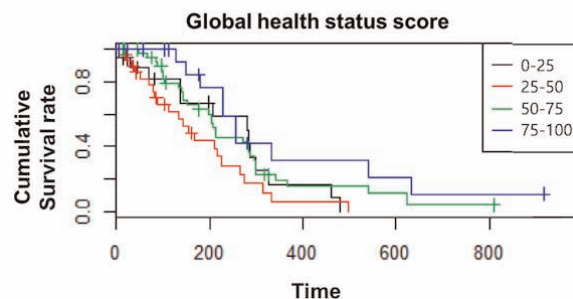
Background and Aims: To study the prognostic value for overall survival (OS) of the self-reported health-related quality of life (HRQOL) at diagnosis in very elderly patients with advanced non-small-cell lung cancer (NSCLC).

Methods: From 2014 to 2017, we retrospectively reviewed the prospective lung cancer database of 8 Hospitals of the college of medicine, the Catholic University of Korea. We included 112 patients aged ≥ 75 with advanced NSCLC and evaluated quality of life by using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 at diagnosis to investigate the prognostic value of HRQOL for OS. Also, the presence of comorbidity was assessed and summarized using the Charlson comorbidity index. The Cox proportional hazards modelling was used for analysis of survival. Statistical analysis was performed with SPSS version 25 and survival package of R version 3.3.3

Results: The final multivariate Cox regression model retained nine parameters as independent prognostic factors for survival. In HRQOL, global health status score (25–50 to 75–100) with a hazard ratio (HR) = 2.085 (95% $P = 0.0257$); role function (50–100 to 0–50) with HR 0.203 (95% $P = 0.0004$); cognitive function (0–50 to 50–100) with HR 10.139 (95% $P = 0.0003$). In clinical parameters, CCI (3 to 1) with HR 0.163 (95% $P = 0.0053$); male gender with HR 2.089 (95% $P = 0.0701$); Age (85 < to ≤ 85) with HR 6.384 (95% $P = 0.0001$); chemotherapy group with HR 0.2465 to palliative group (95% $P < 0.0000$); stage (4 to 3) with HR 2.465 (95% $P = 0.0098$). And in pathology, squamous cell carcinoma with HR 0.179 (95% $P = 0.0202$) and adenocarcinoma with HR 0.077 (95% $P = 0.0011$) to other pathologies.

Conclusion: The results suggest that patients' self-reported HRQOL at diagnosis provide independent prognostic information for survival in very elderly patients with advanced non-small-cell lung cancer. This findings support that the collection of HRQOL is important in clinical practice with very old age patients.

Covariates		β	exp(β)	p-value
Pathology	Other	0	1	-
	Adenoca	-2.564	0.077	0.0011
	Sqca	-1.719	0.179	0.0202
Stage	3	0	1	-
	4	0.902	2.465	0.0098
Chemotherapy	No	0	1	-
	Yes	-1.585	0.205	0.0000
CCI	0	0	1	-
	3	-1.813	0.163	0.0053
Age	75-85	0	1	-
	>85	1.854	6.384	0.0001
Sex	Female	0	1	-
	Male	0.737	2.089	0.0701
Role function	0-50	0	1	-
	50-100	-1.595	0.203	0.0004
Cognitive function	0-50	0	1	-
	50-100	2.316	10.139	0.0003
Global health status	75-100	0	1	-
	25-50	0.735	2.085	0.0257



AP526

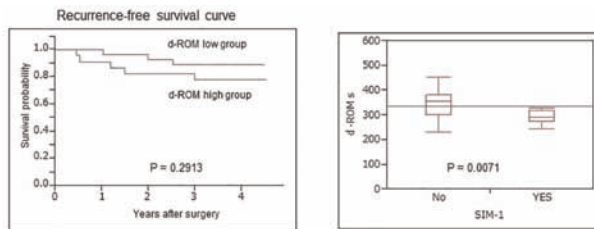
CLINICAL CORRELATION BETWEEN PREOPERATIVE SERUM OXIDATIVE STRESS LEVEL AND ABERRANT DNA METHYLATION IN PERIPHERAL BLOOD OF PATIENTS WITH STAGE I LUNG ADENOCARCINOMA; A PILOT ANALYSIS

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Background and Aims: Although the underlying specific mechanism still needs to be elucidated, reactive oxygen species have considerable effect on various features of malignant tumours. Hence, serum oxidative stress level has been recognized as a significant risk factor for poor clinical outcome. Because epigenetic gene silencing through DNA methylation has a significant role in progression of diverse human cancers, the aim of this study was to investigate whether serum oxidative stress level is associated with DNA methylation profile in preoperatively collected peripheral whole blood samples from patients with curatively resected node-negative lung adenocarcinoma.

Methods: Forty-five patients who had been subjected to curative resection for pathological Stage I lung adenocarcinoma were enrolled in this study. Serum reactive oxygen metabolite (ROM) levels were measured. Methylation-specific PCR analysis was performed to determine the DNA methylation status of 12 genes (*RARB*, *MDF1*, *HOXD11*, *SIM-1*, *PCDH10*, *GDNF*, *Rec8p*, *HS3ST2*, *DCC*, *miRNA137*, *KLK10*, *TIMP3*) in peripheral whole blood samples collected preoperatively. The clinical relevance of the methylation profile and serum ROM level to the outcome of the disease was evaluated.



Results: Patients with high serum ROM level showed poorer recurrence-free survival and overall survival than patients with low serum ROM level (log rank test; $P = 0.2913$ and $P = 0.1016$). DNA methylation profiling revealed that serum ROM level was significantly associated with aberrant *SIM-1* methylation ($P = 0.0355$). The average levels of serum ROM were $306. \pm 4.7$ in patients with methylated *SIM-1* ($n = 17$) and 348 ± 3.9 in patients without *SIM-1* methylation ($n = 33$) ($P = 0.0071$).

Conclusion: Although further investigation using larger sample size is required, the results of this study indicate that inducing epigenetic gene silencing through DNA methylation in specific genes may be one of the underlying mechanisms by which reactive oxygen species are implicated in various features of malignant tumours.

AP527

A STUDY OF CASES WITH POSTOPERATIVE RECURRENT LUNG CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Background and Aims: The development of cancer immunotherapy in recent years has been remarkable, and many studies have been published on clinical effects of immune checkpoint inhibitors. These drugs are also effective in advanced or recurrent non-small cell lung cancer (NSCLC) resistant to cytotoxic anticancer drugs or molecular-targeted drugs and are excellent treatment options that can prolong overall survival of patients. However, to date, few studies have specifically examined treatment outcomes of immune checkpoint inhibitors in recurrent NSCLC.

Methods: We retrospectively reviewed 18 cases with postoperative recurrent NSCLC treated with immune checkpoint inhibitors in our hospital.

Results: The 18 cases comprised 14 males and 4 females with a median age of 71 years [range, 65–75 years]. The histological type of cancer was squamous cell carcinoma in 7 cases and adenocarcinoma in 11. Those with adenocarcinoma included 1 EGFR-mutation-positive case and 1 case with ROS1 translocation. The treatment drug used was pembrolizumab in 1 case and nivolumab in 1 case. The treatment was administered as first-line therapy in 1 case, second-line therapy in 10 cases, third-line or later therapy in 7 cases. Best overall response was CR in 2 cases, PR in 4 cases, SD in 8 cases, and unevaluable in 1 case, with a response rate of 33% and a disease control rate of 50%. Adverse events were interstitial pneumonia in 2 cases, colitis in 1 case, sarcoidosis in 1 case, skin rash in 1 case, and eosinophilic fasciitis in 1 case.

Conclusion: Although the sample size in this study was small, the response rate and the disease control rate were 30% and 50%, respectively, which were superior to those reported by past studies. We intend to further investigate in a larger sample size the treatment effects and safety of immune checkpoint inhibitors in actual clinical settings along with a statistical analysis.

GENETIC VARIANTS IN THE TNF/TNFR SIGNALING PATHWAY GENES ARE ASSOCIATED WITH SURVIVAL OF NONSMALL-CELL LUNG CANCER PATIENTS

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Background and Aims: Genetic variants in biological pathways are likely to influence survival of non-small cell lung cancer (NSCLC) patients. We hypothesized that single nucleotide polymorphisms (SNPs) in the TNF/TNFR pathway genes related to apoptosis are associated with NSCLC survival.

Methods: Study populations included 1,185 NSCLC patients in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial and 984 NSCLC patients in the Harvard Lung Cancer Study (HLCS) as the discovery and validation datasets, respectively. We selected 6788 SNPs in 71 genes in the TNF/TNFR signalling pathway and extracted genotyping data from the PLCO genome-wide association study (GWAS) dataset. We performed Cox proportional hazards regression analysis to evaluate associations between the identified SNPs and survival and validated the significant SNPs, which were further analyzed for their functional relevance.

Results: Thirty-three SNPs in the PLCO dataset were found to be statistically significant in the single-locus analysis, of which rs4978754 IKBKAP CT+TT and TNFRSF1B rs677844 TC+CC genotypes of two validated SNPs (rs4978754 C>T and rs677844 T>C, respectively) predicted a better overall survival (OS) ($P = 0.004$ and 0.002 , respectively). The number of their combined genotypes predicted a better OS in a genotype dose-response manner ($P < 0.001$) in a multivariable Cox model. The meta-analysis of these two validated SNPs showed a favourable overall survival associated with the rs677844 C and rs4978754 T alleles ($P < 0.05$). These two validated SNPs were predicted by the RegulomeDB score to be potentially functional. IKBKAP mRNA expression levels were significantly higher in lung cancer tissues than in normal tissues ($P < 0.001$), while TNFRSF1B mRNA expression levels were significantly lower in lung cancer tissues than in normal tissues ($P < 0.001$).

Conclusion: In a pathway-based analysis of genetic variants in PLCO and Harvard GWAS datasets, we identified TNFRSF1B rs677844 T>C and IKBKAP rs4978754 C>T to be associated with survival in NSCLC patients.

AP529

IMPROVED TREATMENT OUTCOME OF PEMBROLIZUMAB IN NSCLC PATIENTS WITH COPD

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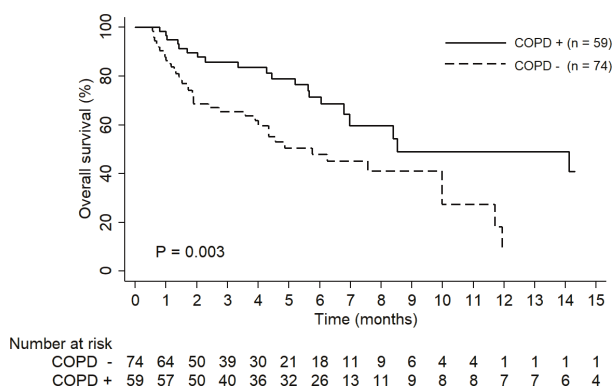
Background and Aims: Chronic obstructive pulmonary disease (COPD) is well-established risk factor of developing and dying from non-small cell lung cancer (NSCLC). Recent studies with small number of patients reported increased progression-free survival (PFS) in immune checkpoint inhibitors (ICIs)-treated NSCLC patients with COPD. This study aimed to confirm the association between the presence of COPD and enhanced treatment response of ICI therapy with large number of NSCLC patients.

Methods: Among advanced-stage NSCLC patients who received palliative pembrolizumab between July 2014 and January 2018 at Samsung

Medical Center, 133 patients with spirometry test results within 3 years were retrospectively identified. COPD were defined as pre-bronchodilator FEV1/FVC less than 0.7, and overall survival (OS) and PFS were analyzed according to the presence of COPD. Objective response rate was also compared between patients with or without COPD.

Results: Spirometry-based COPD were present in 59 (44%) patients. Compared with non-COPD, those with COPD were older, more likely to be male, former or current smokers, had relatively higher prevalence of squamous cell carcinoma, and less lines of previous chemotherapy. COPD patients had better OS (hazard ratio [HR] for death, 0.45; 95% confidence interval [CI], 0.26–0.78; $P = 0.004$) and PFS (HR for disease progression or death, 0.51; 95% CI, 0.32–0.81; $P = 0.004$) than those without COPD. These associations persisted after adjusting for potential confounders including smoking history. The response rate was higher in patients with COPD than in those without COPD (38.2% vs 20.5%, $P = 0.028$).

Conclusion: In NSCLC patients treated with palliative pembrolizumab, spirometry-based COPD was associated with significantly longer OS and PFS. Identifying coexisting COPD could help predict better treatment outcome in NSCLC patients treated with ICIs.



AP530

ONCOGENIC AND IMMUNE PATHWAYS CORRELATED WITH MOLECULAR PROGNOSTIC MARKER SIALYLTRANSFERASE ST3GAL3 IN NON-SMALL CELL LUNG CANCER

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Background and Aims: Aberrant O-glycosylation represents a common feature during oncogenesis in various tumor types. Our previous high throughput RNA-seq analysis revealed that low expression of ST3GAL3 (ST3 β -Galactoside α -2,3-Sialyltransferase 3), an O-glycan related terminal sialyltransferase, was an independent prognostic marker for poor overall survival. Therefore, we conducted a pathway analysis to further elucidate the underlying molecular mechanism of ST3GAL3 expression in lung cancer cells.

Methods: Eighty-one (adenocarcinoma $n = 44$, squamous cell carcinoma $n = 37$) archived non-small cell lung cancer (NSCLC) surgical samples from 1996 to 2008 underwent genome-wide RNA-seq analysis. We conducted Gene Set Enrichment Analysis (GSEA) by comparing patients

with ST3GAL3 low expression to those with high expression. Curated pathways including Reactome and Oncogenic pathways from MsigDB were examined for enrichment. Pathways were considered positively enriched by the criteria of nominal $P < 0.05$ and false discovery rate $q < 0.25$. To validate the results, we validated the pathway analysis in two independent NSCLC cohorts from public databases (TCGA-LUAD/LUSC from the United States and GSE81089 from Europe).

Results: Reactome pathway analysis revealed gene sets involved in immune system interaction, cell surface interaction, and Semaphorin4D among lung cancer samples with ST3GAL3 low expression. Oncogenic pathways related to EGFR, ERB2, KRAS, RAF, MEK and TP53 mutation were enriched in samples with ST3GAL3 low expression. Validation was done in TCGA-LUAD/LUSC ($n = 1019$) and GSE81089 ($n = 199$). Immune system interaction and Toll-like receptor pathways were enriched in TCGA and GSE81089 cohorts. KRAS pathway enrichment was seen in both validation cohorts. EGFR, RAF, MEK and TP53 mutation-related pathways were also enriched in TCGA cohort.

Conclusion: We have identified interrelated cellular/immune interaction and oncogenic pathways with regard to ST3GAL3 low expression. Alterations in sialylation of receptors in these pathways may contribute to altered cancer cell behaviours. This provides further mechanistic targets for validation on the role of ST3GAL3 in prognostic and possibly therapeutic applications in NSCLC.

AP531

THE EFFECT OF EGFR MUTATION TO METASTASIS IN STAGE III-IVB LUNG ADENOCARCINOMA

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Background and Aims: Lung cancer considered as leading cause of cancer related death all over the world. Epidermal Growth Factor Receptor (EGFR) mutation in lung adenocarcinoma influenced treatment options and prognosis. Metastasis in lung adenocarcinoma generally worsen the prognosis and patient's survival rates. This research aim to determine the effect of EGFR mutation to metastasis in lung adenocarcinoma patients.

Methods: Samples are stage IIIB-IV lung adenocarcinoma patients between January 2017 – February 2018 in Dr. Sardjito Hospital Yogyakarta. The patient then divided into EGFR mutation group and wild type group. The effect of EGFR mutation to metastasis will be determined retrospectively by Fisher's Exact Test, and odds ratio. The relation of demographical and clinical status to EGFR mutation will be determined by Logistic regression analysis. Then P value < 0.05 with confidence interval 95% considered as significant.

Results: Total of 71 lung adenocarcinoma patients consist of 26 (36.6%) patients with EGFR mutation (Exon 19, 20, and 21) and 45 (63.4%) wild type. The EGFR mutation frequency significantly higher in patients with 2 or more metastasis sites (50% vs 26.6%; $P = 0.047$, OR = 2.75). Further analysis to specific metastasis location showed that brain metastasis (11.53% vs 6.66%; OR = 1.82) and bone metastasis (30.76% vs 13.33%; OR = 2.88) are more frequent in EGFR mutation group than wild type group. Logistic regression analysis of EGFR mutation status to age, sex, performance score, and stage did not show any significance.

Conclusion: This research show significance relation between EGFR mutation to the sum of metastasis sites in stage IIIB - IV lung adenocarcinoma independent to age, sex, performance status and cancer stage. EGFR mutation could be a predictive factor of brain and bone metastasis in stage IIIB-IV lung adenocarcinoma patients.

AP532

FIRST GENERATION EGFR-TKIS COMPARISON IN NON-SMALL CELL LUNG CANCER PATIENTS HARBOURING SENSITIVE EGFR MUTATIONS

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Background and Aims: Lung cancer is the leading cause of mortality in all patients with cancer. The standard first line treatment of lung adenocarcinoma harbouring sensitive epidermal growth factor receptor (EGFR) mutation is EGFR-tyrosine kinase inhibitors (TKIs). Several studies compared treatment response rate, survival, and side effect among different EGFR-TKIs and the results showed gefitinib was the least effective one among EGFR-TKIs. However, in our practice, the response rate between gefitinib and erlotinib was similar. Thus, we conduct this study for clarified this issue.

Methods: This is a retrospective cohort study of non-small lung cancer (NSCLC) patients harbouring sensitive EGFR mutation receiving 1st line EGFR-TKIs in National Taiwan University Hospital Hsinchu branch from January 1, 2010 to Dec 31, 2015. Clinical response and survival after receiving first line erlotinib or gefitinib were compared using logistic and Cox regression analyses, respectively.

Results: There were 175 patients enrolled, including 140 (80%) patients received gefitinib, and 35 (20%) patients received erlotinib. Erlotinib group were more likely to be non-adenocarcinoma cell type, and chronic kidney disease. In survival analysis, patients receiving erlotinib or gefitinib were associated with similar progression free survival (PFS) (9.5 vs 9.7 months; HR, 1.14; 95% CI, 0.75 to 1.75) and overall survival (OS) (16.8 vs 18.9 months; HR, 1.26; 95% CI, 0.78 to 2.04). However, in patient with L858R mutation, lower PFS in erlotinib compared with gefitinib (9.2 vs 6.0 months; HR, 2.43; 95% CI, 1.27 to 4.66), and OS (17.7 vs 13.2 months; HR, 3.75; 95% CI, 1.84 to 7.66) were found.

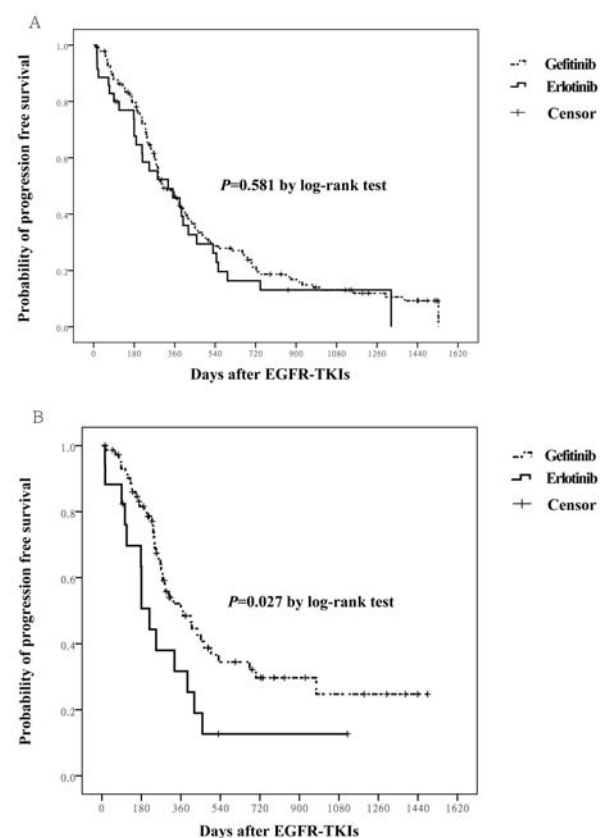
Conclusion: In NSCLC patients harbouring sensitive EGFR mutation, first line erlotinib and gefitinib showed similar clinical response. However, in L858R subgroup, gefitinib seems more effective than erlotinib. Further large scale randomized controlled trials are necessary for confirming the result.

Impact of Erlotinib vs. Gefitinib on Progression Free Survival and Overall Survival in Different EGFR mutation and adenocarcinoma by Multivariate Cox Proportional Hazards Regression Analysis

Erlotinib Versus Gefitinib	Progression Free Survival			Overall Survival		
	HR	95% CI	p value	HR	95% CI	p value
Whole cohort (n = 175)	1.14	0.75-1.75	0.522	1.26	0.78-2.04	0.352
L858R (n = 91)	2.43	1.27-4.66	0.007	3.75	1.84-7.66	<0.001
Exon 19 deletion (n = 76)	0.72	0.36-1.44	0.357	0.42	0.15-1.13	0.086
Adenocarcinoma (n = 159)	1.64	1.03-2.63	0.038	1.33	0.79-2.23	0.279

Multivariate Cox regression adjusted for sex, age, comorbidities (chronic obstructive pulmonary disease, diabetic mellitus, chronic kidney disease, tuberculosis, liver cirrhosis, hypertension, coronary artery disease, cerebral vascular disease, and other malignancy). Abbreviations: EGFR, epidermal growth factor receptor

Kaplan-Meier curves for (A) progression free survival in erlotinib versus gefitinib and (B) progression free survival in erlotinib versus gefitinib in L858R subgroup.



AP533

PEMBROLIZUMAB AS THE FIRST THERAPY FOR SYNCHRONOUS DOUBLE CANCER OF LUNG CANCER AND GASTRIC CANCER. A CASE REPORT

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Background and Aims: Immunocheckpoint inhibitors (ICI) are effective for several malignant tumor including lung cancer. A few cases are reported that ICI are effective to multiple primary cancer, and to our knowledge, an efficacy of pembrolizumab as the first therapy to synchronous double cancer of lung cancer and gastric cancer had not been reported.

Methods: A 69-year-old man was presented to our hospital because of a cough lasting 3 months in March 2017. He had a smoking history of 80 pack years. Chest CT showed tumor in the right upper lobe and mediastinal lymph node enlargement with superior vena cava invasion,

abdominal CT showed gastric wall thickening and multiple small lymph nodes enlargement around the stomach. Lung tumor was diagnosed as adenocarcinoma, cT4N2M1a (PLE), EGFR negative, ALK negative, PD-L1 (TPS) 90%. Gastrointestinal endoscopy revealed advanced gastric cancer with multiple ulcers, which TPS was negative. Surgical treatment was not selected for gastric cancer because of high risk of anaesthesia, chemotherapy for both of lung cancer and gastric cancer was preceded. Pembrolizumab was administered as the first line therapy in April 2017. After administration, the lung tumor was reduced, and the lesions of gastric cancer are also stable without exacerbation or bleeding. The patient has continued pembrolizumab for 1 year and 2 months without disease progression.

Results: In present case, pembrolizumab are effective to both of lung cancer and gastric cancer. It is believed that environmental factors such as smoking are cause of multiple cancers and related to high numbers of mutation of tumor genome. As smoking is one of the prognosis factor of anti-PD-1 therapy, the present case might demonstrate an effectiveness of pembrolizumab even for gastric cancer though its TPS is negative.

Conclusion: ICI such as pembrolizumab might be effective in synchronous multiple cancers, especially in smoking patients.

AP534

PREVENTING AND TREATING BRAIN METASTASES WITH THREE FIRST-LINE EGFR-TYROSINE KINASE INHIBITORS IN PATIENTS WITH EGFR MUTATION-POSITIVE ADVANCED NON-SMALL CELL LUNG CANCER

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Background and Aims: Brain metastases (BM) are common in advanced non-small cell lung cancer (NSCLC), and the prognosis is poor with few therapeutic options. This study evaluated the efficacy of three epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) in preventing and treating BM in patients with EGFR mutation-positive advanced NSCLC.

Methods: Patients with EGFR mutation-positive advanced NSCLC who visited a tertiary referral center from December 1, 2013, to November 30, 2017, were analyzed retrospectively. They received gefitinib, erlotinib, or afatinib until disease progression, death, or intolerable adverse events. The cumulative incidence of subsequent BM of initial non-BM patients, progression-free survival (PFS), and overall survival (OS) of the BM and non-BM patients were estimated and compared using the Kaplan-Meier and log-rank tests.

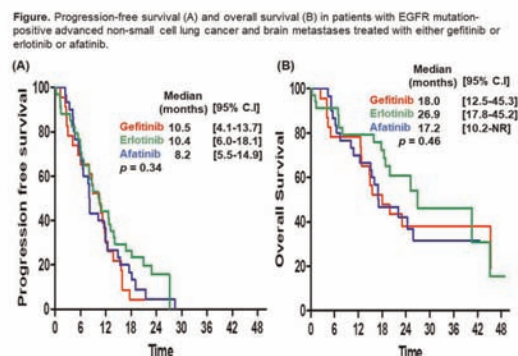
Results: 306 NSCLC patients were enrolled, with 116, 75, and 115 receiving first-line gefitinib, erlotinib, and afatinib, respectively. The afatinib group had a better PFS (12.7 vs 9.8 months; HR 0.59, $P = 0.001$) and OS (39.1 vs 22.0 months; HR 0.64, $P = 0.035$) than the gefitinib group. Afatinib tended to provide better BM prevention than gefitinib (BM cumulative incidence, HR 0.49; 95% CI: 0.34–0.71, $P < 0.001$) according to a Cox model adjusted for possible confounders. Patients with initial BM had a shorter PFS ($P < 0.001$) and OS ($P = 0.015$) than those without initial BM. Among the former, there were no differences in median PFS ($P = 0.34$) and median OS ($P = 0.46$) in the three EGFR-TKI groups.

Conclusion: Our data suggested that, compared to gefitinib, afatinib provided significant benefits in terms of PFS and OS in treating BM. Both had the same effectiveness in preventing subsequent BM.

Table 1. Cox proportional hazards regression for progression-free survival and overall survival of patients with initial brain metastases.

		Progression-free survival		Overall survival	
		HR (95% CI)	p value	HR (95% CI)	p value
Age	>60 versus <60	1.13 (0.59–2.15)	0.709	1.04 (0.50–2.19)	0.910
Sex	male versus female	1.70 (0.94–3.09)	0.081	2.48 (1.20–5.16)	0.015
ECOG PS	≥2 versus <2	1.81 (0.93–3.52)	0.082	2.59 (1.18–5.71)	0.018
Tumor size	>3cm versus <3cm	3.16 (1.17–8.53)	0.023	5.52 (1.12–27.1)	0.035
Smoking	positive versus negative	1.59 (0.68–3.73)	0.283	1.42 (0.57–3.57)	0.452
EGFR mutation	Del 19 versus others	1.63 (0.89–3.00)	0.114	0.91 (0.45–1.84)	0.784
Treatment	Erlotinib versus Gefitinib	0.56 (0.27–1.14)	0.108	0.92 (0.39–2.14)	0.840
	Afatinib versus Gefitinib	0.61 (0.30–1.23)	0.168	1.16 (0.50–2.71)	0.726

ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; PS, performance status.



AP535

A CASE OF PRIMARY PULMONARY MONOPHASIC SYNOVIAL SARCOMA

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Background and Aims: Primary Pulmonary Synovial Sarcoma is a highly aggressive and extremely rare tumor. A 31-year-old female, Overseas Filipino Worker, underwent routine chest radiograph wherein a left sided pleural effusion was found incidentally. The patient denied any respiratory symptoms. She had pleural biopsy and was advised for further work up however she decided to go back to the Philippines. Few days prior to admission, she had difficulty of breathing prompted consult to our institution and was subsequently admitted. The Patient arrived in the emergency room in cardiopulmonary distress. She was pale and chest examination revealed asymmetrical chest expansion, no retractions, absent tactile and vocal fremitus and absent breath sounds on the left lung field.

Methods: To report a case of 31 years old asymptomatic female with primary Pulmonary Synovial Sarcoma.

Results: A massive pleural effusion with contralateral mediastinal shifting was seen on Chest radiograph. On Contrast Enhanced Computed Tomography of thorax showed multiple heterogeneous lesion of the pleural fluid contained within the thickened contrast-enhanced rim septations occupying almost the entire left hemithorax. Patient underwent video-assisted thoracoscopic surgery with frozen section biopsy and chest tube thoracostomy. Pleural fluid analysis revealed predominance of segmenters (60%), exudative with haemorrhagic pleural fluid. Furthermore, the pleural fluid was negative for acid fast bacilli and no growth on culture. Histopathologic findings were consistent with Monophasic Synovial Sarcoma. Immunohistochemical (IHC) analysis was BCL-2, CD99 positive, and show focal positivity with Epithelial Membrane Antigen (EMA), Cytokeratin (CK) 7, Cytokeratin AE1/AE3 while CD8, Cytokeratin 5/6, desmin, CK 18, CK 19, CD 34, S100 were negative

Conclusion: Primary Pulmonary Synovial Sarcoma is a rare tumor. It should be considered as one of the differentials of primary lung cancer in middle-aged patients. More than academic interest, recognizing synovial sarcoma is essential for appropriate management, considering that this tumor carries a poor prognosis

AP536

EFFICACY OF SALVAGE CHEMOTHERAPY AFTER IMMUNE CHECKPOINT INHIBITOR IN NON-SMALL CELL LUNG CANCER PATIENTS

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Background and Aims: Immune check point inhibitors (ICIs) have been developed and showed dramatic effect in some non-small cell lung cancer patients. Moreover, some retrospective studies suggested improvement of responses to chemotherapy after use of ICIs. We evaluate efficacy of salvage chemotherapy after exposure to ICIs.

Methods: Eligible patients were adults with NSCLC who received ICIs (Nivolumab or Pembrolizumab) as second or later line therapy, then received single-agent salvage chemotherapy from January 2016 to April 2018. Clinical data were retrospectively analyzed.

Results: 26 patients were eligible. Patients mean age were 68. 20 were males vs 6 female. 14 were adeno, 11 squamous, and 1 NOS. 20 patients received Nivolumab, 6 patients were Pembrolizumab. 14 patients received ICIs as 2nd line therapy, 6 patients as 3rd line, 6 patients as 4th or later line. As for salvage chemotherapy, tegafur/gimeracil/oteracil (61.5%), DOC+ RAM(15.3%), DOC (7.7%), nab-PTX (3.8%), GEM (3.8%), CPT-11(3.8%) and VNR (3.8%) were used. Over all response rate (ORR) was 11.50%, Disease control rate (DCR) was 57.7%. Median progression free survival (PFS) was 3 months. Grade 1 interstitial lung disease was observed at 1 patient.

Conclusion: Although our data include heavily treated patients who received ICIs as third or later line, ORR/DCR and PFS were comparable to historical data of second line chemotherapy. ICIs might improve efficacy of salvage chemotherapy.

AP537

THE EGFR MUTATION PATTERN AFTER EPIDERMAL GROWTH FACTOR RECEPTOR-TYROSINE KINASE INHIBITORS THERAPY IN PATIENTS WITH NON-SMALL-CELL LUNG CANCER HARBOURING ACTIVATING UNCOMMON EGFR MUTATIONS

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Background and Aims: Around 10–15% EGFR-mutated non-small-cell lung cancer (NSCLC) harbour uncommon EGFR mutations. After excluding T790M and exon 20 insertion, the remaining uncommon EGFR mutations are recognized to be sensitive to epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs). However, the EGFR mutation pattern of NSCLC patients with activating uncommon EGFR mutation who failed first-line EGFR-TKI therapies remained unknown.

Methods: From January 2011 to July 2017, NSCLC patients with EGFR mutation other than exon 19 deletion and L858R in National Taiwan University Hospital, National Taiwan University Hospital Yun-Lin

Branch, and Far Eastern Memorial Hospital were included. The patients with de novo T790M or exon 20 insertion were excluded. The EGFR mutation data were recorded and analyzed in patients who received a second EGFR mutation test on disease progression after first-line EGFR-TKIs therapies.

Results: The EGFR mutation data of NSCLC patients ($n = 1984$, National Taiwan University Hospital 1490 patients; National Taiwan University Hospital Yun-Lin Branch 91 patients; Far Eastern Memorial Hospital 403 patients) were retrieved. A total of 162 patients had activating uncommon EGFR mutation. Among them, 17 patients received EGFR mutation tests for disease progression after first-line EGFR-TKIs therapies. Five patients (29.4%) had T790M mutation, and 4 of them were obtained via liquid biopsy. Five patients (29.4%) lost their initial uncommon EGFR mutations. One patient (5.9%) had EGFR mutation shifted from E709V to L858R. Six patients (35.3%) remained their initial uncommon mutations. One patient (5.9%) had transformed into small-cell lung cancer but retaining the same EGFR mutation (S768I and L858R).

Conclusion: The proportion of acquired T790M in patients with activating uncommon EGFR mutation who failed first-line EGFR-TKIs may be relatively lower as compared to that reported in the previous literatures. Further large-scaled studies for validation are warranted.

AP538

DIABETES IS ASSOCIATED WITH THE RISK OF PROGRESSION AND PROGNOSIS IN LUNG CANCER

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Background and Aims: Lung cancer ranks the second in all cause of death (Mortality & Causes of Death, 2016) and in first place of all new malignancies, both in the incidence and deaths, while diabetes is expected to reach 439 million in 2030. While in present, the clinical prognosis of lung cancer is mainly determined by its clinical stage (Liang et al., 2013), and its staging factors are not included in the merger of diabetes. However, studies have shown that combined diabetes can increase the local recurrence rate (Varlotto et al., 2012). The study is designed to investigate the role of diabetes in lung cancer invasion and prognosis.

Methods: Patients with first diagnosed non-small cell lung cancer and without a second primary cancer were recruited from April 2015 to May 2016. There were 109 patients were diagnosed with diabetes (the diabetes group) and 335 patients without diabetes. All patients were followed up for 2 years. The outcome evaluation was independently by the clinical stage. The Kaplan–Meier method was used to compare survival curves for patients with and without diabetes. The Cox proportional hazards model was used to estimate hazard ratios for the association between diabetes, other prognostic factors and patient survival.

Results: The baseline characters of these patients showed no significant difference beside BMI. The median follow-up was 23 months (range, 3–36 months). Compared with those who with normal glucose and insulin level, patients with diabetes not only had a shorter period of progression free survival but also had a higher risk of all-cause mortality.

Conclusion: For our results diabetes was confirmed to be an independent factor of the risk of non-small cell lung cancer which was considered to associated with the risks of progression and prognosis. A further discover the underlying mechanisms may provide a new approach to cancer treatment.

AP539

PRIMARY THYMIC MALIGNANT LYMPHOMA SUSPECTED OF THYMOMA: A REPORT OF TWO CASES

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Background and Aims: According to the Japanese Association for Thoracic Surgery, the occurrence of lymphoid tumor among mediastinal tumours is not many: 5.3% in 2000 and 6.4% in 2008. It is said to be difficult to differentiate lymphoid tumor from other mediastinal tumours based only on the image findings.

Methods: We operated on two cases of anterior mediastinal tumours which were eventually diagnosed as malignant lymphoma.

Results: One of the cases was a 50-year-old woman who had undergone operation for sigmoid colon cancer. In a follow up, anterior mediastinal tumor of 15 mm in diameter was detected on chest CT scan. Chest MRI revealed the low intensity mass on T1 imaging, and high intensity on T2 imaging at the anterior mediastinum. We suspected it to be thymoma and performed VATS-thymectomy. The histopathological findings revealed lymphoepithelial lesion, and CD20(+) and CD3(-) by immunostaining. Thus we diagnosed her as MALT lymphoma. There is no report of recurrence 21 months after the operation.

Another case was a 45-year-old woman who was pointed out an abnormal shadow on chest X-ray in a medical check-up. A mass of 10 cm in diameter was detected on chest CT scan and MRI, and we suspected it to be thymoma. As invasion to pericardium and left lung was found during the operation, we performed VATS-extended thymectomy, partial pericardiectomy and left upper lobectomy. The histopathological findings revealed alveolar aggregation of tumor cells. Based on the immunostaining, we diagnosed her as diffuse large B-cell lymphoma. Because surgical margin was partially positive, combined modality therapy has been planned following the operation.

Conclusion: We experienced two cases of primary thymic malignant lymphoma which were first considered to be thymoma. We will report them with some literature consideration.

AP540

ESTABLISHMENT OF PRIMARY PATIENT-DERIVED CANCER CELLS OF LUNG CANCER

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Background and Aims: Lung cancer is the leading cause of cancer death in Taiwan. The 5-year survival rate was 15.9%, with a median survival of 13.2 months. The prognosis is poor and how to improve the survival remains an important issue. Patient-derived cancer cells are valuable tools for studying the molecular basis of lung cancer and evaluating therapeutic strategies. In this study we develop cell lines directly from lung cancer patients with malignant pleural effusion (MPE) no matter these patients had treatment or not. We hope pharmacological profiling of patient-derived cells could be an efficient way to direct therapeutic choices for individual cancer patients.

Methods: The MPE samples were consecutively collected from lung cancer patients in National Taiwan University Hospital (NTUH). Primary patient-derived cancer cells were directly cultured from MPE. After successful culture, genetic testing of driver mutation was performed by MALDI-TOF mass spectrometry assay.

Results: Until now total 417 MPE samples with cytology positive of malignant cells were used to generate primary cancer cells. 117 primary cancer cells were successfully established (success rate was 28%). These cells include 3 histological subtypes: 2 cells were squamous cell carcinoma, 7 cells were small cell carcinoma and 105 cells were adenocarcinoma. Driver mutation detection of adenocarcinoma was performed by MALDI-TOF mass spectrometry assay. Account of 105 primary cancer cells of adenocarcinoma, 29% was EGFR L858R mutation (8 with T790M mutation), 21% was EGFR exon 19 deletion (5 with T790M mutation), 6% was EGFR exon 20 insertion, 4% was KRAS mutation, 2% was BRAF mutation and 2% was EML4-ALK translocation.

Conclusion: We successfully established 117 primary cancer cells and performed the driver mutation testing. Most of these cells are derived from patients who failed to chemotherapy or EGFR-TKIs therapy. These cells will be used to study the mechanism of drug resistance and evaluate the therapeutic strategies.

AP541

AN AUTOPSY CASE OF RUPTURED LIVER METASTASES FROM SMALL CELL LUNG CANCER: CASE REPORT AND LITERATURE REVIEW

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Background and Aims: Liver is the most common site of metastasis from small cell lung cancer (SCLC), however, rupture is rare. Here, we describe an autopsy case of SCLC who died of this condition.

Methods: A 50-year-old male visited our hospital because of an abnormal shadow on a chest X-ray. He complained of dry cough and slight fever for three weeks. He had bulbar conjunctiva, and many petechias on his lower extremities. Laboratory tests revealed anaemia, elevation of hepatic enzymes, and ProGRP. CT scan revealed a mass in the right upper lung lobe, and pleural effusion on both sides. Multiple liver tumours were also detected and some were located at the subcapsular region. Histological examination of the tumor specimen obtained by bronchoscopy confirmed the diagnosis of SCLC, and antitumor chemotherapy was started. Several h after completion of the chemotherapy on day 1, he suddenly complained of nausea and general malaise. Laboratory tests showed anaemia, elevation of hepatic and biliary enzymes, acute renal insufficiency, and hyperpotassemia. Thereafter, his condition deteriorated rapidly, and died the next morning. An autopsy revealed distributed liver metastases with necrosis, subcapsular liver hematoma, and haemorrhagic ascites, and ruptured liver metastases was thought as a cause of death.

Results: Ruptured liver metastases from SCLC is rare, and several contributing factors have been proposed, including hypervascularity, necrotic tendency, subcapsular location, congestion of the local hepatic vein, increased intra-abdominal pressure, coagulopathy, and rapid tumor growth. Our patient had some of these risk factors, and from his clinical course, the chemotherapy was also considered to be one of the triggers of this condition due to tumor necrosis.

Conclusion: We comprehensively reviewed the literature and found 11 similar cases with this condition. Physicians need to pay attention to this condition, especially after chemotherapy has initiated.

AP542

DIFFERENCES IN SMALL CELL LUNG CANCER GENETIC PROFILE BETWEEN DISEASE PROGRESSION (PD) AND PARTIAL REMISSION (PR) PATIENTS AFTER THE STANDARD FIRST-LINE CHEMOTHERAPY

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Background and Aims: Small-cell lung cancer (SCLC) is an aggressive lung tumor subtype with high malignancy, frequent metastases and poor prognosis. SCLC patients are relatively sensitive to radiotherapy and chemotherapy, which are mainly therapies in the clinical of SCLC. However, the puzzle in the therapy was the rapid resistance of tumor cells against chemotherapy and the failure of second-line chemotherapy. The purpose of this study was to use the method of precision medical detecting the genes related to SCLC and the key molecular markers that are suitable for the curative effect of chemotherapy, resulting in realize the molecular prediction of small cell lung cancer.

Methods: 24 patients with first-line treatment of SCLC receiving standard chemotherapy (EP) were included, whom were reviewed and categorized into two groups: Disease progression (PD) and Partial remission (PR). Tumor tissues DNA of the patients were detected by using specific target gene capture sequencing technology to discover the gene variation in SCLC and SCLC chemotherapy curative effect related genes were analyzed by bioinformatics methods.

Results: TP53, CYP2C19, ZFX3, BCL2 are the common gene mutations in Chinese SCLC patient population; Common Genes for Copy number variations (CNV) in small cell lung cancer in China: FDPS, SOX2, MAP2K2, PSMA8, MALAT1; The comparative analysis in patients with CNV between PD and PR groups showed EGFR gene copy number variation was detected only in the PR group, and there was a significant difference between the two groups ($P < 0.05$, Fisher test); The tumor tissue DNA somatic cells single nucleotide variants (SNV), genotypes associated with first-line chemotherapy (EP), Tumor Mutational Burden (TMB) and Copy number instability (CNI) of tumor tissues showed no significant difference between two groups.

Conclusion: There was a significant EGFR gene copy number variation difference between the PD and PR groups. The SNV, TMB and CNI of tumor tissues showed no significant difference between two groups.

AP543

ANALYSIS OF ADVANCED OR POSTOPERATIVE RECURRENT NON-SMALL CELL LUNG CANCER CASES TREATED WITH NIVOLUMAB AT HOSPITALS IN NAGASAKI, JAPAN

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Background and Aims: Nivolumab which was approved in December 2015 in Japan, is a PD-1 immune check point inhibitor antibody that disrupts PD-1 mediated signalling and restores antitumor immunity. It showed survival benefit with improved safety profile compared to Docetaxel treatment in advanced non-small-cell lung cancer, however, some immune-related adverse events (irAE) including lung injury can be severe and risk factors of irAE are not identified.

Methods: Ninety three consecutive advanced non-small-cell lung cancer patients treated with nivolumab who attended Nagasaki University Hospital and affiliated hospitals between January 2016 and December 2017 were enrolled. We analyzed these patients' background, tumor type, performance status, tumor response and treatment related adverse events retrospectively.

Results: The number of men and women are 71 and 22, and median age is 67 (31–89). The number of patients of performance status 0, 1, 2 and 3 is 20 (21.5%), 56 (60.2%), 15 (16.1%) and 2 (2.1%) respectively. The numbers of Squamous cell carcinoma (Sq) and non-Squamous cell carcinoma (non-Sq) are 28(30.1%) and 65(69.9%). Response rate is 27.3%. (CR 0%, PR 27.3%). Median-progression free survival of Sq and non-Sq is 66 and 127 days ($P = 0.0667$). Grade3–5 IrAE occurred in 16 (7.4%) patients and Grade5 IrAE occurred in 3 (3.3%). Additionally, grade 3–5 adverse events of lung injury occurred in 8 (8.6%) patients. The proportion of each lung injury patterns were as follow: OP, NSIP, HP and AIP/ARDS is 62.5, 12.5, 0 and 25%. Patients with OP pattern were successfully treated with corticosteroids otherwise, patients with AIP/ARDS pattern have poor prognosis. All lung injury events occurred within 16 weeks, especially AIP pattern occurred within 4 weeks. All patients with lung injury were men and have smoking history.

Conclusion: There was no significant difference for tumor response and treatment related adverse events compared to previous study however, the incidence of lung injury was a little higher than previous study.

AP544

FACTORS ASSOCIATED WITH CRIZOTINIB EFFICACY IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER HARBORING DIFFERENT ALK FUSION VARIANTS

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Background and Aims: Whether different anaplastic lymphoma kinase (ALK) fusion variants or BIM (Bcl-2-like 11) polymorphism influences crizotinib efficacy for advanced non-small cell lung cancer (NSCLC) is still controversial. We aimed to analyze factors associated with clinical outcome in crizotinib-treated patients with known ALK variant.

Methods: We included all patients with known ALK fusion variant received crizotinib for advanced NSCLC. The patients' baseline characteristics, clinical courses and responsiveness to crizotinib were recorded. ALK fusion gene were analyzed using reverse transcription polymerase chain reaction and BIM deletion was checked by polymerase chain reaction and fragment length analysis.

Results: During December 2010–December 2017, there were 54 patients with known ALK variants received crizotinib for advanced NSCLC. 30 of them had successful BIM deletion analysis. Patients with ALK variant 2 had a trend for longer crizotinib progression free survival (PFS) (median, not reached vs 6.1 months, 95% confidence interval [CI], 1.15 – 9.46, $P = 0.10$ by Log-rank test). Multivariate Cox regression analysis found previous anticancer therapy (adjusted hazard ratio [aHR] 1.37, 95% CI, 1.04–1.81 for every one more line therapy, $P = 0.03$) and Eastern Cooperative Oncology Group (ECOG) performance status ≥ 2 (aHR 7.32, 95% CI, 1.65 – 32.48, $P = 0.01$) were independent factors for

crizotinib PFS. Neither different ALK fusion variants nor the presence of BIM deletion was associated of crizotinib PFS.

Conclusion: More prior anticancer therapies and ECOG ≥ 2 were associated with poorer crizotinib outcome. Different ALK variants and BIM polymorphism were not independent factors for crizotinib PFS in this study.

AP545

A CASE OF THYMIC CARCINOMA FOUND IN MARIE-BAMBERGER SYNDROME

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Background and Aims: Marie-Bamberger syndrome (MBS), also known as pulmonary hypertrophic osteoarthropathy, is characterized by clubbing of the fingers and toes, symmetrical proliferation of the periosteum at the end of the long tubular bone, and bilateral joint swelling. Many MBS are associated with lung carcinoma as paraneoplastic syndrome.

Methods: A 65-year-old woman was admitted to our hospital for abnormal chest shadow.

Results: She had noticed a clubbed finger 10 months ago. Bilateral pain occurred in the knees, ankles, and lower leg bones 6 months ago, which symmetrically spread to the left and right anterior chest and back. Chest computed tomography (CT) showed an anterior mediastinal tumor that diffused into the right thoracic cavity. Pathological findings through percutaneous biopsy of the tumor revealed thymic carcinoma. Although the origin of bilateral pain in the whole body was unknown, the metastatic bone tumor was not diagnosed with CT and X-ray. The pain was then diagnosed as MBS, and chemotherapy with CBDCA + PTX was started. One month later, the primary tumor was reduced, and bilateral pain completely disappeared. The chemotherapy has been continued in the outpatient department. Thymic carcinoma is well controlled, and signs of MBS were not observed.

Conclusion: Approximately 80% of MBS cases are derived from the lungs and 20% occur due to cyanotic heart disease. Most MBS that originated from the lungs are caused by lung cancer. Thymic carcinomas are rare. Treatment of the original disease is the best management option for pain. Administration of anti-inflammatory analgesics and radiotherapy for the pain was not effective. It should be noted that MBS symptoms sometimes occur before the discovery of a malignant disease, and not all symptoms occur at once.

We reported a case of thymic carcinoma that took 10 months to diagnose after the occurrence of MBS signs at the first outpatient visit.

AP546

LIPID DROPLETS SUPPORT THE CELL GROWTH AND PROLIFERATION AND ALLEVIATE THE STARVATION INDUCED CELL DEATH IN THE LUNG CANCER CELLS

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Background and Aims: For the rapid and continuous cell growth and proliferation, cancer cells as nutrient sink within body require large quantities of nutrient supply. Many metabolic pathways, including lipogenesis, are reprogrammed and upregulated to meet their demands. Since lipid storage in the normal adult can only be found in cells or tissues where de

novo lipogenesis take place, whether lipid storage could be found in the lung cancer and its roles in tumorigenesis are investigated.

Methods: in vitro cell line studies using techniques including the histochemistry, western blot, and flow cytometry.

Results: Lipid droplets can be found in the majority of lung cancer cell lines, but their presences are not correlated to the driver mutation types of the cells. These neutral lipids in the lipid droplets could either come from the de novo lipogenesis or extracellular source. Perturbation of the lipid droplet formation inhibits lung cancer cell growth and survival. This result indicates that the neutral lipids stored are important for the lung cancer cell growth and survival.

Conclusion: The upregulation of lipogenesis in the lung cancer has been known for a long time, but whether lipid droplet can be found in lung cancer is not clear. The current study demonstrates for the first time that the lipid droplets are present in the most majority of lung cancer cells. Active store neutral lipids within the nutrient sink cancer cells may be a growth advantage selected during tumor evolution and help cancer cell survive during the tumorigenesis. Further studies will be required to answer whether blocking of neutral lipid storage help improve the cancer treatment.

AP547

THE SUM OF TUMOR SIZE PREDICTS THE EFFICACY OF IMMUNE CHECKPOINT INHIBITORS IN NON-SMALL CELL LUNG CANCER

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Background and Aims: Immune checkpoint inhibitors (ICIs) have become standard treatment for advanced non-small cell lung cancer (NSCLC). The predictors for the efficacy of ICIs such as PD-L1 expression and tumor mutation burden were in clinical use. Tumor size was associated with the efficacy of ICIs in melanoma, but little was known in NSCLC. In this study, we investigated the relationship between the efficacy and safety of ICIs and tumor burden in NSCLC.

Methods: We retrospectively reviewed NSCLC patients treated with ICIs (Nivolumab or Pembrolizumab) at a single center between 2016 January to 2018 March. Tumor burden was defined as the sum of the longest diameter of measurable target lesions evaluated by Response Evaluation Criteria in Solid Tumor ver1.1. We assessed progression-free survival (PFS), overall survival (OS) and adverse event (especially immune-related adverse event (irAE)). The threshold of the sum of tumor diameter for clinical response (CR/PR/SD) was determined using receiver operating characteristic curve analysis. PFS and OS were analyzed by log-rank test using Kaplan-Meier curve after dividing two subgroups according to this threshold.

Results: In total, 53 patients were included in the final analysis. Median age was 68 years old, 41 (77.4%) were male, 14 were squamous cell carcinoma (SCC) and 39 were non-SCC. 35 patients were treated with Nivolumab, 18 with Pembrolizumab. Disease control rate was 29/53 (54.7%). Low tumor burden group (<80 mm) was associated with a significantly longer OS than high tumor burden group (>80 mm) (not reached [95% confidence interval (CI): 10.9-not reached] vs 4.4 months [95% CI: 1.9–11.6][$P < 0.001$]). PFS was also longer in low tumor burden group (7.0 months [95% CI: 2.0–11.3] vs 1.3 months [95% CI: 0.5–3.6][$P = 0.03$]). There was no difference in irAE between the two groups.

Conclusion: Tumor burden was associated with PFS and OS in NSCLC patients treated with ICIs.

AP548

PRIMING OF ANTI-PD-1/ PD-L1 THERAPY BY ANTI-METABOLITE CHEMOTHERAPEUTIC AGENTS IN NSCLC
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Background and Aims: The breakthrough of PD-1/ PD-L1 blockade immunotherapy have brought huge benefit for many types of cancer patients especially those with PD-L1 highly expressed. However 60–70% of patients didn't response because of low or no PD-L1 expression. Find a solution to upregulate tumor PD-L1 expression is critical to increase overall response rate. We attempt to identify which kind of chemotherapeutic drugs could prime tumor PD-L1 expression and would provide a rationale for combination immunotherapy.

Methods: We first focused on identifying whether the chemotherapeutic drugs used in first-line advanced Non-Small-Cell Lung Cancer (NSCLC) treatment has the ability to prime PD-L1 expression in NSCLC cell lines at their sub-lethal dosages by immunoblotting, RT-PCR, FACS analyses, and xenograft tumor assay. We then identify whether their PD-L1 priming ability could affect T cells functions by, in vitro T cells activation assay and T cell-mediated cytotoxicity assay. The syngeneic mouse tumor model used to confirm the effect of combined chemotherapeutic agents and anti-PD-L1 antibody approach.

Results: The anti-metabolite chemotherapeutic agent (Pemetrexed, FU, and Gemcitabine), especially Pemetrexed showed a dose-dependent effect on PD-L1 priming. Tumor PD-L1 priming ability of these agents could further affect T cells activity and T cell-mediated cytotoxicity. Silencing of Thymidylate Synthase (TS), the target of Pemetrexed and 5-FU or Ribonucleotide Reductase Catalytic Subunit M1 (RRM1), the target of Gemcitabine, in cancer cells also showed PD-L1 priming effect and suppressed T cells activation. Interferon-gamma (IFN- γ) mediated JAK1/2 signalling was not involved in the priming of anti-metabolites on PD-L1 expression. Finally, mouse syngeneic model confirmed the combination of Pemetrexed and PD-L1 antibody have a better therapeutic effect compared with anti-PD-L1 antibody alone or Pemetrexed alone.

Conclusion: Our result provides a proof of concept on selecting anti-metabolite chemotherapeutic agents for which had PD-L1 priming ability and could enhance the therapeutic effects by combining anti-PD1/PD-L1 antibodies therapy in NSCLC.

AP549

THE RELATIONSHIP OF MELANO-ASSOCIATED ANTIGEN (MAGE) A3 EXPRESSION AND BRONCHOALVEOLAR LAVAGE (BAL) CYTOLOGICAL RESULTS NSCLS AT DR. SOETOMO REGIONAL HOSPITAL OF SURABAYA
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Background and Aims: Lung cancer still becomes a worrying health issue, the major of death in malignant disease and the incidence rate may increase continuously. Most patients with lung cancer have been diagnosed with advanced stage lung cancer. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. To increase the cure

rate and life expectancy, the lung cancer should be detected early when the cancer is still small and localized. Tumor antigen is tumor marker (bio-marker) that provides information of growing cancer, which has been developed for early detection of lung cancer and therapy (immunotherapy) target. MAGE expression becomes sensitive marker in some type of cancer including lung cancer. Previous research stated that there is significant relationship between MAGE expression and histopathology of lung cancer and stage of lung cancer. The purpose of this research was to analyze the relationship between MAGE A3 expression and BAL specimen cytological result on NSCLC at Dr. Soetomo Regional Public Hospital of Surabaya

Methods: A total of 14 patients with NSCLC who underwent bronchoscopy for the removal of BAL in pulmonary ward of Dr. Soetomo Regional Public Hospital that met the inclusion and exclusion criteria were included in this research, they were analyzed with Fisher's exact test.

Results: There was only 1 (7.1%) subject with BAL cytological results of cancer cells (adenocarcinoma) of the 14 research subjects. Positive MAGE A3 expression only occurred in 4 subjects (28.6%) of 14 subjects who were diagnosed with NSCLC.

Conclusion: There was no significant relationship between MAGE A3 expression and histopathologic type. But, a promising result for improvement diagnosis lung cancer with biologic molecular technique.

AP550

APSR MEMBERSHIP SURVEY OF EGFR MOLECULAR TESTING OF NSCLC IN THE ASIA-PACIFIC REGION

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Background and Aims: Around 1 million new lung cancer cases occur annually in the Southeast Asian and Western Pacific regions combined, comprising more than half the global new cases each year. In recent years several key oncogenic driver alterations have been identified in non-small cell lung cancer (NSCLC), including epidermal growth factor receptor (EGFR) gene mutations, which is detected in up to 60% of adenocarcinoma (ADC) in Asian populations. Compared to platinum-based doublet chemotherapy, first-line treatment of EGFR mutant advanced NSCLC with EGFR tyrosine kinase inhibitors is associated with superior progression-free survival, response rate, symptom control and quality of life. EGFR mutation testing to optimise therapy and outcomes has become the standard of care in all cases of advanced NSCLC, in particular ADC although there are wide variations in testing rates and testing methods across countries the Asia-Pacific region.

Aims: This study aims to survey the variation of EGFR mutation testing in NSCLC across the Asia-Pacific region. The APSR membership will be surveyed with a series of questions that address characteristics of the respondents and details of EGFR mutation testing that will inform a report on the patterns and variations across the region.

Methods: The survey was designed based on (1) face-to-face discussions at APSR Congress meetings, (2) expert exchange of views and (3) electronic circulation of draft questions to the entire APSR Lung Cancer Assembly ($n = 176$). The survey will be administered to the entire APSR membership electronically. The study was approved by the St Vincent's Human [CL1] Research Ethics Committee (HREC 15/252).

[CL1] Is this St Vincent Hospital, Sydney?

Results: Results of the study will inform an APSR position paper on EGFR mutation testing in the Asia-Pacific region.

Conclusion: This study will assist with future work on identifying gaps, deficiencies and areas of need in populations with a high incidence of a key oncogenic mutation.

AP551

INCIDENCE OF HEPATITIS B REACTIVATION DURING EGFR TYROSINE KINASE INHIBITORS TREATMENT IN NON-SMALL-CELL LUNG CANCER PATIENTS

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Background and Aims: Reactivation of Hepatitis B virus (HBV) is a documented risk during cytotoxic chemotherapy in patients with lung cancer. There were some case reports regarding HBV reactivation in non-small-cell lung cancer (NSCLC) patients receiving EGFR tyrosine kinase inhibitors (TKIs) treatment. However, the incidence of HBV reactivation in patients treated with EGFR TKI has not yet been reported.

Methods: We enrolled 143 patients who were diagnosed as NSCLC from 2011 through 2015 and had positive hepatitis B surface antigen (HBsAg). All patients had received EGFR-TKIs as anti-cancer treatment during their treatment courses. Reactivation of HBV is defined as one of following: increase in HBV DNA by at least a 10-fold compared to baseline, absolute increase to > 10⁸ IU/mL or HBV viral load > 2000 IU/mL and ALT level > 5 times the upper limit of normal.

Results: The median duration of EGFR TKI treatment is 10.8 months (95% confidence interval [CI]: 7.6–14.0). A total of 12 (8.4%) patients met the criteria of HBV reactivation during EGFR TKI treatment with an annual incidence of 6.96%. Eight of the 12 reactivations occurred during gefitinib or osimertinib treatment.

Conclusion: NSCLC patients receiving EGFR TKIs treatment may have a noticeable risk of HBV reactivation during the treatment period. Thus, Monitoring liver function and HBV viral load during EGFR TKI therapy is recommending in NSCLC patients with positive HBsAg.

AP552

SOMATIC GENE MUTATIONS IN PATIENTS WITH ADENOSQUAMOUS CELL CARCINOMA OF THE LUNG

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Background and Aims: Adenosquamous cell carcinoma (ADSQCC) of the lung is a rare subtype of non-small cell carcinoma that is composed of at least 10% by volume each of squamous cell carcinoma and adenocarcinoma cells. There is few literature addressing the frequency of epidermal growth factor receptor (EGFR) and echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase (EML4-ALK) rearrangement in this subset of lung carcinomas. We analyzed the detection rate of somatic gene mutations in ADSQCC of lung, focusing the EGFR mutation and EML4-ALK rearrangement.

Methods: We retrospectively analyzed patients with adenosquamous cell carcinoma of the lung who underwent surgical resection or biopsy between January 2012 and December 2017. EGFR mutations and EML4-ALK rearrangement were assessed in all of the patients. Detection of the EGFR mutation status was performed by direct sequencing or a commercial real-time PCR kit and EML4-ALK rearrangement was performed by fluorescence in situ hybridization (FISH).

Results: A total of 16 patients were selected in study period. The patients included 14 men and 2 women, mean age 75.9 years (range 61–86 years). In 8 cases (50%) underwent surgical resection and the others (8 cases) underwent percutaneous needle biopsy.

Overall, 3 (18.8%) of 16 patients had EGFR mutations: two patients had an exon 19 deletion and one had an exon 21, L858R mutation. There were no T790 M mutations. Only one cases (6%), there were EML4-ALK rearrangement.

Conclusion: EGFR mutations occur in lung ADSQCC in the lower percentages as in conventional adenocarcinoma in the Asian population. EML4-ALK rearrangement is less common.

AP553

CLINICAL PERSPECTIVES ON THE UNCOMMON EGFR P. L747P AND P.L747S MUTATIONS IN LUNG

ADENOCARCINOMA: A CASE SERIES STUDY

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Background and Aims: Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) have been strongly proved as first-line standard therapy for advanced lung adenocarcinoma with mutant *EGFR*. However, uncommon mutations p.L747P and p.L747S on the exon 19 of *EGFR* could be detected as 19DEL by using commercial kits. We would like to investigate the efficacy of the patients with uncommon mutations of EGFR p.L747P and p.L747S treated with different *EGFR* TKIs.

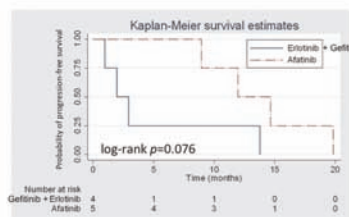
Methods: From 2004 to 2017, we retrieved lung adenocarcinoma patients with *EGFR* p.L747P and p.L747S by method of direct sequencing and recorded their clinical demographic data at National Taiwan University Hospital, a tertiary hospital in Taipei, Taiwan.

Results: Fourteen lung adenocarcinoma patients with *EGFR* p.L747P and p.L747S were identified. Of 14 patients, 11 patients were stage IV lung adenocarcinoma and received *EGFR* TKIs. Five patients received afatinib with 100% objective response rate (ORR), but 4 patients used first-generation *EGFR* TKIs (gefitinib or erlotinib) with 0% of ORR. The median PFS of first-generation *EGFR* TKIs and afatinib, were 1.97 (95.0% confidence interval [CI]: 0.04–3.90) and 11.97 (95.0% CI: 6.38–17.56) months, respectively ($P = 0.076$).

Conclusion: Patients with p.L747P and p.L747S, had primary resistance to first-generation *EGFR* TKI. The irreversible inhibitor, afatinib, could provide better ORR and PFS benefit in treating *EGFR* p.L747P and p.L747S lung adenocarcinoma.

Case	Age(y)/Sex	Smoking	Dx of year	Histology	cStage	EGFR status	EGFR TKI use	Treatment Response to EGFR TKIs	PFS of EGFR TKI (days)
1	63/M	Never-smoked	2006	LUAD	IV	p.L747P	Gefitinib	PD	30
2	36/M	Smoker	2008	LUAD	IV	p.L747P	Erlotinib	PD	90
3	76/M	Smoker	2009	LUAD	IV	p.L747S	Erlotinib	SD	420
4	60/M	Never-smoked	2010	LUAD	IV	p.L747P	Erlotinib	PD	60
5	69/M	Never-smoked	2013	LUAD	IV	p.L747P	Atatinib	PR	365
6	82/M	Never-smoked	2014	LUAD	IV	p.G719S + p.L747S	Atatinib	PR	447
7	58/F	Never-smoked	2016	LUAD	IV	190EL + p.L747S	Atatinib	PR	273
8	49/M	Smoker	2016	LUAD	IV	p.L747P	Atatinib	PR	605
9	61/F	Smoker	2017	LUAD	IV	p.L747P	Atatinib	NE	-
10	64/F	Never-smoked	2011	LUAD	IIA	p.L747P	None	-	-
11	76/M	Smoker	2011	LUAD/SqCC	IIA	p.L747P	None	-	-
12	93/M	Smoker	2014	LUAD	IV	p.L747P	None	-	-
13	72/M	Never-smoked	2015	LUAD	IV	p.L747P	None	-	-
14	65/M	Smoker	2017	LUAD	IIA	p.L747P	None	-	-

cStage, clinical stage; EGFR, epidermal growth factor receptor; PR, partial response; F, female; LUAD, lung adenocarcinoma; M, male; NE, non-evaluable; PD, progressive disease; PFS, progression-free survival; SD, stable disease; SqCC, squamous cell carcinoma; TKI, tyrosine kinase inhibitor



AP554

RISK FACTORS FOR DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN PATIENTS WITH LUNG CANCER

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Background and Aims: The mortality rate from disseminated intravascular coagulation (DIC) is higher in patients with lung cancer than in non-lung cancer patients. Moreover, the prevalence of DIC varies among the pathologic types of lung cancer. This study analyzed the relationship between blood coagulation factors and pathologic types of lung cancer, with the aim of preventing DIC in lung cancer.

Methods: Twenty-six patients with progressive, inoperable stage IIB or higher lung cancer (20 men, 6 women; mean age 71 years; 11 Adeno, 10 squamous cell carcinoma, and 5 small cell carcinoma) and five healthy volunteers without respiratory disease (3 men, 2 women; mean age 72 years) were enrolled in the study. Blood samples were collected at lung cancer diagnosis, before treatment.

Results: White blood cell count, platelet count, serum C-reactive protein, fibrin/fibrinogen degradation products, fibrinogen, thrombin-antithrombin complex, and D-dimer levels differed significantly between lung cancer patients and the control group, but not among the pathologic types of lung cancer. Thrombomodulin levels were significantly higher in patients with Adeno and squamous cell carcinoma than in those with small cell carcinoma ($P < 0.05$ and $P < 0.01$, respectively). Antithrombin levels were significantly lower in patients with squamous cell carcinoma than in those with Adeno ($P < 0.05$).

Conclusion: Coagulation disorders may develop secondary to chronic inflammation in patients with progressive lung cancer. DIC in lung cancer may be attributed to changes in anticoagulation factors, such as thrombomodulin and antithrombin, but not in other coagulation factors.

Characteristic	Patients (%)	Controls (%)
Subjects	26	5
Mean age (years)	71.0 ± 6.3	72.0 ± 4.8
Male/Female	20/6	3/2
Smoking		
Smoker	12 (46.2)	0 (0.0)
Ex-smoker	11 (42.3)	0 (0.0)
Never-smoker	3 (11.5)	5 (100)
Lung cancer group		
Adeno	11 (42.3)	
SqCC	10 (38.5)	
SCC	5 (19.2)	
Stage		
I-II	2 (7.7)	
III-IV	8 (30.8)	
IV	5 (19.2)	
IV	11 (42.3)	

Adeno, adenocarcinoma; SCC, squamous cell carcinoma; SqCC, small cell carcinoma.

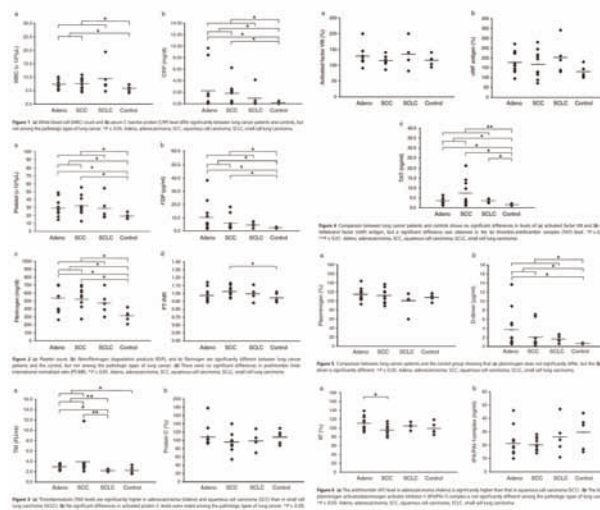


Figure 1. (a) Prothrombin time (PT), (b) activated partial thromboplastin time (APTT), (c) fibrinogen, (d) D-dimer, (e) thrombin-antithrombin complex (TAT), (f) antithrombin (AT), (g) TAT/AT, (h) TAT/AT/AT, (i) TAT/AT/AT/AT, (j) TAT/AT/AT/AT/AT, (k) TAT/AT/AT/AT/AT/AT, and (l) TAT/AT/AT/AT/AT/AT/AT. The values are mean ± SD. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

AP555

THE SURVIVAL ANALYSIS OF INOPERABLE STAGE III NON-SMALL CELL LUNG CANCER WITH THE FIRST-LINE THERAPY IN SOUTHERN OF TAIWAN

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Background and Aims: In recent decades, the gold-standard treatment for the inoperable stage III NSCLC is concurrent chemoradiotherapy (CCRT). But some physicians and patients were afraid of CCRT toxicity in Taiwanese or Asians. We analyzed the overall survival and progressive free survival in clinical practice and observe the difference with treatment guidelines.

Methods: More than 6000 patients of lung cancer between 04/2002 and 04/2014 were treated in our institute. Among these patient, 609 cases were stage III disease (AJCC 7th. ed). The choice of first-line therapy, tumor size, smoking status, EGFR mutation and other clinical factors were collected for analyzing the influence of the survival.

Results: The 418 patients (68.6%) were male and 191 (31.4%) patient are females. 411 patients had never received curable surgery. In these inoperable patients, 219 (53.2%) patients had received first line chemotherapy, 135 (32.8%) patients had received CCRT or sequential chemoradiotherapy. Besides, 57 patients (13.9%) took oral TKI as first line therapy. The median PFS in CT, Combined, Target groups were 5.6, 7.9, 17.3 months respectively ($P < 0.001$). The OS in these groups were 14.7, 14.8, 36.4 months respectively ($P < 0.001$). In this retrospective analysis, sequential chemoradiotherapy had longer PFS (9.5 vs 5.83 months, $P = 0.005$) than CCRT and had trends of longer OS (20.1 vs 12.1 months, $P = 0.098$).

Conclusion: Further analysis is necessary for the choice of first line therapy of inoperable stage III NSCLC in Taiwanese. More data may

need to evaluate the toxicity, side effect, response rate and clinical factors influencing the survival.

AP556

RBM10 INHIBITS PROLIFERATION OF LUNG ADENOCARCINOMA VIA RAP1A-AKT-CREB SIGNALING PATHWAY

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Background and Aims: RNA binding motif 10 (RBM10) is a tumour suppressor gene that modulates apoptosis through the regulation of alternative splicing of apoptosis-related genes. Our previous studies suggested that RBM10 overexpression inhibited lung adenocarcinoma cancer cell malignant behaviour in vitro and complementary DNA microarray analysis identified Rap1A was the most downregulated gene by RBM10 overexpression. As one of Ras-associated proteins, Rap1A has been linked to cancer initiation and development. This study aimed to investigate the relationship between RBM10 and Rap1A and the downstream pathways involving in RBM10 induced biological process.

Methods: Studies were carried out to explore the correlation of RBM10 and Rap1A. Firstly, lentivirus-mediated RBM10 overexpression was employed in lung adenocarcinoma cell line A549 and SPC-A-1. Then, activated GTP-bound form of Rap1A using pull-down isolation was detected by Rap1A activity assay. Western blotting was carried out to detect RBM10, Rap1A and its downstream factors, phospho-AKT and phospho-CREB which were selected in our previous complementary DNA microarray analysis. Finally, rescue experiment was conducted by up-regulating Rap1A expression using 8-pCPT-2'-OMe-cAMP (Epac-selective agonist). Cell viability was assessed using CCK8 assay and expression of downstream factors of Rap1A, phospho-AKT and phospho-CREB were detected by western blot analysis.

Results: We observed that viability of A549 and SPC-A-1 cells was markedly reduced in RBM10-expressed cells compared to corresponding negative controls and expressions of GTP-bound Rap1A, phospho-AKT and phospho-CREB protein were significantly reduced in RBM10 overexpression group by Rap1A activity assay and western blot analysis. It was found that viability of cells was significantly increased by Rap1A rescue experiment using 8-pCPT-2'-OMe-cAMP and expressions of GTP-bound Rap1A, phospho-AKT and phospho-CREB protein were significantly increased.

Conclusion: This result suggests that RAP1A-AKT-CREB signalling pathway may play an important role in the inhibition of lung cancer induced by RBM10, and it could be an useful predictive signalling pathway, indicating a potentially therapeutic strategy for lung cancer.

AP557

FIRST-LINE GEFITINIB, ERLOTINIB, AND AFATINIB PROVIDED SIMILAR CLINICAL EFFICACY IN PATIENTS WHO HAD STAGE IV LUNG ADENOCARCINOMA HARBORING RARE EGFR MUTATION IN TAIWAN

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Background and Aims: The first-line epithelial growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) had proved significantly longer progression free survival (PFS) in patients who had advanced lung adenocarcinoma harbouring common susceptible EGFR mutation as

compared to cytotoxic chemotherapy. However, the efficacy of the first-line EGFR TKI in patients having rare mutation is still unclear.

Methods: We retrospectively reviewed patients with advanced lung adenocarcinoma who had their specimens tested for EGFR mutation in three Kaohsiung Medical University affiliated hospitals from 2009 to 2017. We recorded their basic characteristics, the response to the EGFR TKI, PFS and overall survival (OS).

Results: Totally, 2958 patients had their specimens tested for EGFR mutation. In 67 patients having rare mutations and having anti-cancer treatment, 57 patients with stage IV cancer received EGFR TKI, including gefitinib ($n = 31$), erlotinib ($n = 9$), and afatinib ($n = 17$), as the first-line therapy. The mutations in these patients included mutation only in exon 18 ($n = 21$), exon 20 ($n = 16$), and exon 21 ($n = 13$), and mutations in multiple exons ($n = 7$). The response rates to gefitinib, erlotinib, and afatinib were 41%, 29%, and 33%, respectively ($P = 0.7450$). There were no significant differences between patients receiving different EGFR TKIs in PFS (The median PFS of patients receiving gefitinib, erlotinib, and afatinib were 6.2, 9.0, and 5.5 months, respectively ($P = 0.3025$)) and in OS (median OS of patients receiving gefitinib, erlotinib, and afatinib were 16.1, 12.1, and 20.5 months, respectively; $P = 0.9116$).

Conclusion: First-line gefitinib, erlotinib, and afatinib provided similar clinical efficacy, in terms of response rate, PFS, and OS, in stage IV lung adenocarcinoma patients harbouring rare EGFR mutation. This study may be one of the largest studies comparing the efficacy of different EGFR TKIs to rare mutation. Further large-scale prospective study is warranted.

AP558

A CASE REPORT ON LUNG ADENOCARCINOMA IN A PREGNANT PATIENT

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Background and Aims: Cancer diagnosed during pregnancy is rare with a rate of only 0.02–0.1% annually, and lung cancer during pregnancy is even more rare, with only around less than 70 cases reported in the literature. Non-small cell lung cancer (NSCLC) is the most common histological type accounting for 80–85% of all gestational lung cancer

This is the case of a 34 year old pregnant female seen at 27 weeks gestational age who presented with a recurrent pleural effusion.

Methods: The patient underwent repeated thoracenteses. Histopathology and Immunohistochemistry revealed a metastatic adenocarcinoma from a primary pulmonary lesion which was EGFR negative. Chest CT scan showed left parahilar soft tissue fullness, as well as mediastinal and left axillary lymphadenopathies.

Results: A pleural catheter was inserted and a multidisciplinary team was put together to decide the best course of action. The definitive plan was to carry the pregnancy closer to term then to proceed with palliative treatment for the mother with chemotherapy.

Conclusion: Unfortunately, the pregnancy spontaneously terminated before the planned delivery time and the mother proceeded with palliative chemotherapy.

AP559

1-YEAR SURVIVAL OF NON-SMALL CELLS LUNG CARCINOMA (NSCLC) PATIENTS AND INFLUENCING FACTORS

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Background and Aims: NSCLC which accounts for 85% cases of lung cancer, have a low rate of 1-year survival especially in developing countries. In Indonesia, there are still limited data on survival of NSCLC patients and reported from various hospital-based study.

Objective: To evaluate 1-year survival rate of NSCLC patients and influencing factors.

Methods: Retrospective cohort with survival analysis was conducted on NSCLC patients at Dr. Wahidin Sudirohusodo hospital in Makassar, Indonesia, from January 1st until December 31st 2015.

Results: There were 75 NSCLC patients, age range 19–76 years, 74.7% men, 58.7% normal BMI, 70.7% smoking and ECOG 3-4, 50.7% CCI score >1, and 62.7% non-adenocarcinoma. The median survival is 135 days and the 1-year survival rate is 13%. Bivariate analysis showed that age 40–49 years (180 days and 19%, $P = 0.036$), normal BMI (198 days and 20%, $P = 0.015$), on targeted therapy (240 days and 33%, $P = 0.000$), ECOG 1–2 (270 days and 32%, $P = 0.000$), CCI score <1 (218 days and 24%, $P = 0.000$), and normal albumin (180 days and 13%, $P = 0.024$). Have significant impact on median and high rate of 1-year survival. Median survival was high in subjects with pleural effusions (180 days), but the likelihood rate was high in subjects without pleural effusion (20%, $P = 0.0260$). Multivariate analysis showed that performance status and therapy had the most dominant impact on the 1-year survival.

Conclusion: 1-year survival rate of NSCLC patients in Dr. Wahidin Sudirohusodo hospital is 13% and influenced mainly by the performance status and therapy.

AP560

PATIENTS WHO DEVELOP FEBRILE NEUTROPENIA (FN) IN THE INITIAL REGIMEN IN PATIENTS WITH SMALL CELL LUNG CANCER(SCLC) HAVE A POOR PROGNOSIS

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Background and Aims: Small cell lung cancer (SCLC) is more effective against chemotherapy and radiotherapy than lung cancer of other cell types. On the other hand, FN is an adverse event caused by treatment with anticancer drugs and is often fatal. We examined the relationship between SCLC and FN this time.

Methods: This subject was a patient diagnosed with SCLC and treated with anticancer drug on April 1, 2013 to March 31, 2017. We compared FN cases with those who did not develop FN during treatment of the first regimen. This study is a retrospective study and data was collected from medical records. Differences between responders and non-responders were screened by the Mann-Whitney U test. Prognosis was studied over the entire survival period.

Results: We examined this case in 20 patients who developed FN in the first regimen. 35 cases did not develop. The median age was 71.5, the median MASCC score was 19.5 points, and the low risk group was 12 cases of FN patients who developed on the first regimen. In FN onset cases and in non-onset cases with FN, radiation therapy combined was 3 cases and 3 cases respectively. There was no significant difference between the LD and 6 cases and 10 cases respectively. FN cases had a median overall survival time of 239 days, 587 days who did not develop FN, and FN cases had poor prognosis. HR 2.42 (95% IC: 1.29–4.56)

Conclusion: Patients who develop febrile neutropenia (FN) in the initial regimen in patients with small cell lung cancer (SCLC) have a poor prognosis.

AP561

PINK1 REGULATES PD-L1 AND MHC-I EXPRESSION IN LUNG CANCER WITH GLYCOLYTIC PHENOTYPE

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Background and Aims: The success of immune checkpoint blockade highlights the importance of tumor microenvironment (TME) and host immune systems. PD-L1 can be upregulated in hypoxic or acidic TME. PINK1 is a mitochondrial serine/threonine kinase that has ambiguous roles in cancer. PINK1 loss of function reduces mitochondrial OXPHOS and reshapes tumor cells into a glycolytic phenotype. These suggest the role of PINK1 in TME and PD-L1 regulation. In the current study, we aim to investigate whether PINK1 regulates PD-L1 and its potential role in lung cancer immunotherapy.

Methods: As the expression of PD-L1 can be influenced by the tumor cell itself and the surrounding TME, we first investigated whether PINK1 affects PD-L1 expression in four lung cancer cell lines, CL1-0, CL1-5, A549 and EKVX. Cells were transfected with siPINK1 or PINK1 plasmid for PINK1 manipulation. Changes of metabolic phenotypes upon PINK1 manipulation were investigated by Seahorse XF96 Analyzer. Changes of PD-L1 expressions were examined by RT-qPCR and immunoblots. Related mechanisms were explored by immunoprecipitation and immunoblots.

Results: The results showed that PINK1 knockdown upregulated PD-L1 transcription and translation in CL1-5 and EKVX cells, but not CL1-0 or A549 cells. When compared with A549 cells, CL1-5 cells were assigned to be of glycolytic phenotype and the degree of glycolysis-dependency increased with PINK1 knockdown. The change of MHC-I expression was in concordance with that of PD-L1 upon PINK1 manipulation. We also showed that the regulation was mediated in part by STAT family proteins or HIF-1 α , dependent on different cellular contexts.

Conclusion: PINK1 regulates PD-L1 and MHC-I expression in lung cancer with glycolytic phenotype. As MHC-I and PD-L1 play pivotal roles in cancer immunotherapy, our discovery facilitates therapeutic development not only for TME reshaping but also for immune escape modulation.

AP562

RISK FACTORS ASSOCIATED WITH THE OCCURRENCE OF LUNG CANCER IN WOMEN IN PERSAHABATAN HOSPITAL, JAKARTA

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Background and Aims: Lung cancer is the second leading cause of cancer-specific death among women in Indonesia and the incidence increases continuously from year to year. The main cause of lung cancer is smoking, but it is unlikely occurred in women, especially in Asia and Indonesia. Lung cancer is caused by multifactor, and about 10–15% of lung cancer in the world are found in non-smokers. This study aims to determine the risk factors associated with the occurrence of lung cancer in women in Persahabatan Hospital, Jakarta.

Methods: A case-control study involving 46 subjects with lung cancer as well as 62 subjects with no lung cancer at pulmonology clinic, Persahabatan Hospital, Jakarta between July 2016 and October 2017 was done. The data regarding ages, jobs, active smokers, passive smokers, history of cancer in their families, history of chronic lung diseases, and EGFR mutation in subjects with lung cancer were obtained. Descriptive statistics, chi square hypothesis test, and logistic regression were used for analysis.

Results: A total of 108 subjects ranged in age from 19–90 years. All the subjects in the case group showed the histopathology of adenocarcinoma, and 67.4% of them showed EGFR mutations. Subjects in the control group were mostly diagnosed with pulmonary tuberculosis (43.5%). The result of bivariate analysis showed that there is a significant association between passive smoker ($P = 0.038$, OR = 2.613; 95% CI: 1.038–6575) and age ($P = 0.002$; OR = 5378; 95% CI: 1698–17,029) with lung cancer in women. From multivariate analysis, it was found that there was a significant association between passive smoker ($P = 0.047$, aOR = 2.639, 95% CI: 1.012–6878) and age ($P = 0.005$; aOR = 5.417; 95% CI: 1.685–17,412) with the occurrence of lung cancer in women.

Conclusion: We concluded that adenocarcinoma is the most common types of lung cancer in women and age above 40 years is the factor most associated with the occurrence of lung cancer in women at Persahabatan Hospital.

AP563

REAL-WORLD CLINICAL OUTCOMES AND PATHOLOGIC FEATURES OF BRAF V600E-MUTATED LUNG

ADENOCARCINOMA PATIENTS IN TAIWAN

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Background and Aims: There is limited information on clinical outcomes and pathologic features in real-world treated lung adenocarcinoma (ADC) patients harbouring BRAF-V600E mutation.

Methods: We retrospectively reviewed medical record of BRAF V600E-mutated lung adenocarcinoma at a Taiwan academic medical center between 2008 and 2016. The clinical data and pathological features were retrieved. In addition, we used immunohistochemistry (IHC) assay to confirm the expression pattern of BRAF V600E protein in lung ADCs harbouring the BRAF V600E mutation.

Results: In total, we identified 33 lung ADC patients with BRAF V600E mutation. The median age was 67.5 years, 51.5% were male, 39.4% were current/former smokers, and 78.8% had Stage IV NSCLC. IHC demonstrated that the majority of lung ADC harbouring BRAF V600E exhibited a moderate to strong cytoplasmic expression. In only 3 of 30 (10%), IHC staining failed to identify BRAF V600E. Most of BRAF V600E positive IHC cases had micropapillary histological pattern with diffuse cytoplasmic distribution. For clinical outcomes, four patients did not relapse after treatment and still survive for 12.8 (Stage IB), 21 (Stage II), 27.5 (Stage IIIA) and 34.1 (Stage IIIB) months after diagnosis. At time of review, 29 had metastatic status (M1 disease) and 25 patients were deceased. Median (95%CI) OS from date of the metastatic disease was 10.8 (0.7, 20.9) months. Twenty-six patients received ≥ 1 line of systemic therapy for metastatic disease. Pemetrexed-platinum doublet chemotherapy was the most common first-line (1L) regimen (20 patients, 53.8% of 1L recipients). Patients received pemetrexed-based chemotherapy demonstrated a significant longer OS [23.6 ($n = 18$) vs 2.9 ($n = 11$) months, Log-rank test = 0.0014].

Conclusion: These findings indicate that BRAF V600E antibody had high sensitivity (90%) to detect BRAF V600E mutation. Conventional chemotherapy, particularly pemetrexed containing regimens may be still

considered as an important care for the metastatic BRAF V600E-lung ADC patients who were unable to receive the combination of dabrafenib and trametinib treatment.

AP564

PRIMARY ATYPICAL NEUROENDOCRINE TUMOR OF THE THYMUS: A CASE REPORT

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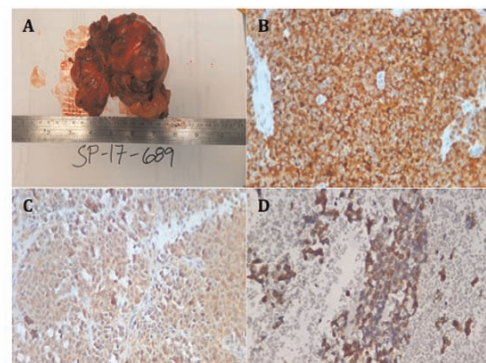
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Background and Aims: Neuroendocrine tumours of the thymus are previously known as carcinoid tumours of the thymus, which are very rare neoplasms. These tumours have a complex aetiology and biology causing difficulties in classifying them histologically. Neuroendocrine tumours are classified as typical carcinoids, atypical carcinoids, small cell or large cell carcinomas. The detailed clinical features are still unknown but several studies suggest that they are usually associated with systemic symptoms due to secretion of biogenic amines from metastatic lesion whereas others are primary tumours of the thymus. Data as to the trend of management and prognosis are scarce due to limited number of studies.

Methods: CASE PRESENTATION: We report a case of a primary neuroendocrine tumor of the thymus in a 41 year-old male who had on and off chest pain with easy fatigability, diagnosed with anterior mediastinal mass. Chest CT-scan showed a left anterior mediastinal mass to consider thymoma that was resected surgically. Immunohistochemical studies showed neoplastic cells positive to Pancytokeratin, Neuron Specific Eolase and Chromograinin test.

Results: Chest CT-scan showed a left anterior mediastinal mass to consider thymoma that was resected surgically. Immunohistochemical studies showed neoplastic cells positive to Pancytokeratin, Neuron Specific Eolase and Chromograinin test.

Conclusion: This neoplasm is reported to have symptoms that may vary due to various endocrine abnormalities. Surgical resection offers the best chance for a definitive diagnosis and remains the treatment of choice. Aggressive chemotherapy maybe helpful for the improvement of the quality of life, delaying local recurrence, and increasing survival.



(A) The gross findings of the anterior mediastinal mass shows tan-red, globular soft to firm tissue with attached fatty tissue measuring 13x8x5cm 220 grams. (B) Immunohistochemical staining for pancytokeratin showing neoplastic cells with strong reactivity. (C) Neoplastic cells stained with Neuron Specific Eolase and (D) Chromograinin showing granular cytoplasmic reactivity.

AP565

ANALYSIS OF INVASIVE RISK FACTORS FOR PURE SUB-CENTIMETER GROUND-GLASS NODULES

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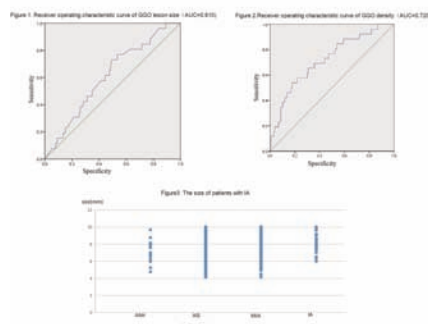
Background and Aims: Most of the pure glass nodules (GGNs) ≤ 10 mm in diameter on computed tomography (CT) are considered as non-invasive adenocarcinoma. However, some of them are invasive adenocarcinomas (IAs). These cases should be treated differently in terms of surgery because they have different prognosis. Therefore, it is necessary to study the predictive factors for IA when pure GGN 10 mm or less in diameter is present.

Methods: A retrospective study was conducted on the clinical data of 2261 patients with lung cancer who underwent surgical resection. We selected 450 patients of lung adenocarcinoma with pure ground-glass nodules 10 mm or less in diameter. We compared the clinical, surgical, and pathological characteristics of non-IA with those of IA.

Results: Among the 450 patients, 14 (3.11%) were AAH, 228 (50.67%) were AIS, 182 (40.04%) were MIA, 26 (5.78%) were IA. The age of the IA was older than the non-IA (60.19 vs 51.37 years; $P < 0.001$). The mean axial diameter of the GGN lesions in IA was larger than that in non-IA (8.02 vs 7.46 mm; $P = 0.043$). The mean density of CT value in IA was higher than that in non-IA (-514.15 vs -606.24 HU; $P < 0.01$). The IA had more EGFR mutation than non-IA (58.8% vs 29.7%; $P = 0.02$). Univariate logistic regression analysis identified the age, unsmooth margin, axial size and mean density, EGFR mutation of GGNs as predictive factors for IA. Multivariate logistic regression analysis identified the age, unsmooth margin, axial size and mean density of GGNs as predictive factors for IA.

Conclusion: The differences between IA and non-IA in age, lesion size, mean density and margin was significant.

Item	Non-IA (n=436)	IA (n=14)	P-value
Age (years)	51.37 ± 10.12	60.19 ± 12.34	<0.001
Sex (male/female)	218/218	7/7	0.985
Smoking status (yes/no)	156/280	1/13	<0.001
Family history of lung cancer (yes/no)	12/424	1/13	0.854
Operative method (VATS/OT)	436/0	14/0	0.000
Pathological type (AAH/AIS/MIA/IA)	14/228/182/26	0/0/0/14	0.000
Mean axial diameter (mm)	7.46 ± 1.23	8.02 ± 1.15	0.043
Mean density (HU)	-606.24 ± 25.12	-514.15 ± 32.45	<0.01
EGFR mutation (yes/no)	128/308	8/6	0.02
Unsmooth margin (yes/no)	156/280	1/13	<0.001
Other factors			



AP566

EFFECTS OF RODENT TUBER EXTRACT CAPSULES (TYPHONIUM FLAGELLIFORME) INPATIENTS WITH LUNG CANCER WHO REFUSED CHEMOTHERAPY

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Background and Aims: Chemotherapy is one kind of therapy solutions for lung cancer, Chemotherapy is the main treatment option for lung cancer. This study aims to determine the effect of Rodent tuber Extract Capsules (*Typhonium flagelliforme*) in patients with lung carcinoma who refuse chemotherapy.

Methods: This study was conducted in Unit infection Centre RSUP. DR. Wahidin Sudirohusodo Makassar. Data retrieval prospectively in a limited population, by inspected the objective and subjective responses, and analyzed using Chi-Square test, correlation test and Mann-Whitney test.

Results: The results were obtained samples of 30 patients of 10 patients who refused chemotherapy (treatment group) and 20 patients undergoing chemotherapy (control group).the incidence of lung cancer is related to the age of 75% in patients aged >40 years, while 15% of cases aged <40 years, on the response of the subjective test Chi-square, the chemotherapy patients gained significant value in the variable ECOG $P < 0.05$ ($P = 0.00$) and chest pain $P < 0.05$ ($P = 0.004$) which shows both variables showed significant differences, whereas the treatment group gained significant value in the variable ECOG $P < 0.05$ ($P = 0.00$), chest pain $P < 0.05$ ($P = 0.00$) and vomiting $P < 0.05$ ($P = 0.02$) of the three variables showed significant differences. The Mann-Whitney test results obtained $P < 0.05$ ($P = 0.00$) showed that the difference in the results of MSCT scan thorax treatment group and control group.

Conclusion: this results proved that the rodent tuber extract capsule (*Typhonium flagelliforme*) at a dose of 2 times a day 2 capsules (1.5 g) can improve subjective and objective response of lung carcinoma patients who refused chemotherapy.

AP567

TREATMENT OF NON-SMALL CELL LUNG CANCER WITH ATEZOLIZUMAB: A CASE SERIES STUDY

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Background and Aims: Atezolizumab, an anti-programmed death ligand 1 (PD-L1) antibody, was approved to use for non-small lung cancer (NSCLC) patients from April 2018 in Japan. In this study, we report clinical experiences of usage of atezolizumab in a single center. The aim of study is investigation of clinical outcomes and safety in treatment of NSCLC patients with atezolizumab.

Methods: A single-center, case series study was conducted. NSCLC patients treated with atezolizumab from April to May 2018 were entered in the study. Patient characteristics, response rate, and adverse events were retrospectively analyzed.

Results: 14 patients in total were reviewed. Average age of patients was 70. $\pm$ 4 years. Histological types were eight patients (57.1%) had adenocarcinoma, four patients (28.6%) had squamous, one patient (7.1%) had adenosquamous, and one (7.1%) had NOS histological type. All patients had received one or more previous therapies (median, 3) before treatment with atezolizumab. Nine patients (64.3%) were previously treated with one or more anti-programmed cell death 1 (PD-1) antibodies. Immunohistochemical analysis showed that four (28.6%), three

(21.4%), three (21.4%), and four (28.6%) patients had high ($\geq 50\%$ TPS), low ($1\% \leq \text{TPS} < 50\%$), negative ($\text{TPS} < 1\%$), and unknown expression of PD-L1, respectively.

Conclusion: Atezolizumab could be used for patients who had received three or more previous therapies including anti-PD-1 antibodies.

AP568

ORAL VINORELBINE AND CISPLATIN PLUS CONCOMITANT CHEMO-RADIO THERAPY AS INDUCTION THERAPY IN STAGE III NON-SMALL CELL LUNG CARCINOMA: RESULTS OF A MULTI-CENTER PHASE II TIAL

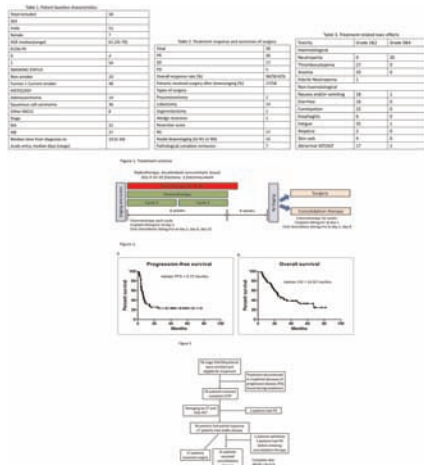
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Background and Aims: Concurrent chemotherapy plus radiation therapy (chemoRT) is an optimal and recommended treatment strategy for stage III non-small cell lung cancer (NSCLC) currently. Here, we sought to investigate the efficacy and safety of oral vinorelbine and cisplatin plus concomitant chemo-radiotherapy in treating stage III NSCLC patients.

Methods: A prospective, open-label, single-arm clinical trial was performed during January 2010 to September 2016. Patients were treated with two cycles of chemotherapy with intravenous cisplatin 60 mg/m² on day 1 and oral vinorelbine 50 mg/m² on days 1, 8 and day 15, and radiotherapy was administrated concurrently since the day 1 when chemotherapy started. A total dose of 66 Gy radiotherapy was delivered in daily fractions of 2 Gy for 6.5–7 consecutive weeks. Tumor response will be assessed after completing 2 cycle of concomitant treatment, and patients were referred to surgery or consolidation therapy based on the assessment.

Results: Fifty-eight patients were enrolled and analyzed, 31 of the 56 patients had stage IIIA and the other 27 had stage IIIB NSCLC. Thirty-six patients had partial response (PR) to the therapy and the overall response rate was 62.1%. The median progression free survival (PFS) was 6.73 months and median overall survival (OS) was 24.83 months. Seventeen patients received surgery after induction concurrent chemoradiation therapy (CCRT), and the median PFS was 25.67 months for patients received surgery. For safety, no adverse effects related mortality was recorded in this trial, and 20 patients ever experienced grade 3&4 neutropenia, and only one patient had febrile neutropenia. Forty-eight patients finally had complete treatment course of this trial, and the complete rate was 82.6%.



Conclusion: Concurrent chemoradiotherapy with the regimen of weekly oral vinorelbine plus triweekly cisplatin was an effective treatment for stage III NSCLC patients. Most patients in this study tolerated the treatment well and had complete treatment courses. The safety profile was also acceptable for patients.

AP569

STUDY OF COMPARISON AMONG DIAGNOSTIC MODALITIES TO ESTABLISH THE DIAGNOSIS OF LUNG CANCER : CEA MARKER, CT-SCAN IMAGING, AND BRONCHOSCOPIC METHOD

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Background and Aims: Lung cancer was a highly aggressive malignancy causing high morbidity and mortality. It was the leading cause of cancer-related deaths worldwide with an overall 5-year survival rate of 17% after diagnoses. Carcinoembryonic Antigen (CEA) marker, Computerized Tomography (CT) Scan imaging, bronchoscopy, and biopsy of bronchial brushing play an important role in the diagnosis of lung cancer. The aims of this study were to assess sensitivity and specificity of diagnostic modalities for lung cancer.

Methods: A retrospective study with descriptive analytic approach of 169 cases of suspected pulmonary mass that admitted to Wahidin Sudirohusodo Hospital Makassar Indonesia during January until December 2015. The patient were examined for CEA marker level, CT-scan imaging, bronchoscopy, and confirmed by biopsy of bronchial brushing. The correlations were assessed with statistical formula that analyzed by using SPSS 22.0.

Results: This Study predominantly male patients (72.7%), while mean age was 61 (24–97) years old. CEA level showed the significant correlation ($P < 0.005$) with poor sensitivity rate of 69.5% but high specificity rate of 96%. CT-scan imaging ($P < 0.005$) showed lower of sensitivity (44%) and specificity (89.7) rate compared with CEA marker. Bronchoscopic modalities carried the highest diagnostic yield ($P < 0.005$), with pooled sensitivity rate of 90% and specificity rate of 94%. The definitive diagnosis was established by biopsy of bronchial brushing.

Conclusion: Bronchoscopy showed potential for increasing the diagnostic yield of lung cancer with the highest sensitivity and specificity rate compare with the other modalities. The adequate tissue acquisition for histological and precise interpretation by expert from CT-scan imaging and bronchoscopy is very important to confirm diagnosis of lung cancer.

APL013

REAL-WORLD FIRST-LINE TREATMENT PATTERNS AND OUTCOMES AMONG PATIENTS WITH ADVANCED OR METASTATIC NON-SMALL CELL LUNG CANCER IN TAIWAN: A POPULATION-BASED RETROSPECTIVE STUDY

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Background and Aims: Lung cancer is the most deadly cancer in Taiwan. Knowledge of the real-world data can complement evidence acquired in clinical trials. The objective of this study is to describe the choice of regimens and survival outcomes for the first-line treatment among patients with advanced and metastatic non-small cell lung cancer (NSCLC).

Methods: We captured data from the National Health Insurance Database between 2010 and 2015. The impact of the treatment regimens on overall survival was assessed.

Results: Total 20693 patients with advanced NSCLC were identified, 15,346 (74.16%) of which were adenocarcinoma. Approximately 50.6% of the patients was administered with cytotoxic chemotherapy as the first line treatment, whereas 49.4% was administered with target therapy as the first line treatment. Among all chemotherapies, pemetrexed with platinum (31.2%) was the most common. The second common regimen is docetaxel with platinum (9.2%), whereas the third common regimen is gemcitabine with platinum (6.3%). On the other hand, among patients administered with target therapy as first line treatment, the most common regimen is pemetrexed with platinum (60%). Among patients with adenocarcinoma histology, pemetrexed with platinum regimen demonstrates longer OS than other chemotherapy regimens.

Conclusion: We found that the most commonly-prescribed initial chemotherapy for NSCLC was pemetrexed/ platinum regimen. In patients with adenocarcinoma histology, the overall survival for patients with pemetrexed and platinum was significantly higher than those with other platinum-based chemotherapy.

Characteristics		ALL		Adenocarcinoma		SCC*		Others	
		N	%	N	%	N	%	N	%
Total		20,693	100.00	15,346	74.16	3,341	16.15	2,006	9.69
Gender	Male	11,881	57.42	7,610	49.59	2,862	85.66	1,409	70.24
	Female	8,812	42.58	7,736	50.41	479	14.34	597	29.76
Age	Mean(SD**), years	66.68(12.68)		65.97(12.83)		68.97(11.47)		68.28(12.82)	
	<70	11,365	54.92	8,800	57.34	1,587	47.50	978	48.75
	≥70	9,328	45.08	6,546	42.66	1,754	52.50	1,028	51.25
Stage	IIIB	2,770	13.39	1,331	8.67	1,087	32.54	352	17.55
	IV	17,923	86.61	14,015	91.33	2,254	67.46	1,654	82.45
EGFR type	+	8,004	38.68	7,597	49.50	74	2.21	333	16.60
	-	5,163	24.95	4,422	28.82	211	6.32	530	26.42
	NA***	7,526	36.37	3,327	21.68	3,056	91.47	1,143	56.98
Year of diagnosis	2011	4,862	23.50	3,537	23.05	851	25.47	474	23.63
	2012	5,166	24.96	3,841	25.03	825	24.69	500	24.93
	2013	5,156	24.92	3,864	25.18	794	23.77	498	24.83
	2014	5,509	26.62	4,104	26.74	871	26.07	534	26.62
Facility Type	Medical center	12,532	60.56	9,551	62.24	1,884	56.39	1,097	54.69
	Non-medical center	8,161	39.44	5,795	37.76	1,457	43.61	909	45.31

SCC*: squamous cell carcinoma

SD**: standard deviation

NA***: not available

Paediatric Lung Disease 2

AP570

ASSOCIATION BETWEEN PNEUMONIA IN PRETERM INFANTS AND GENITAL MYCOPLASMAS IN PLACENTAS

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Background and Aims: among respiratory diseases in the neonatal period pneumonia takes a special place due to big frequency, severe current, possibility of complications and failures. The genital mycoplasma species are the most common organisms isolated from infected placentas and they contribute to adverse pregnancy outcomes including preterm birth and neonatal morbidities. We determined the association between

neonatal pneumonia and genital mycoplasmas (*Ureaplasma* species, *Mycoplasma hominis*) in placental tissue of preterm infants.

Methods: This study enrolled 34 infants who were born at 30–36 weeks' gestation. Morphological, histological and molecular genetic study of 34 placentas was performed. Polymerase chain reaction (PCR) techniques was carried out by real-time method. Patients were divided into two groups according to detection of genital mycoplasmas in placentas.

Results: Among 34 placentas, 19 samples (55.9%, group I) had mono- and mixed infections; 15 samples (44.1%, group II) was non-infected. In group I, *Ureaplasma* species was detected in a concentration of 102 to 106 GE/mL, *Mycoplasma hominis* - in a concentration of 103 to 10 6 GE/mL. Various morphological manifestations of inflammatory processes were detected in a larger number of cases in the placentas of group I compared to those found in the group II [17/19 (89.5%) vs 4/15 (26.7%), $P < 0.001$]. Neonatal pneumonia was identified in the group I more often than in the group II in 5.5 times [7/19 (36.8%) vs 1/15 (6.7%), $P < 0.05$].

Conclusion: Pneumonia in preterm infants was significantly associated with the detection of genital mycoplasmas (*Ureaplasma* species, *Mycoplasma hominis*) in placental tissue. These results may be important for obstetricians and neonatologists.

AP571

THE AVAILABILITY OF VITAMIN D TO THE AMUR REGION CHILDREN AND ADOLESCENTS WITH PATHOLOGY OF THE LUNGS

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Background and Aims: Many authors report a widespread Hypovitaminosis D among different age groups and indicate connection between vitamin D and respiratory disease. Due to high incidence of respiratory disease in children from the Amur region, a study of vitamin D in children with acute (community-acquired pneumonia, CAP) and chronic (bronchial asthma, BA) bronchopulmonary pathology was conducted.

Methods: 20 children with CAP and 21 children with BA were examined. The control group consisted of 44 healthy children whose average age was $11. \pm .63$ years. The concentration of vitamin D in the blood serum was investigated using sets of 25-OH vitamin D (ELISA EVROIM-MUN AG) by enzyme immunoassay.

Results: the amount of vitamin D in children with CAP was $33.2 \pm .46$ ng/mL, in children with BA – $29.6 \pm .41$ ng/mL, that was 1.2 times lower than in healthy children ($40.4 \pm .62$ ng/mL, $P < 0.05$). The deficiency was detected in 9% of the examined children with BA, moderate deficiency of vitamin D and its sufficient content was revealed in equal number of cases – 45.5%.

The connections of vitamin D level with its intake in the daily diet ($r = 0.36$, $P < 0.05$), with serum calcium content ($r = 0.94$, $P < 0.05$) and with a child's body length ($r = 0.3$, $P < 0.05$) were detected. The results confirm the regulatory effect of vitamin D on growth processes.

Conclusion: the conducted studies correlate with the literature data that patients with pulmonary diseases often have a reduced level of vitamin 25(OH)D in the blood serum, which is associated with increased cases or deterioration of asthma control, with increased respiratory infections and require further study of the effect of deficient conditions in children with somatic pathology.

AP572

INVESTIGATION ON THE RELATION BETWEEN CHRONIC COUGH AND MYCOPLASMA PNEUMONIA CHLAMYDIA PNEUMONIA INFECTION IN CHILDREN

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Background and Aims: Objective To investigate the relation between children chronic cough and *Mycoplasma pneumonia* (MP), *Chlamydia pneumoniae* (CP) infection, in order to provide a basis for treatment.

Methods: 70 cases diagnosed as children with chronic cough and 50 cases in control group were detected by enzyme -linked immunosorbent assay of plasma M P, CP-specific IgM antibodies, and group comparison was made.

Results: MP infection in study group were 32 cases(45.7%), CP infection were 9 cases (12.8%); M P infection in control group were 3 cases(6.0%), CP infection 2 cases (4.0%), the mixed infection in study group were 4 cases (5. 7%), and none in control group, there is statistically significant difference between the two groups .

Conclusion: The relation between chronic cough in children and *Mycoplasma pneumonia*, *Chlamydia pneumonia* infection is close . MP-IgM, CP-IgM should be routinely detected in looking for causes of chronic cough in children, to provide a basis for clinical treatment.

AP573

CURATIVE OBSERVATION ON CHILDREN WITH MYCOPLASMA PNEUMONIA TREATED BY AZITHROMYCIN AND HUMAN- R- GLOBULIN

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Background and Aims: To compare the efficacy of uniting azithromycin and human- r- Globulin vs Using azithroyin only for treating children with *Mycoplasma pneumoniae pneumonia* (MPP).

Methods: 90 cases were divided into group A and B, 56 cases in each group. Group A was given azithromycin plus human- r - globulin, Group B was given azithromycin only.

Results: Duration of fever, cough and rales was noted. Two weeks after, another chest X-ray was given. Data were analyzed. Patients with clinical signs and symptoms in group A and B were nearly all controlled. Shadows in their lungs were absorbed. There was no significant difference in therapeutic efficacy between two groups ($P > 0. 05$) . Duration of fever, cough and rales in group A was shorter in comparison with that of group B. There was great significant difference between the two groups ($P < 0. 01$) .

Conclusion: Children with MPP treated with azithromycin plus human- r-globulin were favourable. It is worthy of being widely used.

AP574

PULMONARY SEQUESTRATION: AN UNUSUAL CAUSE OF RESPIRATORY DISTRESS IN A NEWBORN

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Background and Aims: To present a case of a term male neonate diagnosed with pulmonary sequestration.

To define pulmonary sequestration, its manifestations, diagnostics, treatment and complications.

Methods: We present a case of a term male neonate with respiratory distress. Prenatal ultrasound at 28 weeks AOG revealed a congenital

cystic adenomatoid malformation. The patient stayed for 28 days at the NICU. CT scan of the chest showed diffuse ground glass opacity in both lungs with consolidation in both lower lobes and a decreased attenuation and enhancement of the left lower lobe consistent with congenital cystic adenomatoid malformation. Patient then underwent left postero-lateral thoracotomy and left lower lobe lobectomy. Biopsy showed extra-pulmonary Broncho-pulmonary Sequestration. The patient's clinical and laboratory presentation supported the diagnosis of pulmonary sequestration. Patient developed pneumonia during the course of admission and was treated accordingly. Patient was discharged improved.

Results: None.

Conclusion: Patients with pulmonary sequestration needs urgent treatment to the avoid complications and death.

AP575

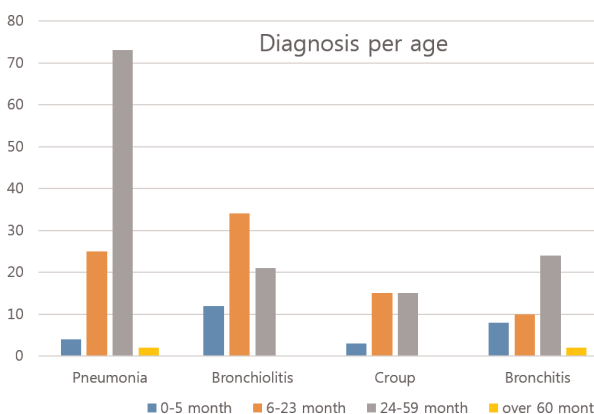
OUTBREAK OF HUMAN METAPNEUMOVIRUS INFECTION OF CHILDREN IN BUSAN, SOUTH KOREA

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Background and Aims: Human metapneumovirus was recently discovered in children with acute respiratory infection. We have studied the occurrence of human metapneumovirus and report clinical findings of 248 human metapneumovirus infected children who were hospitalized during an outbreak in Busan, South Korea.

Methods: During 4 months from February 1, 2016 to May 31, 2016 we collected nasopharyngeal aspirate specimens from children admitted because of respiratory tract infection. Samples were analyzed for human metapneumovirus, influenza virus A/B, parainfluenza, coronavirus, bocavirus, respiratory syncytial virus, adenovirus, and rhinovirus by polymerase chain reaction.



Results: Human metapneumovirus was identified in 248 of 899 children (27.6%). The median age of human metapneumovirus infected children was 24 months (range, 1–15 years), 122 of children are male (49.2%), 127 (51.2%) had pneumonia, 65 (26.2%) had bronchiolitis, 15 (6.0%) had croup and 41 (16.5%) had an upper respiratory tract infection such as rhinopharyngitis, tonsillitis. Lower respiratory tract infection was higher proportion than upper respiratory tract infection. The most common diagnosis in children younger than 2 years old was bronchiolitis and second was pneumonia. 4 of the children with pneumonia (3.1%) were treated by intravenous immunoglobulin. 18 of the children with bronchiolitis (27.7%) needed oxygen therapy. 2 of 65 (3.1%) were treated with continuous positive airway pressure. Most of human metapneumovirus infected children (244, 98.4%) were under 5 years old.

Conclusion: Human metapneumovirus was the most common virus in children who were hospitalized for respiratory tract infection in Busan during the 2014 spring season. The outbreak of human metapneumovirus infection of children in Busan this year caused more severe pneumonia or bronchiolitis than the human metapneumovirus outbreak in South Korea in 2014.

AP576

A TEN YEARS OLD GIRL PRESENTED WITH JIA INDUCED ILD

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Background and Aims: Interstitial lung disease is a rare presentation of juvenile idiopathic arthritis. There are a few reports of patients with JIA induced ILD including this case.

Methods: This 10 years old girl got admitted in our hospital on October, 2017. She was diagnosed as a case of polyarticular, RA positive JIA seven years back. She was treated then with injection methotrexate, tablet leflunomide, tablet prednisolone. After 3 months, she developed fever and cough for which she was diagnosed as a case of pulmonary tuberculosis. She was treated with paediatric anti-TB regimen for six months. For the last one year, she developed exertional shortness of breath and productive cough. On examination, the girl was ill-looking with puffy face, mildly anaemic, clubbing present, respiratory rate 34 breaths per minute. Chest examination shows symmetrically diminished chest movement. There was bilateral diffuse end-inspiratory fine crepitation unaltered with coughing. CVS examination showed features of pulmonary hypertension.

Results: Investigation showed haemoglobin% 9.5 g/dl, ESR 40 mm in 1st hour, sputum for AFB and GeneXpert were negative. Chest X-ray PA view showed bilateral diffuse reticulonodular opacities with enlarged cardiac shadow. Echocardiography showed features of cor pulmonale and HRCT chest findings include reticulo-nodular opacities in all lobes of both lungs. Finally the patient was diagnosed as a case of JIA induced ILD with Cor pulmonale. Then she was treated with oxygen inhalation, injection methylprednisolone, tablet pirfenidone, tab N-acetylcysteine. But the patient did not improve and later developed respiratory failure and was shifted to ICU. Ultimately she died.

Conclusion: This patient is a rare case of JIA induced ILD. The prognosis of this case is very poor.

Pulmonary Circulation 2

AP577

RATIONAL AND DESIGN OF THE LARGEST PROSPECTIVE MULTICENTER REGISTRY STUDY ON PULMONARY EMBOLISM IN CHINA: THE CURES STUDY

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Background and Aims: Pulmonary embolism (PE) is a global health issue. Recent years, the incidence, mortality, and disease burden of PE dramatically increase along with the social aging, awareness of the disease and diagnosis technique advances in China. In order to provide the latest nationwide data in PE, we initiated a prospective, multicentre and ongoing registry study on PE since Jan 2008, which is the China Pulmonary Thromboembolism Registry Study (CURES).

Methods: The CURES is a three-stage designed study, recruiting adult patients presenting with symptomatic PE alone or PE with deep venous thrombosis (DVT) confirmed by objective tests. Stage I of the study started from Jan 2008 to Jun 2011, and consecutively enrolled about 3000 eligible PE or PE with DVT patients. Stage II continued to enrol about 5,000 patients with three month follow-up between Jul 2011 and Jul 2016. Stage III started from Aug 2016 and expected to last until Dec 2019, intending to further recruit 3000 patients with regular follow-up visit every three months. In the meanwhile, blood samples were also collected in Stage III to investigate thromboembolism relevant genetic susceptibility and potential biomarkers. Demographic data, medical history, risk factors of the disease, symptoms and signs on presentation, diagnostic methods and results, treatment options and clinical outcomes were collected. All patients provided written consent to their participation.

Results: Until now, the CURES study has included over 10,000 PE or PE with DVT patients from 94 medical centres from the China PE-DVT network. The collected data could be further analyzed and reveal epidemiological characteristics, patterns of clinical care and outcomes of the disease in the real-world setting.

Conclusion: CURES is the largest prospective multicentre registry study on PE in China, which provides us valuable data and insights into the disease, and achieves the ultimate goal of improving disease control and management.

AP578

HYDROGEN GAS INHALATION IS A NOVEL TREATMENT FOR PULMONARY HYPERTENSION

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Background and Aims: Reactive oxygen species and inflammation contribute to the pathogenesis of pulmonary hypertension (PH). Therapy with hydrogen gas is reported to have both anti-oxidant and anti-inflammatory effects in various diseases, yet whether and how inhaled hydrogen gas affects the pathogenesis of PH is unclear.

Methods: Hydrogen gas inhalation was given to experimental rat model of PH induced by monocrotaline (MCT) injection at two time point: (1) immediately after MCT injection (prevention model); (2) 16 days after MCT injection (treatment model). The parameters indicating development of PH; right ventricular systolic pressure (RVSP), right ventricle weight, and right ventricular hypertrophy index

Results: For mice received hydrogen immediately after MCT injection, hydrogen gas inhalation significantly reduced RVSP, right ventricle weight, and right ventricle hypertrophy. Increased production of IL6 and malondialdehyde (MDA) were found in lung tissues and plasma from rats injected with MCT, these parameters were abrogated in those receiving hydrogen gas inhalation. Anti-inflammatory effects were also indicated by less macrophage infiltration in lungs from rats receiving hydrogen gas inhalation. Furthermore, in cultured rat pulmonary arterial smooth muscle cells (PASMCs), hydrogen gas prevented IL-6 secretion induced by hydrogen peroxide. In lung tissues from MCT-injected rats and hydrogen peroxide (H₂O₂) treated PASMCs, hydrogen gas up-regulated the levels of nuclear factor-erythroid 2-related factor 2 (Nrf2) and its target protein

heme oxygenase 1 (HO-1). For mice receiving hydrogen gas 16 days after MCT injection, the survival rate was significantly increased compared to mice without hydrogen inhalation (65% vs 41%, $P = 0.02$)

Conclusion: Hydrogen gas inhalation prevents MCT-induced PH progression by improving Nrf2 functions and impairing inflammatory responses in PASMCs, and hydrogen gas also increased the survival of mice with PH.

AP579

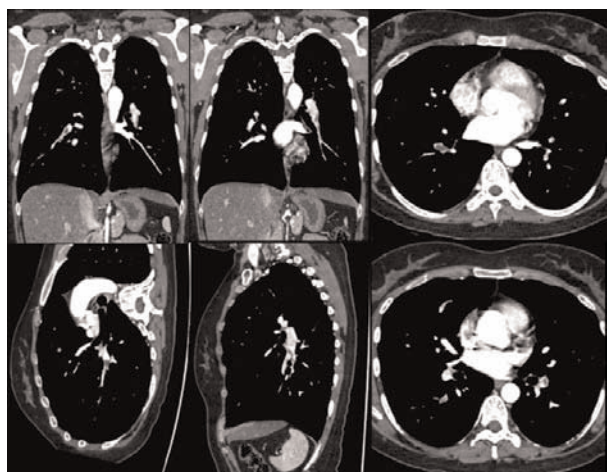
A CASE OF PULMONARY EMBOLISM FROM SUPERFICIAL VENOUS THROMBOSIS WITH AN UPPER EXTREMITY SOURCE IN A 35-YEAR-OLD FEMALE ON ORAL CONTRACEPTIVE PILLS

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Background and Aims: Venous Thromboembolism accounts for a significant cause of morbidity and mortality, both in the general and at risk populations. Certain risk factors put patients at an increased propensity to develop VTE, including a prior history of pulmonary embolism (PE), immobility, malignancy, obesity, smoking, and oral contraceptive pill (OCP) use. Superficial vein thrombosis (SVT) is a relatively uncommon form that is only starting to be recognized to have significant association with deep vein thrombosis (DVT) and PE. PE secondary to upper extremity SVT in the absence of any DVT are rare.

A 35-year-old female with a brief history of OCP use, presented with dyspnoea and palpitations at the emergency department (ED). She had no history of immobility, thromboembolic events, trauma or malignancies. Upper and lower extremity venous Doppler were done which showed SVT in the left cephalic vein. CT angiogram confirmed PE. Patient was treated conservatively with enoxaparin and rivaroxaban, which afforded resolution of symptoms.



The pathophysiology of SVT involves multiple factors, such as changes in haemostasis, external or endothelial trauma, and inflammation. The great saphenous vein is most commonly affected in 60–80% of cases. A study in people with suspected pulmonary embolism showed an odds ratio (OR) of 4.90 with concurrent OCP use. Another found a mean-weighted prevalence for PE and SVT at 6.9%. Only a handful of cases of PE with upper extremity SVTs have been reported. No case of upper extremity SVTs evolving to PE is found with only OCP as the known risk factor.

It is emphasized that a lower extremity DVT is the major source of PEs, however, sources from upper extremities or superficial veins remain a possibility. Physicians should have a high index of suspicion in order to diagnose and initiate treatment for this potentially life threatening condition.

AP580

GENETIC VARIANT OF CYP4V2 ASSOCIATED WITH VENOUS THROMBOEMBOLISM: A CASE-CONTROL STUDY

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Background and Aims: Genome-wide association studies have identified the CYP4V2 (rs13146272) as a risk candidate gene associated with venous thromboembolism (VTE). However, the limitation of small sample size and some relevant genetic analysis models failed to correlate the relationship between VTE with rs13146272. Here, we performed this case-control study in Chinese population to analyze the associations between rs13146272 and VTE and to compare the difference among various ethnicity.

Methods: In total, 226 VTE patients and 205 healthy controls were recruited and analyzed for the allele frequency of variant rs13146272 by Mass ARRAY SNP genotyping assay. In addition, 9 case-control cohorts from 5 studies, involving 6667 VTE-affected individuals and 8716 controls subjects, were used for the meta-analysis comparison. Pooled odds ratios and 95% confidence intervals were calculated for assessing the association using different genetic models.

Results: Our result showed no significant association between VTE and rs13146272 under additive model (OR 0.92, 95% CI: 0.70–1.21, $P = 0.55$) in Chinese population. Compare among various ethnicity showed significant association between VTE risk and rs13146272 under additive model, recessive model and dominant model. And in two of these models, the association reached the threshold of genome-wide significance ($P < 5.0 \times 10^{-8}$).

Conclusion: Our study demonstrated that the genetic of different ethnicity carried genetic diversity of the association between SNP rs13146272 with VTE risk. Further validation of this association in larger sample size study with multi-ethnicities should be warranted.

APL014

ACUPUNCTURE INDUCED PULMONARY THROMBOEMBOLISM AND DEEP VEIN THROMBOSIS: A CASE REPORT

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Background and Aims: Acute pulmonary thromboembolism (PE) with deep vein thrombosis (DVT) of the lower extremities is very common disease. But a few cases reported about the acupuncture induced PE and DVT.

Methods: We introduce a case report of the PE and DVT due to acupuncture, an ancient alternative medical treatment in East Asia.

Results: A 57-year-old man presented to the emergency room with a 1 day history of acute dyspnoea. He received several acupuncture treatments for leg muscle pain three times a week from one month before admission. A chest radiograph and ECG showed normal. Transthoracic echocardiogram performed in the emergency room showed mild

increased right ventricular (RV) size without D-shape. Computerized tomography of 3D angio pulmonary artery and deep vein thrombosis demonstrated multifocal intraluminal filling defects both main pulmonary arteries, right distal femoral vein and popliteal vein. Initial investigations revealed a normal complete blood count, creatinine, coagulation panel, cardiac marker, D-dimer and thrombophilia testing. He was treated with low molecular weight heparin in therapeutic dosage and at the time of discharge he replaced oral rivaroxaban.

Conclusion: Acupuncture is widely used in East Asia as a medical therapy. Serious side effects associated with acupuncture are reported such as PE with DVT, recently. So physicians should keep in mind acupuncture-related complications.

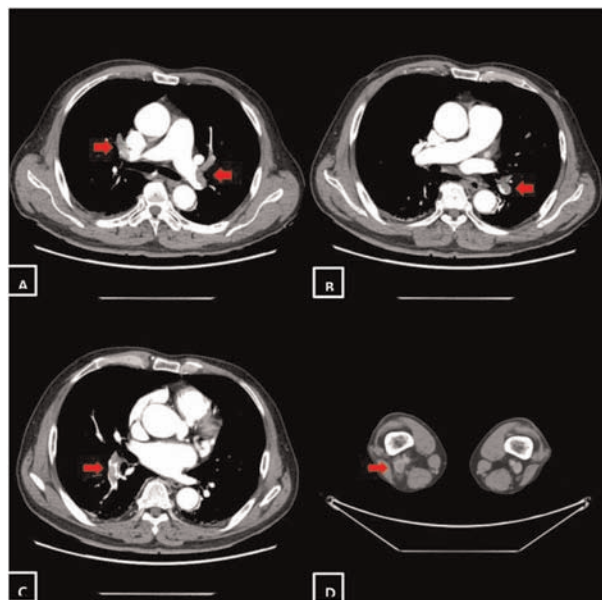


Figure 1. The 3D angio pulmonary artery and deep vein thrombosis CT. A) The intraluminal filling defect due to thrombi in main pulmonary arteries, B,C) Thrombus in both lobar bronchial arteries, D) Thrombi on right popliteal vein

Respiratory Infections (Non-Tuberculous) 2

AP581

THE CLINICAL FEATURES ANALYSIS OF TRACHEOBRONCHIAL FUNGAL INFECTIONS WITH TUMOR-LIKE LESION

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Background and Aims: Tracheobronchial fungal infections (TBFI) are life-threatening complications in immunocompromised hosts, but are rarely reported. Misdiagnosis and delayed antifungal treatment are associated with the high mortality rate of TBFI. This study analyzed the bronchoscopic features of TBFI and their roles in the early diagnosis of TBFI.

Methods: The demographic, clinical, radiological, and bronchoscopy data of 53 patients diagnosed with TBFI in our department during a 15-year period were retrospectively analyzed.

Results: Most of the TBFI patients were male, and mass was the most common radiologic abnormality in TBFI. Obvious predilection in primary bronchus distributions was observed. 41.9% of the 43 *Aspergillus* Tracheobronchitis (AT) patients, 70% of the 10 tracheobronchial mucormycosis (TM) patients, and 100% of the 3 endobronchial cryptococcosis

patients had been misdiagnosed with cancer under bronchoscopy because of tumour-like lesions. The most common features of AT were bronchial occlusion with mass or mucosal necrosis, or bronchial stenosis with mucosal hyperplasia or uneven mucosa. The majority descriptions of TM were bronchial stenosis or obstruction due to mucosal necrosis, uneven mucosa or mass. The endoscopic characteristics of endobronchial cryptococcosis included occlusion due to uneven mucosa or mass, external compressive stricture.

Conclusion: The immunocompromised patients with tumour-like lesions under bronchoscopy should be differentially diagnosed with cancer. Biopsy specimen by bronchoscopy is indispensable for early diagnosis of TBFI.

AP582

PROSPECTIVE INVESTIGATION OF ELDERLY NON-TUBERCULOUS MYCOBACTERIA (NTM) LUNG DISEASE: THE ACTUAL TREATMENT AND THE PROGNOSIS IN CLINICAL SETTING

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Background and Aims: The incidence of nontuberculous mycobacteria (NTM) has increased over the last decades. Given the importance of NTM infection in the current clinical setting, there are concerns about how to treat/manage NTM pulmonary infection in elderly subjects. However, the most prescribed regimen, persistent rate and efficacy of the treatment, the prognosis after the treatment and/or the adverse effect caused by the treatment for NTM in elderly patients remains unclear.

The aim of this study was to evaluate the clinical course of NTM infection, the treatment condition for NTM and the prognosis in elderly patients.

Methods: We retrospectively reviewed the clinical records of consecutive 161 patients diagnosed with NTM lung disease in our hospital (a regional central hospital in Japan), between January 2007 and December 2017. The patients were divided into two group in age (<75 or ≥75). The patient characteristics, administered treatment including palliative care, the adverse effect of treatment, the change in radiological and clinical findings were evaluated.

Results: Among enrolled 161 patients, there were 74 patients with age ≥ 75, and 87 patients who are younger than age < 75. There were 26 patients treated among these elderly patients. The median overall survival of elderly patients was 1208 days and 365 days for treated group and non-treated group, respectively ($P = 0.0166$).

Conclusion: These results suggest that antibiotics therapy may have a favourable outcome in elderly patients with NTM lung disease.

AP583

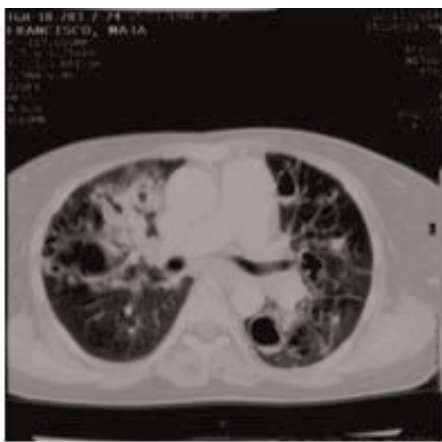
JOB'S SYNDROME: RECURRENT PULMONARY INFECTIONS IN PRIMARY IMMUNODEFICIENCY, A CASE REPORT

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Background and Aims: Primary immunodeficiency disorders are less encountered but should be a consideration in patients with recurrent pulmonary infections. One of these is the so called Autosomal Dominant Hyperimmunoglobulin E syndrome or Job's syndrome, coined after a biblical figure Job who got afflicted with boils. HyperIgE syndrome is a primary immunodeficiency diagnosed by the combination of the triad of recurrent skin infections, and lung infections and elevated serum IgE levels.

Methods: Our patient is a case of Autosomal Dominant Hyper IgE Syndrome diagnosed 30 years ago based on clinical presentation of frequent recurrent craniofacial skin infections and elevated IgE levels. Thereafter, there was decreased frequency of skin infections, however, with increasing episodes of recurrent upper and lower respiratory tract infection occurring approximately 2–3 times yearly. 2 months before admission, when she complained of intermittent frontal headache. She underwent Cranial CT scan with contrast which revealed Moderate Communicating Hydrocephalus; Chronic Non-haemorrhagic infarct of the left putamen and head of the left caudate nucleus and Bilateral mastoid disease. She underwent High Resolution Chest CT scan with contrast which revealed Cystic bronchiectasis, bilateral with bullae (6.3 × 6.1 cm), both upper lobes with a few containing minimal fluid levels suggestive of infection; pneumonic consolidation and lung abscess, (3.6 × 3.4 cm) middle lobe.



Results: Recurrent pneumonias start early in life, and are frequently complicated by the development of pneumatoceles and bronchiectasis. HIES is characterized by dermatitis and recurrent infections (bacterial sinopulmonary and skin infections). Patients often have chronic upper airway infections with persistent and/or recurrent episodes of sinusitis, suppurative otitis media, and mastoiditis.

Conclusion: Job's syndrome is a rare primary immunodeficiency syndrome characterized by the triad of recurrent skin infections, lung infections and elevated IgE levels. Recurrent pulmonary infections could lead to cardiovascular and neurologic complications and the cornerstone for management is mainly supportive and must involve a multidisciplinary approach.

AP584

PROGNOSIS OF PATIENT WITH BRONCHIECTASIS AFTER HOSPITALIZED EXACERBATION

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Background and Aims: Pneumonia is one of the major reason of hospitalization for patients with bronchiectasis, but there is little literature about the prognosis of the patients who survived after the hospitalized exacerbation. The aim of this study was to investigate the mortality and the affecting factors in patients with bronchiectasis after hospitalized exacerbation.

Methods: This retrospective study comprised 74 patients survived from hospitalized exacerbation of bronchiectasis due to bacterial pneumonia from January 2011 to February 2017. Demographic data, comorbidity, severity of the disease, sputum microbiology and modified Medical Research Council (mMRC) Dyspnoea Scale were examined, and their impact on mortality were assessed.

Results: On univariate analysis, male sex ($P = < 0.01$), BMI ($P = 0.02$), chronic Candida infection ($P = 0.029$), high score (3 or 4) on mMRC at discharge ($P = < 0.01$) were associated with poor survival after the admission. Seven patients with high mMRC score have followed by 1-month rehabilitation after the discharge and 5 out of the 7 patients successfully achieved improved mMRC scale up to 1 or 2.

Conclusion: Male sex, BMI, chronic Candida infection, high score (3 or 4) on mMRC at discharge were associated with poor survival. However, proceeding rehabilitation may successfully improve mMRC.

AP585

GENOTYPIC CHARACTERISTICS OF CARBAPENEM-RESISTANT ENTEROBACTERIACEAE IN ONE OF SECONDARY REFERRAL HOSPITAL IN SOUTH KOREA

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Background and Aims: Carbapenem-resistant *Enterobacteriaceae* (CRE) infections are associated with poor outcomes and treatment options are limited because of resistant to nearly all antibiotics. CRE infections are typically seen in patients with prior healthcare exposure rather than home residents. Hospitalization patients with initially CRE positive have been increasing in our hospital. The aim of this study was to investigate clinical features of patients with initially CRE positive in emergency room (ER) of one of secondary referral hospital in South Korea.

Methods: Patients visiting ER were conducted a surveillance study of CRE colonization, from NOV 24, 2016 to DEC 31, 2017. A total of 251 patients tested PCR for CRE with rectal swab.

Results: Sixty four patients (25%) were colonized with CRE. Most of the patients were referred from long-term care hospitals (70%, $P < 0.001$) (Figure). It was the patients referred from sanatoria that colonized CRE and true pathogens were the same (39%, $P = 0.004$). *K. pneumoniae* and *E. coli* were main species (each 36%). *Klebsiella pneumoniae* carbapenemase (KPC) gene was detected in 30 patients, imipenemase (IMP) gene in 22, Oxacillinase-48-type carbapenemases (OXA-48) gene in 5, New Delhi Metallo- β -lactamase (NDM) gene for 14, and Verona Integron-encoded Metallo- β -lactamase (VIM) gene for 6. Both KPC and NDM genes were produced by 4 strains, KPC and IMP genes by 2 strains, KPC and VIM genes by 2 strains, NDM and IMP genes by 2 strains, NDM and OXA-48 genes by 1 strain, VIM and IMP genes by 1 strain, and KPC, IMP and NDM genes by 1 strain, and one strain was not identified genotype. NDM gene was mainly detected in patients referred from hospitals (22%, $P = 0.008$).

Conclusion: The incidence of CRE colonized and infection were increasing in ER admitted patients referred from sanatoria in our hospital. NDM-positive CRE has to be also keep in mind in hospital environment.

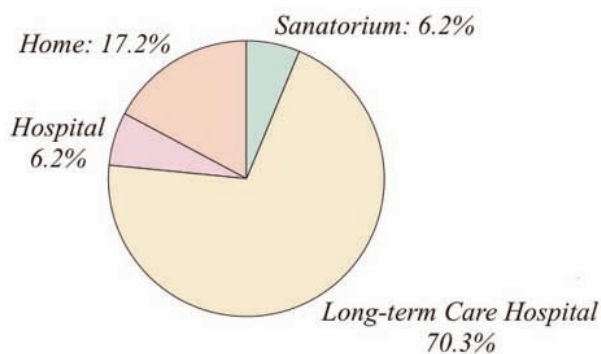


Figure. Distribution of Residence

AP586

THE LIMITED IMPACT OF PSYCHIATRIC DISEASE AND PSYCHOTROPIC MEDICATION ON THE OUTCOME OF HOSPITALIZATION FOR PNEUMONIA

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Background and Aims: Psychotropic medicine has been suggested to be a risk factor for the onset of pneumonia, especially aspiration pneumonia. However, the impact of coexisting psychiatric disease and psychotropic medication on the outcomes of pneumonia patients in the respiratory care unit setting is less well-known.

Methods: We conducted a single-centre retrospective study of 209 consecutive patients who were hospitalized due to pneumonia. Using the patients' records, coexisting psychiatric diseases and the use of psychotropic medicines were reviewed to examine their association with the clinical course of inpatients with pneumonia.

Results: Psychotropic medicines, including agents for insomnia, were used in 73 (34.9%) patients, and there were 35 (16.9%) patients who had psychiatric disease. Among the 12 (5.7%) fatal cases, 4 patients were treated with psychotropic medicines, all of which were agents for insomnia. However, the rate of psychotropic medicine usage in the fatal cases (33.3%) was equivalent to that of the survivors (35%), and the coexistence of psychiatric disease did not affect survival. The duration of hospitalization of the patients who received psychotropic medicines (median 17 [range: 7–89] days) was also equivalent to that of the other patients (14 [2–55] days, $P = 0.081$).

Conclusion: While the present study was a single-centre study and had a small population, coexisting psychiatric disease and psychotropic medicine use did not have a strong impact on the outcomes of pneumonia patients who were hospitalized in the respiratory unit of a university hospital. Further prospective studies targeting a larger cohort are needed.

AP587

PREDICTORS OF 30 DAYS MORTALITY AMONG COMMUNITY-ACQUIRED PNEUMONIA PATIENTS WITH COMORBIDITY IN TERTIARY CARE HOSPITAL

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Background and Aims: Community-acquired Pneumonia (CAP) is one of the leading cause of death from infectious disease in developing

countries. The prediction of outcome is important in decision-making process. Several studies to developed or evaluated scoring system has been done, but the scoring system performance was not superior in some groups of patients especially patients with comorbidity. According to the fact, we need to studied predictors that affect the 30 days mortality among CAP patients with comorbidity. The purpose of this study was to determine the predictors of 30 days mortality in CAP patients with comorbidity in the biggest referral hospital in Indonesia.

Methods: We performed a prospective cohort study among 267 CAP patients with comorbidity in Cipto Mangunkusumo Hospital between October-November 2017. Data were collected at initiation of hospitalization period and the main outcome was all-cause mortality during 30 days. Chi-square test were used to determine the association between variables. Multiple logistic regression analysis was used to determine independent risk factors for mortality. The odds ratio (ORs) and corresponding 95% confidence intervals (Cis) for each variable were calculated.

Results: Among 267 patients there were 31.5% of 30 days mortality rate. The independent predictors of mortality were confusion ($P < 0.01$ OR 1.7 [95% CI 1.2–2.4]), respiratory rate $\geq 30/\text{min}$ ($P < 0.01$ OR 3.3 [95% CI 2.5–4.4]), pulse $\geq 125/\text{min}$ ($P < 0.01$ OR 3.0 [95% CI 2.3–4.0]), low blood pressure systolic < 90 mmHg or diastolic ≤ 60 mmHg ($P < 0.01$ OR 2.0 [95% CI 1.4–2.9]), albumin < 3.5 g/dL (P 0.02 OR 2 [95% CI 1.1–3.7]), platelet count $< 100,000/\text{L}$ ($P < 0.01$ OR 1.8 [95% CI 1.2–2.6]).

Conclusion: Confusion, respiratory rate $\geq 30/\text{min}$, pulse $\geq 125/\text{min}$, low blood pressure systolic < 90 mmHg or diastolic ≤ 60 mmHg, albumin < 3.5 g/dL, platelet count $< 100,000/\text{L}$ were independent predictors of 30 days mortality among CAP patients with comorbidity.

AP588

MALNUTRITION ALTERS PERFORMANCE STATUS OF ELDERLY PATIENTS WITH PARAPNEUMONIC EFFUSION

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Background and Aims: Parapneumonic effusion (PPE) is one of the common complications in pneumonia, and may get seriously ill. Performance status (PS), a measure of general well-being or activities of daily living of patients, may also get worse in spite of the recovery from PPE, especially in elderly patients. The aim of this study is to evaluate the alteration of PS among patients with PPE.

Methods: Patients were eligible for this study if they were 60 years or older, and were diagnosed with PPE in Yamagata City Hospital Saiseikan from April 2008 to March 2017. Patients were divided into two groups based on alteration of PS during hospital stay: the upkeep of PS (UPS group) and the worse of PS (WPS group). Clinical parameters and laboratory examination of serum, blood or pleural effusion were analyzed in both groups. Data were statistically analyzed using R software (Ver. 3.4.0).

Results: A total of 100 patients (68 male and 32 female) were enrolled in this study. The median age of the patients was 77 years (60 to 100 years). There were 54 patients in UPS group and 46 patients in WPS group. Patients in WPS group were older than those in UPS group (82.9 vs 78.6 years old; $P < 0.05$). WPS group showed significantly lower than UPS group in the values of serum albumin (2.3 vs 2.6 g/dL; $P < 0.05$) and body mass index (BMI; 19.4 vs 21.1 kg/m²; $P < 0.05$). There were no significant differences in other laboratory values of serum, blood, or pleural effusion between both groups. Furthermore, the length of hospital stay in WPS group was longer than UPS group (41.3 vs 24.8 days; $P < 0.05$).

Conclusion: Lower serum albumin or BMI could be the prognostic factors that worsen PS in elderly patients with PPE, suggesting that malnutrition would be unfavourable for clinical course of PPE.

Respiratory Infections (Non-Tuberculous) 2

AP590

A CASE REPORT: THE COEXISTENCE OF PULMONARY CRYPTOCOCCOSIS AND GRANULOMATOSIS WITH POLYANGIITIS

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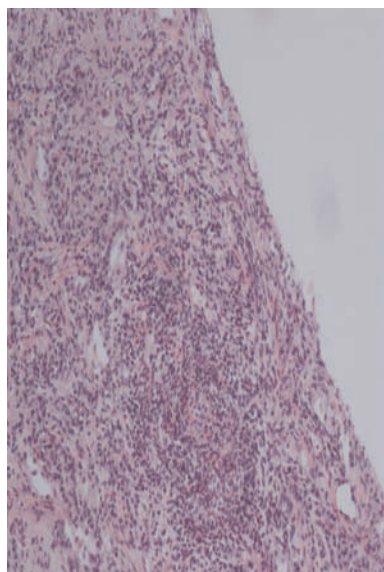
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Background and Aims: Granulomatosis with polyangiitis is a systemic disease of unknown aetiology characterized by the progressive necrosis of granuloma and extensive meningitis. Granulomatosis with polyangiitis combining with infection is not common, especially with pulmonary cryptococcus disease.

Methods: We present a rare case of a 56-year-old Chinese woman who presented with repeated malaise, fever, cough and haemoptysis. Her initial chest CT scan showed multiple subpleural masses with visible cavity. Piperacillin and moxifloxacin were successively applied, however, the drugs were ineffective, and the pulmonary masses became larger than before. Then the antigen of cryptococcus capsule histoplasma was tested positive. After the application of fluconazole, her fever was gone. However, during the treatment, the repeated urine routine indicated RBC (++) . Further investigations of urinary system suggested ANCA-PR3 (+) as well as c-ANCA (+). Whereafter, the percutaneous lung centesis was taken, and granulomatosis with polyangiitis coexisted with pulmonary cryptococcosis was verified by the biopsy eventually. Based on the result, corticosteroid therapy was introduced in the patient. After 1 month of treatment, her symptoms of cough, haemoptysis and malaise were gone, and the chest CT scans showed the masses dwindled down and the cavity was gone. The antigen of cryptococcus capsule histoplasma was tested negative eventually after the application of fluconazole for 13 months.

Results: The case was eventually diagnosed as the coexistence of pulmonary cryptococcosis and granulomatosis with polyangiitis.

Conclusion: This case is aimed at improving the clinician's ability to recognize granulomatosis with polyangiitis complicated with pulmonary infections, and avoid the misdiagnosis of pulmonary cavity.



QUICK SOFA AND PERFORMANCE STATUS SCORING SYSTEMS PREDICT THE PROGNOSIS OF PNEUMOCOCCAL COMMUNITY-ACQUIRED PNEUMONIA

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Background and Aims: Pneumococcus (*Streptococcus pneumoniae*) is one of the most common pathogens that cause community-acquired pneumonia (CAP). Pneumococcal CAP (pCAP) sometimes develops into sepsis and may get seriously ill. Several clinical scoring systems have been widely used for the evaluation of severity of CAP or sepsis. The aim of this study is to evaluate the clinical factors that predict mortality of pCAP.

Methods: Patients were eligible for this study if they were 16 years or older, and were diagnosed with pCAP in Yamagata Prefectural Central Hospital from January 2012 through May 2018. pCAP was defined by single isolation of *S. pneumoniae* from sputum or blood culture among CAP patients. Patients were divided into two groups based on the 60-day mortality: the survivors and the non-survivors. Clinical parameters including performance status (PS) were assessed in both groups. Disease severity was evaluated by A-DROP, CURB-65, and quick Sequential Organ Failure Assessment (qSOFA) scores. Data were statistically analyzed using JMP 11 software.

Results: A total of 192 patients (135 men and 57 women) were enrolled in this study. The median age of patients was 77 years (21 to 97 years). There were 169 patients in the survivors and 22 in the non-survivors. *S. pneumoniae* were more frequently detected in blood cultures from the non-survivors compared to the survivors (27.3% vs 7.7%, respectively; $P = 0.01$, chi-square test). The non-survivors showed poor PS (PS ≥ 3), higher A-DROP score (A-DROP ≥ 3), and higher qSOFA score (qSOFA ≥ 2) compared to the survivors ($P = 0.002$; 0.02; 0.0003, chi-square test, respectively), whereas there was no difference in CURB-65 score between both groups. Multivariate analysis indicated that higher qSOFA score and poor PS were the independent risk factors for the 60-day mortality in pCAP (Odds Ratio 4.0 [95% confidence interval: 1.3–13.3], 4.0 [1.4–10.9], respectively).

Conclusion: qSOFA and PS would be useful scoring systems that could predict the prognosis of pCAP.

AP592

IMPLEMENTING A CARE BUNDLE APPROACH REDUCES DURATION OF LENGTH OF STAY IN COMMUNITY-ACQUIRED PNEUMONIA

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Background and Aims: Community-acquired pneumonia (CAP) is the second leading cause of mortality worldwide and mortality in hospitalized patients is as high as 13%. The effectiveness of prevention bundles on the occurrence and mortality of ventilator associated pneumonia (VAP) was evaluated in many studies. However, there were no similar bundles for CAP. This study aims to evaluate an alternative model of care designed to improve adherence to four evidence-supported interventions (early switch to oral antibiotics, early mobilization, chest physiotherapy and routine malnutrition screen)

Methods: Patients who meet a standard case definition for CAP will be included. Two internal medicine units at one hospital will be

randomized using concealed allocation to: (i) usual medical, nursing and allied health care delivered according to existing organizational practice (usual service, $n = 36$) or (ii) care supported by a dedicated "community-acquired pneumonia service" (CAP service, $n = 36$): a multidisciplinary team deploying algorithm-based implementation of a bundle of the four evidence-based interventions. Multivariable regression models assessed hospital length of stay (LOS), 30-day mortality, total hospital cost, and oral antibiotics duration after discharge.

Results: We calculated multivariate regression models adjusted for age, gender, comorbidities and severity of illness and accounting for clustering within hospitals to compare LOS and outcomes between "usual service" and "CAP service". LOS in CAP service was significantly shorter compared to usual service (6.5 vs 7.8 days, absolute difference 1.3 days [95%CI (-2.000,0.000)]) and decreased total hospital cost (24670 vs 29169 NTD, $P = 0.313$). However, prolongation of oral antibiotic treatment after discharge was noted. (27.8% vs 5.6%, $P = 0.01$). There were no differences in 30-day mortality rates or recurrence rates within 14 days.

Conclusion: Management by a care bundle approach reduced hospital LOS and hospital cost compared with standard of care. However, prolongation of oral antibiotic treatment after discharge was noted in our study. Further studies are required to validate these findings for other patient populations.

AP593

LONG-TERM OBSERVATION OF ANTI-GLYCOPEPTIDOLIPID-CORE ANTIBODY TITER IN PATIENTS WITH MYCOBACTERIUM AVIUMCOMPLEX-POSITIVE LUNG DISEASE

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Background and Aims: The incidence of pulmonary *Mycobacterium avium* complex (MAC) has increased in middle-aged women with a change in its mode of development. For example, cases can show the minimal progression of minor lesions, no change for a long period of time but then rapid progression, and lesion regression despite treatment. We performed the long-term observation of patients in whom pulmonary MAC had been suspected on the basis of clinical presentation, diagnostic imaging, and an antibody assay.

Methods: From January 2012 through December 2013, 109 patients had characteristic lesions found with imaging examinations and positive results of an assay for anti-glycopeptidolipid-core antibody; 90 of these patients with a chronic illness were reviewed regarding the clinical course, imaging findings, bacterial tests, and changes in antibody titre.

Results: During observation MAC disease was definitively diagnosed in 47 patients and was suspected in 62 patients. Imaging findings showed both improvement and worsening in 8 patients, in whom the fluctuation in antibody titre was small.

Imaging findings worsened in 38 patients; the antibody titre increased in some patients, showed no change in most patients, and decreased in 2 patients. Imaging findings improved in 18 patients, in whom antibody titres generally decreased.

Imaging findings showed no change in 62 patients, in whom antibody titres changed only slightly but usually decreased. Although imaging finding showed only a slight change, the antibody titre remained high. In 1 patient, the antibody titre increased despite no change in imaging findings.

Conclusion: Pulmonary MAC can be a chronic condition, but long-term antibody titres have rarely been reported. The present study observed antibody titres for 5 years, but we believe that it tends to be compared with the change of the disease condition. We believe that the antibody titre should be observed.

AP594

SMALL COHORT RETROSPECTIVE STUDY MIXED CO-INFECTION OF FUNGUS IN PNEUMONIA POPULATION

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Background and Aims: The top cause of death in Taiwan in 2016, pneumonia ranked 3rd from statistics of official. Due to global climate change, high temperature, humidity have become common air condition. Fungus distribution and growth under such climatic conditions cannot be ignored in environment. Especially furniture is highly vulnerable to fungal growth in interior decoration. This environmental health issue is worth exploring influenced the airway.

Methods: All cases requested for medical intervention either outpatient or hospitalization objects recruited since 2015 until 2018 now 2 YEARS account of Chest X-ray abnormality with major Respiratory symptoms. Entire cases proved fungal infection in respiratory systems by way of fungus antigen, culture and pathology confirmation. All possible clinical variables included age gender CXR pattern diagnostic methods treatment, performance, Sequelae prognosis, comorbidity variables were included for analysis.

Results: Regardless of Clinical or imaging and fungus species have completely different performance and outcomes. It can be said that the diversification hard to think of once. Simply speaking, it varies from person to person, time to treatment correlated with mortality.

Conclusion: Lack of epidemiological data, about immunity suppression and normal population statistics bring out, this type of infection is often forgotten. Finding the presence of pathogenic bacteria is always a challenge for clinicians, all kinds of diagnostic tools emerged key. For our analysis of mycotic infections in unusual clinical manifestations and chest image, we need to exclude. Clinical guidelines did not record but worthing discussion. Early BAL, tissue biopsy are key points and intervals for diagnosis in symptomatic victims. Proper control of respiratory bacterial infection is priority. Laboratory and pathology must detect over BAL specimen. We speculate that airway fungal colonization from continental airflow dust from desert regions can carry partial source of fungal spores to impact air quality included indoor air in remote area. If fungus or their bio-marker detected by interventional methods, empirical therapy should be aggressively planned to proceed.

AP595

CANDIDAL TRACHEOBRONCHITIS AFTER TOTAL AORTIC REPLACEMENT AND THORACIC ENDOVASCULAR AORTIC REPAIR

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Background and Aims: Candidal tracheobronchitis is a rare disease. Candida species cultured from respiratory tract sample are usually considered as a colonization, however, they can very occasionally be regarded as a pathogen in ICU settings. Thoracic Endovascular Aortic Repair (TEVAR) is a novel therapy for aortic aneurysm. TEVAR is less invasive therapy than vascular graft replacement, and respiratory complications associated with TEVAR are uncommon.

Methods: Here, we report a case of candidal tracheobronchitis after total aortic arch replacement and TEVAR.

Results: The patient is a 77 year old male. He underwent total aortic arch replacement and TEVAR for rupture of thoracic aortic aneurysm. Four stents were placed along the total descending thoracic aorta. Three days after the operation, the respiratory pattern on the ventilator monitor changed to an obstructive pattern. The bronchoscopic findings showed diffuse yellowish-white pseudo-membrane of tracheobronchial trees and partial bronchial obstruction. Pseudo-membrane was localized from trachea to segmental bronchi. Peripheral bronchi were intact and there was no definitive pneumonia. *Candida albicans* was detected by Gram staining and culture of the pseudo-membrane. We diagnosed the condition as candidal tracheobronchitis. We considered that acute ischemic damage of tracheobronchial mucosa due to obstruction of the bronchial artery by stenting graft placement predisposed to the fungal infection. Antifungal agent was administered intravenously and by inhalation. Pseudo-membrane gradually resolved, however, bronchial stenosis developed subsequently and balloon dilation was needed.

Conclusion: Candidal tracheobronchitis is rare, however it is known to occur especially in an immunocompromised patient. Reported predisposing factors include older age, endocrine disorders, malignant neoplasms, alteration of immunologic status, prolonged antibiotic therapy, neutropenia, and aplastic anaemia. In our case, acute ischemic damage of tracheobronchial mucosa was considered to have contributed to the susceptibility to active candidal infection. This case also indicated that respiratory complications can occur after TEVAR.

AP596

PNEUMOCOCCAL URINARY ANTIGEN TEST USE AS A PROGNOSTIC MARKER IN PATIENTS ADMITTED WITH COMMUNITY-ACQUIRED PNEUMONIA: A PROPENSITY SCORE MATCHING STUDY

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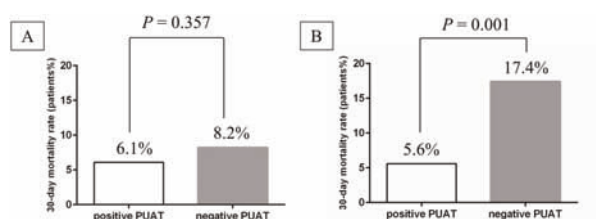
Background and Aims: Although pneumococcal urinary antigen test (PUAT) have widely used for diagnosis of pneumococcal pneumonia, the clinical benefits derived from the results of PUAT have not been fully established. The objective of our study was to determine prognostic performance of the PUAT in patients with community-acquired pneumonia (CAP).

Methods: We conducted retrospectively cohort study of consecutively collected patients diagnosed with CAP. Patients were classified according to the results of the PUAT and were matched using the propensity score matching method. Primary outcome was the 30-day mortality.

Results: A total of 1257 patients were identified and 163 (13.0%) had the positive PUAT. The sensitivity and specificity of PUAT for overall pneumococcal pneumonia were 49.0% and 90.2%, respectively. The positive PUAT group did not show worse clinical parameters compared to negative PUAT group. In the full cohort, there were no significant differences in the 30-day mortality between two groups (6.1% in the positive PUAT group vs 8.2% in the negative PUAT group; $P = 0.357$). Instead, in the propensity matched cohort, the 30-day mortality rates were lower in the positive PUAT group (5.6% vs 17.4%; $P = 0.001$). In subgroup analysis, comparable results of the 30-day mortality were obtained in patients with severe pneumonia. In secondary outcomes, the proportion of patients with potentially drug-resistant pathogens, the change of antibiotics, and failure of initial antibiotic therapy was significantly lower in the positive PUAT group compared to the negative PUAT group of propensity matched cohort (4.3% vs 10.6%; $P = 0.034$, 17.4% vs 26.7%; $P = 0.044$, and 14.9% vs 30.0%; $P = 0.004$, respectively).

Conclusion: Our findings suggest that positive PUAT results may be associated with favourable clinical outcomes in patients with CAP.

Therefore, the PUAT might be considered as an early prognostic marker in these patients.



AP597

ONE CASE OF PNEUMOCONIOSIS ASSOCIATED WITH PULMONARY NOSOCOMIAL INFECTION

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Background and Aims: To understand the clinical manifestations, imaging features and bacteriological examination of pulmonary nocardiosis, so as to improve the understanding of the disease and avoid misdiagnosis and mistreatment.

Methods: In 1 case with cough and expectoration, fever as the main clinical manifestations, sputum positive acid-fast stain, misdiagnosed as tuberculosis lung slave card fungus infection in patients with clinical characteristics were analyzed, and the and retrospective review of relevant literature.

Results: Fever, cough and cough phlegm are the most common symptoms of pulmonary nocardiosis. The imaging features are not specific, and the sputum and secretion are positive for anti-acid staining. Laboratory examination is an important basis for diagnosis.

Conclusion: The clinical features of pulmonary nocardiosis are not specific, and are similar to other pulmonary diseases, which may lead to misdiagnosis and mistreatment. We should be alert in our clinical work.

AP598

THREE CASES OF POM-1 METALLO- β -LACTAMASE PRODUCING *PSEUDOMONAS OTITIDIS* ISOLATED FROM RESPIRATORY SPECIMENS

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Background and Aims: *Pseudomonas otitidis* was first described in 2006 as a causative agent of otic infections. Isolation of this organism from non-otic specimens has not been reported. Genotypically and phenotypically, *P. otitidis* is closely related to *Pseudomonas aeruginosa*. It causes misidentification of *P. otitidis* as *P. aeruginosa*.

Methods: We retrospectively reviewed the clinical data of patients from whom *P. otitidis* was isolated. All specimens were obtained from patients in the Ryukyu University Hospital, Okinawa, Japan.

Results: There were three cases of *P. otitidis* isolated from respiratory specimens. Isolates were originally misidentified as *P. aeruginosa* or *P. putida* by morphological and biochemical characteristics. However, analysis of 16S rRNA sequences and MALDI-TOF MS system revealed

these isolates to be *P. otitidis*. All strains were susceptible to piperacillin and antipseudomonal cephalosporins, although resistance or decreased susceptibility to carbapenems was observed.

Conclusion: *P. otitidis* has a resident metallo- β -lactamase (MBL) gene and produces an MBL, named POM-1. When *Pseudomonas* species shows unusual β -lactam susceptibility, physicians should consider *P. otitidis* and use appropriate methods for identification.

AP599

INCIDENCE AND CLINICAL FEATURES OF COMMUNITY-ACQUIRED PNEUMONIA CAUSED BY MACROLIDE-RESISTANT *MYCOPLASMA PNEUMONIAE* FROM ADULTS IN JEJU

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Background and Aims: *Mycoplasma pneumoniae* is not an uncommon cause of community-acquired pneumonia (CAP), particularly in school-aged children and young adults. Macrolides are generally considered as the treatment of choice for *M. pneumoniae* respiratory tract infections. Although the rate of macrolide-resistant *M. pneumoniae* (MRMP) has been increasing substantially among children, there are very few studies that have focused on MRMP in adult patients with CAP. The purpose of this study is to investigate incidence and clinical features of CAP caused by MRMP from adults in Jeju, the largest island off the southern coast of Korea.

Methods: We retrospectively recruited adult patients with CAP in whom *M. pneumoniae* infections had been confirmed over a 7-year period. MRMP was examined by amplification of macrolide resistance genes using the stored specimens. The patients were divided into the MRMP and macrolide-sensitive *M. pneumoniae* (MSMP) groups.

Results: A total of 70 subjects were included, 34 (48.6%) males and 36 (51.4%) females. The mean age was 46.1 years. There were only 2 patients (2.9%) who carried macrolide resistance mutations in the 23S rRNA gene, and all the mutations were A2063G transitions. No significant differences were observed in age, comorbidities, symptoms, CURB-65 scores, the duration of fever, and length of hospital stay between MRMP and MSMP groups. The number of involved lobes was greater in the MRMP group (3.50 ± 0.71 vs 1.44 ± 0.74 , $P = 0.008$). Pleural effusion was detected in 8 patients (11.4%) of the MSMP group, but not in the MRMP group.

Conclusion: The incidence of CAP caused by MRMP was relatively low in adults in Jeju. Patients with MRMP pneumonia tended to have multilobar pneumonic infiltrates.

Acknowledgments: This work was supported by a research grant from Jeju National University Hospital in 2017.

AP600

ADVANCES IN ESTABLISHMENT OF BRONCHIECTASIS ANIMAL MODEL

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Background and Aims: The incidence and mortality of Bronchiectasis have increased steadily in recent years. A perfect animal model is important for its fundamental research. This review aims to evaluate the present methods of Bronchiectasis rat model and provide basis for further study.

Methods: We searched the PubMed, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Chongqing VIP and Wanfang Data from their inception dates to May 10th, 2018. The literatures were screened and analyzed. Inducing factors/dose, observation time, evaluation standard of animal model were mainly evaluated.

Results: Sixteen literatures were included. Firstly, the model was established by intratracheal instillation of *Pseudomonas aeruginosa* after tracheotomy, thoracotomy surgery and lobar bronchial ligation. The histopathology of this model resembled that of the human disease. However, the rats faced a double risk of operation and infection with great wound and less livability. Then, based on the first method, Shihong Cao's team established the model by intratracheal instillation of *Pseudomonas aeruginosa* with tracheotomy and made the tracheal intubation extending to about 3cm below the sternal Angle, while without thoracotomy surgery and lobar bronchial ligation. This method improved the successful rate and livability. However, operative wound still exist, the survival time of rats was only about 30 days, which wasn't consistent with disease progression. In addition, the concentration (105 CFU/L, 108 CFU/L, 1012 CFU/L) of *Pseudomonas aeruginosa* is not fixed in these studies, which is difficult for us to copy. The animal models were not concluded to be successful or not by Micro CT, which is a gold standard for diagnosis of Bronchiectasis.

Conclusion: The existing methods of Bronchiectasis animal model still have some deficiencies in application of basic research. A rat model with less trauma, higher success rate, and more similar to histopathology of human bronchiectasis is imperative for further study.

AP601

IS BLOOD CULTURE USEFUL IN THE MANAGEMENT OF ASPIRATION PNEUMONIA?

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Background and Aims: Routine use of blood cultures for immunocompetent patients with community-acquired pneumonia are questioned in terms of cost effectiveness, however, little is known about this point in patients with aspiration pneumonia. The aim of this study is to examine the utility of blood cultures in patients with aspiration

Methods: Patients with aspiration pneumonia admitted to our hospital between April 2016 to March 2017 were included. Background characteristics, results of blood cultures, clinical course were extracted from the medical records, and analyzed descriptively.

Results: 141 patients with aspiration pneumonia were included, and all patients had undergone blood cultures on admission. Blood cultures were positive in only 4 patients (2.8%), and antibiotics were changed based on the results of blood cultures in only 1 patient (0.7%). All of these 4 patients were severe pneumonia (PSI class IV-V), and 2 of 4 patients (50%) died in hospital. In patients with recurrent aspiration pneumonia, blood cultures at every admission were all negative.

Conclusion: This study suggests that the utility of blood cultures in patients with aspiration pneumonia was low. Restricted use of blood cultures may be needed in terms of cost effectiveness.

AP602

ORGANIZATION AND CLINIC-EPIDEMIOLOGIC ASSESSMENT OF EFFICIENCY OF THE REGIONAL PROGRAM OF RESPIRATORY INFECTIONS PREVENTION

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Background and Aims: Acute respiratory infections cause high morbidity and mortality among population and are one of the most important problems of epidemiology and pulmonology. Aim: To assess medical and social-economic efficiency of regional programs of respiratory infections prevention.

Methods: 4988 children at the age from 2 till 5 years having risk factors were included in the program of preventive vaccination with the use of pneumococcal vaccine "Prevenar-13" and influenza vaccine. The assessment of program efficiency is done on the basis of the pneumonia morbidity and mortality monitoring for the period of 2010–2017 on the territory of the Amur region of Russia.

Results: During the year two periods of the morbidity growth were registered: at the 4–7th weeks and 42–50th weeks with the peak in March and October. A correlation of annual dynamics of pneumonia morbidity with the level of acute respiratory viral infections (ARVI) ($r = 0.89$) was revealed. Among patients with pneumonia, adults predominated ($72.7 \pm 0.34\%$). But intensive parameters of the morbidity were significantly higher among children and teenagers (1010.9 ± 126.2 per 100000) than among adults (622.3 ± 61.0 per 100000). The disease was more common for children of 0 to 2 years and senior age people (over 65). Among children pneumonia morbidity in the post-vaccination period decreased 2.3 times. For 10 years the number of people vaccinated increased 2.2 times (from 17.5% till 39.7%), and the level of ARVI and influenza got lower by 29.2%. During the period of realization of preventive programs (2013–2017) the level of pneumonia morbidity on the territory of the Amur region decreased by 35.5% and among children by 2.6 times. The mortality decreased by 44.2% and from pneumonia 3.5 times.

Conclusion: The realization of the regional program of monitoring and prevention of acute respiratory diseases with influenza and pneumococcal vaccines has a high level of medical and social-economic efficiency.

AP603

PULMONARY INFECTION CAUSED BY NOCARDIA FARIGINICA IN AN IMMUNOCOMPETENT PATIENT: A CASE REPORT AND REVIEW OF THE LITERATURE

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Background and Aims: *N. fariginica* infections are rare and potentially life threatening. We herein present a case of *N. fariginica* without significant underlying immunodeficiency, and review the clinical features of *N. fariginica* in 22 cases reported in the literature from 2009 through 2017.

Methods: Case outline: We describe the case of bronchiectasis caused by *N. fariginica* in a 47-year-old female patient. She was admitted to our hospital with a two-day history of productive cough and haemoptysis. CT showed bronchial dilatation and inflammation in the middle lobe of right lung and lower lobe of left lung.

Results: Productive cough and haemoptysis did not improve after two-day treatment with Piperacillin-Tazobactam 2.5 g/day. Later, *N. fariginica* was identified as the responsible organism by 16S rRNA sequencing in sputum and bronchial brush samples, and therefore Piperacillin-Tazobactam therapy was replaced by intravenous TMP-SMX. The patient soon recovered and was discharged from the hospital. Oral TMP-SMX was prescribed as a discharge medication to be used continuously at home.

Conclusion: *N. fariginica* is a rare infectious agent mainly affecting immunocompromised patients. In any case, a higher index of suspicion is needed, as diagnosis can easily be missed due to the absence of characteristic symptoms and the several difficulties usually encountered in identifying the pathogen.

AP604

NATURAL HISTORY OF NON-CAVITARY NODULAR BRONCHIECTATIC MYCOBACTERIUM AVIUM COMPLEX LUNG DISEASE

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Background and Aims: This study investigated the natural history of non-cavitary nodular bronchiectatic (NC-NB) *Mycobacterium avium* complex (MAC) lung disease (LD).

Methods: Among patients diagnosed with NC-NB MAC LD between March 2000 and December 2013, 551 patients who were followed until December 2017 were enrolled at a tertiary referral centre in South Korea. Patients were subdivided into the progressive and stationary group according to whether treatment was started within 3 years from the time of diagnosis. We also investigated the rate of spontaneous sputum conversion in the untreated group.

Results: The mean age of 551 patients was 61.1 years. During the median 5.8 years of follow-up, 323 (58.6%) of the patients received treatment within 3 years (progressive group), whereas remaining 228 (41.4%) patients did not (stationary group). Multivariate analysis revealed that age ≤ 60 years, a positive sputum smear, the presence of any systemic symptoms and *M. intracellulare* isolates were predictors of receiving treatment. Moreover, during the median of 5.0 years follow-up, spontaneous sputum conversion occurred in 52.2% patients among those who did not receive treatment.

Conclusion: Among patients with NC-NB MAC LD, approximately 60% of patients received treatment within 3 years of diagnosis. And about 50% of untreated patients experienced spontaneous sputum conversion.

AP605

MICROBIOLOGICAL PATTERN OF PULMONARY INFECTION PATIENTS IN PERSAHABATAN HOSPITAL INTENSIVE CARE UNIT AND IT'S CORRELATION WITH SEVERITY OF THE DISEASE MEASURE WITH APACHE II SCORE

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Background and Aims: Nosocomial pneumonia acquired in Intensive Care Unit (ICU) include Hospital Acquired Pneumonia (HAIP) and Ventilator Associated Pneumonia (VAP) will prolong length of stay, increase mechanical ventilation and mortality or either resistance with multidrug. In this study we evaluate correlation between severity of pulmonary infection cases using Acute Physiology and Chronic Health Evaluation II and the pathogen and the impact with mortality and length of stay in ICU.

Methods: This study used cross sectional methods that held between August 2017-September 2017 in Persahabatan Hospital Intensive Care Unit. Total subjects consist of 59 patients with lung infection base on consecutive sampling. All of the patients diagnosed with pulmonary infection from specialist and confirmed with radiological findings, measure the APACHE II Score and performed sputum culture and resistance.

Results: In our Hospital (Persahabatan Hospital) 32,2 % are diagnose with HAP and only 1.7 % VAP. Mean APACHE II score at the time admission is 15,21 and 18, HAP has APACHE II score > 16 33,3% and only one patient survived and discharge from ICU meanwhile the VAP patient died. The most common isolation found was gram negative (37,2%) with *Acinetobacter baumannii* (13,6%) followed by *Klebsiella pneumoniae* (11,9%) and the most common gram positive bacteria found is *Staphylococcus hemolyticus* (10,2%). Highest Mortality (52%) are from negative bacteria with highest mortality risk is *Acinetobacter baumannii* 75% (APACHE II Score 30–34).

Conclusion: *Acinetobacter baumannii* was pathogen which related with high APACHE II score and mortality.

AP606

This abstract has been withdrawn.

AP607

ANALYSIS FOR DISTRIBUTION RANGE AND DRUG RESISTANCE OF PATHOGENIC BACTERIA IN SPUTUM OF AECOPD INPATIENTS

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Background and Aims: To explore distribution range, drug sensitivity and drug resistance of pathogenic bacteria in sputum from lower respiratory tract of AECOPD inpatients thus providing evidence for selection of antibiotics during clinical practice.

Methods: From January 2017 to December 2017, clinical data (age, gender, sputum cultivation, drug sensitivity test) collected from 850 cases of AECOPD inpatients admitted at respiratory & ICU departments of the second hospital affiliated to Jilin University were retrospectively analyzed to explore type classification, distribution range and drug resistance of pathogenic bacteria.

Results: Among 850 cases of AECOPD patients, sputum samples from 774 cases (91.06%) were submitted for cultivation with positive rate of 53.49% (414/774), Male: 198 cases, Female: 216 cases, Mean Age: 76.62.

Among 414 sputum samples, 526 strains of pathogenic bacteria were cultivated, with 310 strains (58.93%) of gram-negative bacilli headed by top 5 pathogens including *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter cloacae* and *Escherichia coli*. Meanwhile, 27 strains (5.13%) of gram-positive bacilli, predominantly ranked by *Streptococcus pneumoniae* and *Staphylococcus aureus*, were cultivated. The rest were entirely fungus strains (189 strains/35.93%), mainly confirmed as *Albicans saccharomyces*.

Drug sensitivity distribution of gram-negative bacilli were classified as following: highly resistant to 2nd generation cephalosporin, 3rd generation cephalosporin, quinolone and semi-synthetic penicillins without β -lactamase inhibitor; moderate resistant to 4th generation cephalosporin, aminoglycoside, cefoperazone-sulbactam and piperacillin-tazobactam; sensitive to carbapenems.

Conclusion: Though the importance of etiological examination is increasingly accentuated during clinical practice with general examination rate over 90%, detection rate remains to be improved.

Gram-negative bacilli and fungus strains are ranked as major pathogens for infection of AECOPD cases.

Though Gram-negative bacilli infected by AECOPD cases are highly resistant to 2nd generation cephalosporin, 3rd generation cephalosporin and quinolone, 4th generation cephalosporin, compound agents of penicillin and β -lactamase inhibitor and carbapenems should be selected with preference for treatment according to empirical antibiotic therapy.

AP608

DISSEMINATED MYCOBACTERIUM KANSASII DISEASE IN A PATIENT WITHOUT A DIAGNOSIS OF CLINICAL IMMUNODEFICIENCY

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Background and Aims: Disseminated nontuberculous mycobacterial (NTM) disease is uncommon in HIV-negative patients and usually associated with severe immunosuppression. Disseminated NTM infections in immunocompetent patients have been reported to be associated with acquired anti IFN- γ autoantibodies. Disseminated *Mycobacterium kansasii* infections with lymphadenitis are rare in immunocompetent patients and these infections associated with anti IFN- γ autoantibodies have never been reported.

Methods: A 33-year old who is previously healthy presented with cough and fever for 3 weeks, which persisted after treatment of antibacterial drugs. Chest CT showed air-space consolidation in the right middle lobe of his lung and swelling of the supraclavicular, mediastinal and hilar lymph nodes. Tissue samples obtained via mediastinoscopy indicated granuloma with acid-fast bacteria and the culture of the tissue revealed *Mycobacterium kansasii*. He was made a diagnosis of disseminated *Mycobacterium kansasii* disease.

Results: On the Quanti FERON-TB Gold In-tube (QFT-GIT) test, positive control was negative, which suggested the existence of anti-interferon-gamma autoantibodies, and the enzyme-linked immunosorbent assay test for anti-interferon-gamma autoantibodies (IFN- γ Ab) revealed an increased IFN- γ Ab titre. After diagnosis, he started to receive anti mycobacterial agents. After a week from initial treatment, his symptoms (cough and fever) was worsen. Chest CT showed pericardial and pleural effusion, which suggested paradoxical reaction. Two months were required for improvement of his symptoms. He continues outpatient therapy.

Conclusion: Disseminated *Mycobacterium kansasii* infection is very rare NTM disease condition, which suggests some kind of immunosuppressant status. Physicians should keep in mind the possibility of presence of anti IFN- γ antibodies when they encounter disseminated NTM disease.

AP609

LEGIONELLA PNEUMONIA INDUCED ACUTE RESPIRATORY DISTRESS SYNDROME: CASE SERIES OF A TERTIARY MEDICAL CENTER IN TAIWAN

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Background and Aims: The Legionella pneumonia induced severe pneumonia that required intensive care in about 44% of patients, and the mortality rate ranged from 1% to 10%. However, there was limited literature to discuss on Legionella pneumonia induced acute respiratory distress syndrome (ARDS). In this study, we reported 5 patients with Legionella pneumonia induced ARDS, and tried to find out the clinical characteristics.

Methods: We collected all of the patients admitted to medical intensive care units in Chang Gung Memorial Hospital, Linkou branch from November 2017 to May 2018. The diagnosis criteria of ARDS were based on the Berlin definition in 2012. The Legionella pneumonia was diagnosed by one of the following criteria: positive of *Legionella pneumophilla* antigen test of urine, positive polymerase chain reaction (PCR) or culture of Legionella from sputum, tracheal aspirate or bronchoalveolar lavage (BAL).

Results: Totally, five patients that met the diagnosis of Legionella pneumonia induced ARDS were collected. The mean age was 55.2 years (range 50–61 years). Four patients were male. The mean minimal PaO₂/FiO₂ was 103.8 mmHg. The hospital mortality rate was 40% (2/5). Three survival patients were characteristic with no comorbidity, all of them diagnosed by positive urine antigen, and all of them used appropriate antibiotics at the beginning (Levofloxacin in 2 patients and Azithromycin in 1 patient). One of died patients was diagnosed by BAL fastidious culture, and the doxycycline was used by the result. Another one died patient used empiric Tazocin for the pneumonia, and the final BAL culture confirmed Legionella after the patient was expired. Both of the two died patients had underlying diabetes mellitus.

Conclusion: For patients with Legionella pneumonia induced ARDS, factors associated with poor outcome may include inappropriate antibiotic therapy, underlying diabetes mellitus, and higher bacterial load that with positive culture result.

AP610

IATROGENIC PLEURAL EMPYEMA CAUSED BY PROPIONIBACTERIUM ACNES

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Background and Aims: *Propionibacterium acnes* is one of commensals living on the human skin and glands, implicated mainly in acne, but seldom in deep infection. Pleural empyema is rarely complicated with closed thoracostomy. We experienced a case of empyema caused by *P. acnes* after pleural biopsy and closed thoracostomy through percutaneous pigtail catheter.

Methods: A 79-year-old man was admitted for cough, purulent sputum and shortness of breath. Three weeks before, closed thoracostomy and pleural biopsy were performed for the confirmative diagnosis for his recurrent pleural effusion. He had increased amount of right pleural effusion. Through pigtail catheter, pleural effusion was removed. Gram positive rods were visible in gram stain, but not cultured.

Results: By 16S rRNA analysis, *P. acnes* was confirmed as the pathogen. His empyema was repeatedly treated with antibiotics, fibrolysis and irrigation. Pleural decortication was recommended.

Conclusion: We report a case of empyema with *P. acnes*, firstly in Korea, possibly complicated with closed thoracostomic procedures.

AP611

COMPARISON OF GROCOTT-GOMORI METHENAMINE SILVER AND IMMUNOFLUORESCENCE STAINING FOR DIAGNOSING PNEUMOCYSTIS PNEUMONIA: ANALYSIS INVOLVING QUANTITATIVE PCR FOR DETECTION OF PNEUMOCYSTIS JIROVECI IN BRONCHOALVEOLAR LAVAGE FLUID

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Background and Aims: Pneumocystis pneumonia (PCP) can be diagnosed with Grocott-Gomori methenamine silver (GMS) staining and immunofluorescence (IF) staining. In recent years, quantitative polymerase chain reaction (PCR) for the detection of *Pneumocystis jirovecii* in bronchoalveolar lavage fluid (BALF) has been reported to be useful in PCP diagnosis. However, few reports have compared GMS and IF staining by using quantitative PCR. In this study, we performed quantitative real-time PCR of BALF in order to compare the diagnostic sensitivities of IF and GMS staining.

Methods: Quantitative real-time PCR assay for the detection of *Pneumocystis jirovecii* DNA in BALF was performed in PCP patients who had been pathologically diagnosed by GMS or IF staining of transbronchial lung biopsy specimens and BALF in Osaka City General Hospital between January 2015 and December 2016. The amount of fungus was quantitatively evaluated.

Results: PCP was pathologically diagnosed during the study period in 18 patients (HIV/non-HIV: 15/3; male/female: 17/1). Of the 18 patients, 4 were diagnosed by IF staining alone (group I) and 14 were diagnosed by GMS staining (group G). In all patients from group G, *Pneumocystis jirovecii* was also detectable by IF staining. The sensitivities for PCP diagnosis in groups I and G were 100% and 77.8%, respectively. On comparing the quantitative real-time PCR copy number in BALF between group I and group G, we found that the number was significantly lower in group I than in group G (I vs G: range, 40–6900 vs 42–2700000 copies/mL; median, 144 vs 340,000 copies/mL, $P = 0.01$).

Conclusion: Our findings indicate that IF staining is more sensitive than GMS staining for the diagnosis of PCP. IF staining might be able to diagnose PCP with a small amount of fungus, while GMS staining might not be able to diagnose PCP with a small amount of fungus.

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AP612

DIFFERENT PROFILES OF COUGH HYPERSENSITIVITY MEDIATED BY TRPV1, TRPA1 IN PATIENTS WITH CHRONIC REFRACTORY COUGH

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Background and Aims: TRPA1-mediated cough sensitivity in patients with chronic refractory cough (CRC) remain unclear. We tested the hypothesis that cough hypersensitivity mediated by TRPA1 and TRPV1 might exist alone or coexist in patients with CRC, by establishing allyl isothiocyanate (AITC) cough challenge.

Methods: Inhalation cough challenges with TRPA1 agonist AITC and TRPV1 agonist capsaicin were performed in 250 patients with CRC and 56 healthy volunteers (Table 1).

Results: AITC cough challenge was able to detect cough sensitivity in patients with CRC (Figure 1). Patients had an increased cough sensitivity to AITC compared to healthy volunteers (log C₅: 2.40[1.19, 3.00] vs 2.70[2.10, 3.00] mM, $P = 0.000$) (Figure 2a). Capsaicin challenge showed the same result, values were significantly lower for patients with chronic cough compared with control subjects (log C₅: 1.80[0.29, 3.00] vs 2.70[0.89, 3.00] μM, $P = 0.000$) (Figure 2b). Females showed a heightened AITC cough sensitivity compared to males no matter in patients with CRC (log C₅: 2.40[1.19, 3.00] vs 2.57[1.19, 3.00] mM, $P = 0.001$) or healthy volunteers (log C₅: 2.57[2.10, 2.88] vs 2.88[2.40, 3.00] mM, $P = 0.002$) (Figure 3a, 3b). Female patients had an enhanced capsaicin cough

sensitivity compared to male patients (log C5: 1.50[0.29, 3.00] vs 2.39 [0.29,3.00] μ M, $P = 0.000$) (Figure 3c, 3d). Among 234 patients who finished both challenges, 80 (34.2%) presented hypersensitivity to both AITC and capsaicin while 45 (19.2%) showed hypersensitivity solely to AITC, 45 (19.2%) showed hypersensitivity solely to capsaicin, and 64 (27.4%) exhibited hypersensitivity to neither of them (Table 2). A weak correlation was found between AITC and capsaicin cough sensitivity in patients (log C5: $r_s = 0.331$, $P = 0.000$). The cough reflex was not related to age (Figure 4).

Conclusion: There are different profiles of cough hypersensitivity mediated by TRPV1, TRPA1 in patients with chronic cough, suggesting a selective or combined antagonists therapy targeting TRPV1, TRPA1 or other cough receptors might be effective.

AP612

Title: Different profiles of cough hypersensitivity mediated by TRPV1, TRPA1 in patients with chronic refractory cough

TABLE 1 Clinical characteristics of subjects

	Patients with CRC	Healthy volunteers
Number	230	50
Female (%)	112 (48.7)	27 (54.0)
Age (years) *	42 (3.0-73.9)	36 (3.0-73.9)
Cough duration (months) *	24 (2.0-96.0)	-
AITC challenges, n	230	50
Capsaicin challenges, n	234	51

*Data are expressed as mean $\pm$ SD. *Data were expressed as median (min, max). *Median (min, max).

TABLE 2 TRPV1/TRPA1-mediated cough hypersensitivity in patients with CRC

	Capsaicin		Total
	+	-	
AITC	80 (34.2)	45 (19.2)	125 (53.4)
	45 (19.2)	64 (27.4)	109 (46.6)
Total	125 (53.4)	109 (46.6)	234 (100)

Data are expressed as n (%). + = cough hypersensitivity, - = normal cough sensitivity.

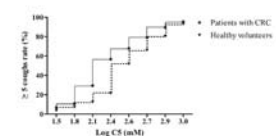


FIGURE 1 Concentration-dependent induction of ≥ 5 cough rate in AITC cough challenge.

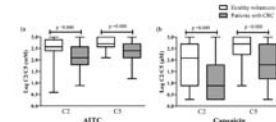


FIGURE 2 AITC and capsaicin cough sensitivity in patients and healthy volunteers. Data are expressed as median (min, max).

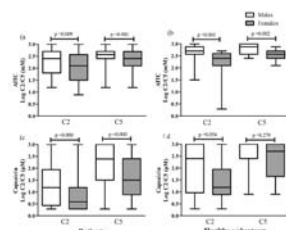


FIGURE 3 Gender difference in AITC/capsaicin cough sensitivity. Data are expressed as median (min, max).

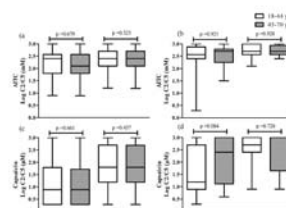


FIGURE 4 Age difference in AITC/capsaicin cough sensitivity. Data are expressed as median (min, max).

AP613

MOTOR UNIT RECRUITMENT IN HUMAN GENIOGLOSSUS DURING FLOW-LIMITED BREATHING IN SLEEP

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Background and Aims: Genioglossus is a pharyngeal dilator muscle crucial for maintaining airway patency during wakefulness and sleep. Human genioglossus motor unit activity show diverse discharge patterns during eupnoeic breathing in wakefulness (inspiratory, expiratory, tonic). No study to date has examined motor unit recruitment strategies in sleep with flow limited breathing.

Methods: Overnight sleep and respiratory data were collected in nine sleep apnoea subjects under CPAP. Genioglossus activity was measured using percutaneously inserted intramuscular fine-wire electrodes inserted at 5 different sites within the tongue. Flow limited breathing was induced by reducing CPAP holding pressures. Genioglossus electromyogram recordings were analysed for single motor unit recruitment with flow-limited breathing.

Results: Twenty two single motor units were discriminated in stable sleep. 20 of the 22 units were silent during CPAP supported breathing but recruited by flow limited breathing. All 20 units exhibited a phasic inspiratory firing pattern upon recruitment, and the vast majority ($N = 15/20$) develop tonic inspiratory activity with increased respiratory drive.

Conclusion: Preliminary findings identify the recruitment of a predominant subtype of genioglossus single motor unit that is active phasically in inspiration with a developing tonic component. This type of recruitment is likely to function to dilate the partially collapsed pharyngeal airway.

AP614

THE HMGB1-RAGE/TLR-TNF- α SIGNALING PATHWAY MAY CONTRIBUTE TO KIDNEY INJURY INDUCED BY HYPOXIA

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Background and Aims: This study aimed to investigate whether high mobility group box 1 protein (HMGB1) signalling pathway play a role in kidney injury due to sleep apnoea.

Methods: Adult Sprague Dawley rats were used to establish hypoxia models: continuous hypoxia, intermittent hypoxia, and intermittent hypoxia with hypercapnia. Histopathological and ultrastructural changes were observed by light and electron microscopy. Immunohistochemical staining was used to detect HMGB1 distribution. qPCR was used to detect the expression of HMGB1, RAGE, TLR4, NF κ B, TNF α , IL6, SIRT1, PPAR mRNA in renal tissues. An ELISA was used to detect the expression of soluble TLR2, TLR4, PPAR- γ , TNF α , IL-6 in peripheral blood.

Results: HE staining showed that there was no serious injury to the kidneys due to hypoxia except a certain degree of renal tubular epithelial cell vacuolation. In contrast, ultrastructural changes by electron microscopy were more significant in the hypoxia groups including foot process fusion in the glomerulus and degeneration of mitochondria in the proximal convoluted tubules. IHC showed increased expression of HMGB1 and nuclear translocation in the hypoxia groups. The results of qPCR showed hypoxia stimulation increased the expression of HMGB1 mRNA, PPAR mRNA, RAGE mRNA and TNF α mRNA and decreased the expression of SIRT1 mRNA in kidney tissues ($P < 0.05$). The results of the ELISAs showed that hypoxia stimulation increased the expression of soluble TLR4, TNF α and IL-6 in peripheral blood, and decreased the expression of soluble TLR2 and PPAR- γ .

Conclusion: Hypoxia stimulation can cause early renal injury at sub-cellular level and increase the expression and translocation of HMGB1. Hypoxia also upregulates the mRNA expression of the HMGB1-RAGE-TNF α pathway in kidney tissue and increased expression of soluble TLR4, TNF α and IL-6 in peripheral blood. It suggested the HMGB1-RAGE/TLR-TNF α pathway may contribute to the molecular mechanisms of early renal injury induced by hypoxia, which might be drug intervention targets in the future.

AP615

COMBINATION OF NON CPAP THERAPY IN PATIENTS WITH OSA

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Background and Aims: Mandibular advancement device (MAD) is a convenient alternative for patients refusing CPAP. However, it is less

effective than CPAP. Positional device has been shown to be effective in some OSA patients and combination therapy might have synergistic effects.

Methods: Position dependent OSA is defined as the overall AHI > 5/h and the supine AHI more than 2 times of AHI in other positions. Patients with positional dependent OSA who were not using CPAP were put on a positional device (Figure 1, NightShiftTM, Advanced Brain Monitoring Inc., CA, USA). It uses vibro-tactile feedback to discourage back-sleeping. Patients using MAD with a residual AHI > 15/h were offered positional device as combination treatment. Both groups of patients had the device switched on and off for 2 weeks respectively with one week of wash out period in between. Sleep studies were performed after the end of each 2 weeks period.

Results: Between January 2015 to December 2017, 54 patients completed a trial of positional device, of which 8 patients were using MAD at the same time. There was no significant difference between the two groups on baseline mean age (55/58), BMI (27/27), ESS (9/9) and AHI (23/25). Table 1 shows outcomes of the two groups. Up to 89% of patients were woke up by the vibration 47% could not fall asleep again.

Conclusion: Non CPAP combination therapy is feasible and effective in selected patients.

	Positional Device (n=46)		Positional Device + MAD (n=8)	
	Device on	Device off	Device on	Device off
Overall AHI(SD)/hr	11.3(11)*	17.8(15)*	14.4(11)*	25.2(20)*
Supine AHI(SD)/hr	9.9(14)	12(21)	18.3(23)	32(13)
Mean % of non-supine sleep time/night(SD)	93(7)*	68(18)*	95(4)*	67(15)*
Mean % time of snoring > 50dB(SD)	22.4(16)*	33.7(19)*	14(21)*	24(19)*
Mean % of nights with compliance $\geq$ 5hrs/night(SD)	65(26)*	77(24)*	65(31)	73(32)
Oxygen desaturation index (ODI)(SD)	11(11)*	18(16)*	14(11)*	25(18)*

Table 1 * p < 0.05 between device on/off within each group



AP616

A RETROSPECTIVE ANALYSIS ON THE DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH EXCESSIVE DAYTIME SLEEPINESS PRESENTING TO THE SLEEP MEDICINE CLINIC HOSPITAL TAIPING

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Background and Aims: Excessive daytime sleepiness (EDS) is due to variable causes. Most patients, after a thorough clinical assessment, need a polysomnography to come to a correct diagnosis. This study is to explore the demographic profile of patients with EDS and any correlation with patients' profile.

Methods: This was a retrospective study looking at patients with EDS attending the Sleep Clinic in Hospital Taiping from April 2017 till February 2018. The data was retrieved from the outpatient notes and

analyzed with SPSS version 21. Mann-Whitney U test was used to explore the association between the different parameters. Patients with an Epworth Sleepiness Score of more than 12 were included. All patients underwent a full night attended polysomnogram. Patients' age, ethnicity, comorbidities, BMI and sleep diagnosis were analyzed.

Results: 105 patient's data were analyzed, 61% were male and 39% were female. 61.9% were Malays, 12.4% were Chinese and 25.7% were Indians. Male patients had more severe OSA compared to females, which was statistically significant. 90.5% of patients were obese. 20% of patients had mild OSA, 15.2% had moderate OSA and 58.1% had severe OSA, 2.9% had primary central sleep apnoea, 1% had idiopathic hypersomnia, 1% had Cheyne Stoke Respiration and 2% had narcolepsy. 61.5% of male patients and 38.5% of female patients had OSA with obesity hypoventilation syndrome (OHS). All the patients with OHS had OSA. 59.1% of patients with severe OSA had hypertension and 85.7% of patients had both hypertension and diabetes mellitus. There was a statistically significant increase in the co-morbidities in patients with severe OSA compared to mild and moderate OSA.

Conclusion: Men develop more severe OSA than women. Patients with severe OSA were more likely to have hypertension and diabetes compared to non-severe OSA. Hence early diagnosis is essential to prevent complications.

AP617

GETTING OLDER IS ASSOCIATED WITH THE INCREASED RISK FOR OSA AND HYPOVENTILATION IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

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Background and Aims: Background: Duchenne muscular dystrophy (DMD) is characterized as progressive muscle wasting and eventually results in respiratory insufficiency. Obstructive sleep apnoea (OSA) and hypoventilation were prevalent in DMD. Nevertheless, nocturnal hypoventilation (NH) has been associated with respiratory failure in DMD. Although early identifying OSA and NH may facilitate early treatment but clinical associated factors have not been fully elucidated.

Aims: To identify clinical factors associated with OSA and percentage of total sleep time spent on transcutaneous CO₂ >50 mmHg (%TSTof PtcCO₂>50 mmHg) in non-invasive-ventilation-naïve DMD.

Methods: Medical records of patients with DMD, 5 to 18 y/o, referred to sleep lab for suspicious OSA from Jan. 2009 to Feb. 2018 were reviewed. OSA was defined as obstructive apnoea-hypopnea (AHI>1 /h) while hypoventilation was defined as %TST of PtcCO₂>50 mmHg higher than 25%. Multivariable logistic regression was applied to identified clinical factors independently associated with OSA and %TST of PtcCO₂>50 mmHg where the result was expressed as (odds ratio (OR) or coefficient; 95% confidence interval (CI)).

Results: Totally, 42 boys with DMD were enrolled with the mean age of 9.65 years and body mass index (BMI) z score of -0.01. 64% had OSA and 10% had NH. OSA patients were older than non-OSA patients and two groups had similar pulmonary function parameters including forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1). NH patients were also older than non-NH patients. Age was the only factor independently associated with OSA (OR 1.637; 95% CI

1.03–12.597) and %TST of $\text{PtcCO}_2 > 50$ mmHg (coefficient 3.537; 95%CI 0.994 to 6.080) after controlling BMI, FVC, and FEV1.

Conclusion: OSA was prevalent in DMD. Age was the independent factors for both of the OSA and %TST of $\text{PtcCO}_2 > 50$ mmHg.

Acknowledgement: The work was supported by grants from National Taiwan University Hospital (NTUH 107-19), Far Eastern Memorial Hospital (FEMH-2018-C-020) and “Center for electronics technology integration (NTU-107L900502)” from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan

AP618

NORADRENERGIC A7 CELL GROUP MODULATES THE CENTRAL REGULATION OF GENIOGLOSSUS IN RATS

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Background and Aims: Neuromuscular compensation of the genioglossus muscle plays a critical role in maintaining upper airway patency in obstructive sleep apnoea. It has been proven that A7 pontine noradrenergic cell group projected to hypoglossal (XII) nucleus and can modulates XII nerve activity. But the precise mechanisms that A7 noradrenergic cell group could modulate GG activity are still unknown in rats. The aim of this work is to investigate role of A7 cell group, α_2 adrenoceptor and G-protein-activated inwardly rectifying K⁺(GIRK) channels on A7 region in central regulation in rats.

Methods: Transcranial magnetic stimulation (TMS) (i.e., changes in latency and amplitude) and electromyogram (EMG) activity in genioglossus were analyzed before and after microinjection each agent in rats. Anti-DBH-saporin (noradrenergic neuron lesioning agent), RS-79948 (α_2 -adrenoceptor agonist), clonidine (α_2 -adrenoceptor antagonists), tertiapin-Q (GIRK channel blocker) and ML297 (GIRK channel activator) were microinjected into the A7 region, respectively.

Results: Lesions of noradrenergic A7 cell group evoked a significant inhibitory effect on GG activity. Microinjection of α_2 -adrenoceptors agonist clonidine evoked a similar effect on GG activity, whereas the effect of clonidine was weakened in rats pre-injected with tertiapin-Q, GIRK channel blocker. In contrast, microinjection of α_2 -adrenoceptors antagonist RS-79948 elicited a significant stimulatory effect on GG activity, whereas the effect of antagonist was weakened in rats pre-injected with ML297, GIRK channel activator.

Conclusion: The present results suggested that A7 cell group can modulate GG activity through GIRK channels by α_2 -adrenoceptor. GG activity can be inhibited by activating α_2 -adrenoceptor on A7 cell group. Moreover, the effect of α_2 -adrenoceptor is functionally linked to GIRK channel regulation. This finding is an effective strategy for reversing upper airway hypotonia in subjects with obstructive sleep apnoea.

AP619

A PREDICTION EQUATION OF OPTIMAL CPAP PRESSURE FOR OBSTRUCTIVE SLEEP APNEA IN MALAYSIA

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Background and Aims: Obstructive sleep apnoea (OSA) if untreated is associated with increment of all-cause mortality and cardiovascular mortality. Manual in-laboratory positive airway pressure (PAP) titration studies are the gold standard method for prescribing PAP pressures for OSA patients but costly and time-consuming. Automatic PAP

(APAP) titration is cost effective alternative for manual titration, however is recommended only for patient without significant comorbidities. Several formulas predicting optimal continuous positive airway pressure (CPAP) for OSA treatment have been developed from Western and Asian studies, with variable parameters used for predictive factors.

Objective: To develop prediction equation for optimal PAP pressure for Malaysians derived from our single center data and compared with current available equations.

Methods: We retrospectively reviewed 92 patients who undergone sleep titration in Sarawak General Hospital. Published prediction equations (Hoffstein, Se crier, Basoglu, Wu, Luo, Choi, Chuang, Liu) were used to calculate the optimal CPAP pressure. Subsequently, we used a step-wise multiple linear regression analysis to develop a predictive equation for optimal CPAP for our patients.

Results: The titrated and calculated pressure were poorly correlated. The intraclass correlation coefficient for the Malaysia cohort was weak for the calculated predicted pressure with the optimal pressure ranging 0.11–0.36. Our prediction equation predicted CPAP pressure (cmH_2O) = $13.666 + 2.361(\text{male}) + (0.154 \times \text{Epworth Sleepiness Score}) - (0.059 \times \text{Nadir } \text{SpO}_2 \text{ (\%)})$. The intraclass correlation coefficient for the derived equation was 0.51 (95% CI: 0.24–0.67). This equation performed poorly for patients required CPAP pressure less than 6 cmH_2O and more than 18 cmH_2O .

Conclusion: Our prediction equation may improve manual titration success by determine starting pressure of CPAP especially during split-night studies. However, this equation usefulness will be limited to some clinical settings.

AP620

SLEEP EFFICIENCY AND NOCTURNAL DESATURATION ASSOCIATED WITH HYPERTENSION

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Background and Aims: Cumulative studies have indicated sleep disorders and increased risk of cardiovascular diseases. Poor sleep may result in sympathetic hyperactivity. Little information reported sleep efficiency and nocturnal desaturation associated with hypertension. Therefore, we investigated the relationship between hypertension and sleep efficiency and desaturation during sleep.

Methods: We evaluated the patients ≥ 20 years receiving in-lab polysomnography in a tertiary sleep centre between 2010 and 2015. We collected demographic characteristics, sleep efficiency (total sleep time [TST] / time in bed * 100%), oxygen desaturation index (ODI, hourly average number of desaturation episodes) in TST, and hypertension. We calculated odds ratios (ORs) and 95% confidence intervals (CIs) to evaluate the effect of potential risk factors on hypertension by using univariate and multivariate logistic regression models.

Results: A total, 5407 patients (4124 men and 1283 women) were recruited. Mean age were 46.4 ± 14.0 years. The majority of patients (73.6%) were overweight and obese. Sleep efficiency among the study patients were $78.1 \pm 15.8\%$. The mean value of ODI were 22.1 ± 24.5 . After adjustment for potential covariates, men, older age, higher BMI, less sleep efficiency, and more ODI in TST were independent risk factors of hypertension.

Conclusion: Less sleep efficiency and more ODI in TST were associated with development of hypertension. Clinicians should educate and improve sleep efficiency and decrease nocturnal desaturation in terms of primary prevention for hypertension.

Table 2. Odds ratios and 95% confidence intervals of variables associated with hypertension

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Sex (men vs women)	1.27 (1.11, 1.44)**	1.42 (1.22, 1.65)***
Age	1.06 (1.05, 1.06+)**	1.07 (1.06, 1.07)***
BMI	1.11 (1.10, 1.13)***	1.14 (1.13, 1.16)***
Sleep efficiency	0.98 (0.97, 0.98)***	0.99 (0.98, 0.99)**
ODI	1.02 (1.01, 1.02)***	1.01 (1.00, 1.01)**

OR: odds ratio; BMI: body mass index; ODI: oxygen desaturation index;
** $P < 0.01$; *** $P < 0.001$

APL015

EPIDEMIOLOGICAL CHARACTERISTIC OF ISCHEMIC STROKE IN ADULTS INDONESIAN OBSTRUCTIVE SLEEP APNEA POPULATION: A PRELIMINARY STUDY

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Background and Aims: Obstructive Sleep Apnoea (OSA) is a major public health problem, largely unrecognized and undiagnosed. OSA could lead to atherosclerosis through direct or indirect process such as cerebrovascular disease. OSA and ischemic stroke had two way association. OSA patients had higher risk to suffer ischemic stroke, and ischemic stroke patients had greater risk to have OSA. This study had purposed to know the characteristic of ischemic stroke among OSA patients at Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.

Methods: This study used cross sectional study design and collected samples based on OSA Registry at Respirology and Critical Illness Division, Internal Medicine Department, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia during five month, August to December 2017. Indonesian version of Berlin Questionnaire is used to interview subjects. Collected data were analyzed using SPSS 20.0.

Results: One hundred fourteen patients were recruited in this study. There were fifteen (13%) OSA patients that suffer ischemic stroke. Eight subjects (53.3%) are male and 86.6% ischemic stroke patients were elderly. We found that 66.6% ischemic stroke patient had smoking habit and 33.3% had concomitant cardiovascular problem. In BMI classification, normal and obese have same amount of subjects which is 6 subjects (40%). The best neck circumference cut-off point for males and females that indicated overweight or obesity among ischemic stroke patients 37 cm and 33 cm, respectively. Of 85% ischemic stroke patients had higher value neck circumference than normal. Abnormal waist circumference were significantly higher in ischemic stroke patients (83%). Seventy seven percent of ischemic stroke patients had hypertension and controlled by antihypertensive drugs. There was 33.3% ischemic stroke patients had renal failure.

Conclusion: Prevalence of ischemic stroke among OSA patients was 13%. Ischemic stroke among OSA patients had characteristic higher in male, elderly population, having smoking habit, had hypertension, having big neck circumference and waist circumference than normal.

Respiratory Structure and Function 2

AP621

EFFECT OF MODERATE ENDURANCE TRAINING ON EXERCISE BIOLOGICAL CALIBRATION

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Background and Aims: Biological calibration (BC) is an integral process to ensure the validity of the cardiopulmonary exercise testing (CPET) system. In a pragmatic setting, BC subject is recruited from healthy hospital staffs, which may increase physical activities for social or personal reasons. The effect of exercise on important CPET variables during BC is not known. We aimed to study the effect of endurance training on the result of BC.

Methods: Our BC protocol comprised of 3 stepped constant work exercise at 20W/min, 60W/min and 100W/min (5 minutes each) on a cycle ergometer (*Ergoline*) with continuous oxygen uptake (VO_2), carbon dioxide output (VCO_2), heart rate (HR) and minute ventilation (MV) monitoring via the *Carefusion Vmax Encore* system. A sedentary BC subject underwent self-paced endurance exercise; BC was performed after 3 months of training and compared with historical results.

Work Rate, W/min	VO_2 , L/min		VCO_2 , L/min		HR, beats/min		MV, L/min	
	Baseline	After training	Baseline	After training	Baseline	After training	Baseline	After training
Rest	0.31 (0.02)	0.44*	0.28 (0.03)	0.35*	79 (2)	74*	9.3 (1.4)	11.5*
20	0.65 (0.02)	0.64	0.60 (0.01)	0.56*	86 (1)	79*	17.4 (1.0)	17.9
60	1.10 (0.02)	1.05	1.21 (0.04)	0.94*	108 (4)	95*	29.9 (0.8)	25.0*
100	1.63 (0.03)	1.64	1.82 (0.03)	1.64*	138 (3)	115*	47.9 (3.6)	40.1*

Baseline value expressed as mean (standard deviation). *Increased or *decreased by >2SD of baseline mean.

Results: The subject ran regularly averaging a mean (standard deviation) weekly mileage of 18.8 (8.1) km at a pace of 07:04 (00:26) minutes/km. Exercise training resulted in higher resting VO_2 , VCO_2 and VE but lower HR when compared to historical BC results. During BC, VO_2 were similar to pre-training levels but VCO_2 and HR were consistently lower at all work rates. VE was similar to historical value at 20W/min exercise but lower at higher work rates (see Table). We think these findings can be explained by an improvement in the aerobic capacity with associated delay in the anaerobic threshold.

Conclusion: Short-term moderate endurance training resulted in lower VCO_2 , HR and VE but a relatively stable VO_2 at low-to-moderate work rate when compared to pre-training BC. Therefore, an increase in physical activities in between BCs should be taken into account during the interpretation of results and ideally more than one BC subjects should be recruited.

AP622

EFFECTS OF DIFFERENT-INTENSITY INSPIRATORY MUSCLE TRAINING ON DIAPHRAGM AND ASSISTIVE INSPIRATORY MUSCLE THICKNESS IN HEALTHY INDIVIDUALS

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Background and Aims: The aim of this study was to evaluate the effect of inspiratory muscle training (IMT) of different intensities on diaphragm and neck inspiratory muscle thickness in healthy individuals.

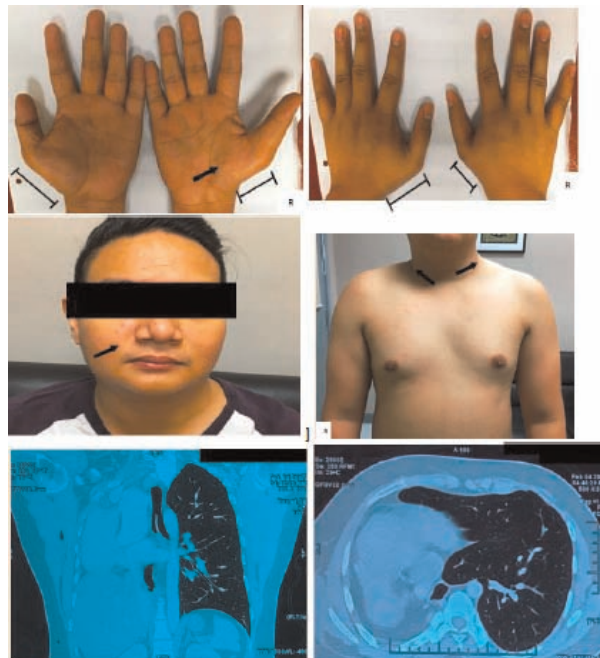
Methods: Thirty-three healthy men were included. They were randomly assigned to three groups: a 10% group, performing IMT at 10% of maximal inspiratory pressure (MIP), and respective 30% and 60% groups. IMT training was performed for 30 breaths $\times$ 2 sets twice a day (four sets in total) for 8 weeks. Baseline and post-training measures of MIP and thicknesses of the diaphragm (Tdi), sternocleidomastoid muscle (Tst), and anterior scalene muscle (Tas) at total lung volume were evaluated using ultrasonography. Differences in measured values were examined by two-way analysis of variance with a split-plot design.

Results: The MIP significantly increased in all groups, and the change was significantly higher in the 60% group. Tas significantly increased only in the 60% group. There was no significant change in Tdi or Tst in any group.

Conclusion: These data suggest that high-load IMT might lead to an increase in the thickness of the anterior scalene muscle, but not that of the diaphragm, in healthy people.

and succeeding branches are absent. Mediastinum is deviated to right occupying right hemithorax. There is decreased intercostal spaces on the right. There is compensatory hyperaeration of the left lung. Radiologic findings were indicative of right pulmonary aplasia. Patient is kept under close follow-up.

Conclusion: A case of 24 year old male, with recurrent childhood respiratory infection, currently asymptomatic noted with asymmetric chest wall, shoulder and limbs worked-up as a case of right unilateral pulmonary aplasia



AP623

RIGHT UNILATERAL PULMONARY APLASIA: A CASE REPORT

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Background and Aims: Pulmonary aplasia is a rare congenital abnormality characterized by absence of lung parenchyma and its supporting pulmonary vasculature alongside with a rudimentary main bronchus. Patients with no other concomitant congenital anomaly survive well into adulthood surpassing respiratory infection through childhood. This case aimed to discuss case of 24-year-old male, with recurrent childhood respiratory infection, currently asymptomatic noted with asymmetric chest wall, shoulder and limbs.

Methods: On physical examination, there was slight shallowness of the right nasolabial fold; unequal shoulder height, left was more muscular than the right. Right hypotenar was atrophied. Trachea was shifted to the right. There was lag on right chest wall, percussion was dull on the right hemithorax, and there was absent breath sounds on right lung field. Heart sounds was heard on right anterior chest wall. Chest X-ray, chest ultrasound, and Chest CT scan were done.

Results: Chest X-ray showed full opacification of right hemithorax with tracheal deviation to the right. Left cardiac border was not appreciated. Ultrasound of right hemithorax showed negative for pleural effusion with ipsilateral cardiomeastinal shift close apposition to the intercostal spaces. Contrast enhanced chest CT scan revealed absence of right lung and its supplying vasculature. Right main bronchus is present but small

AP624

THE EFFECTS OF SCAPULA AND TRUNK MUSCLE TRAINING ON MOUTH PRESSURE

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Background and Aims: Respiratory muscle training is usually carried out through methods that use dedicated equipment to apply direct resistance to breathing. This study investigated the effects of arm and trunk muscle resistance training on mouth pressure.

Methods: The subjects were 25 healthy women (mean age 22 years, mean BMI 20.6). They were divided into the scapula muscle training group (scapula group), the trunk muscle training group (trunk group), and the control group. The scapula group and trunk group carried out training, which comprised 2 sets of 15 repetitions per day at a load of 60% maximum muscle strength for four weeks. Scapula muscle strength, trunk muscle strength, respiratory function, respiratory muscle strength, and respiratory muscle endurance were measured before and after the training period for comparison.

Results: In the scapula group, scapula muscle strength and maximum inspiratory mouth pressure (PImax) (pre: 92.1 ± 12.0 cmH₂O, 4w: $98.7 \pm 1 \pm 3.0$ cmH₂O; $P < 0.05$) increased significantly, and in the trunk group, trunk muscle strength, PImax (pre: 93.1 ± 22.1 cmH₂O, 4w:

98.6 ± 13.0 cmH₂O; $P < 0.05$), and maximum expiratory mouth pressure (PE_{max}) (pre: 100.8 ± 25.5 cmH₂O, 4w: 107. ± 4.5 cmH₂O, $P < 0.01$) increased significantly.

Conclusion: We suggested that muscle training of the scapula and trunk muscles was effective for increasing mouth pressure.

AP625

SWOT ANALYSIS ON THE PROMOTION OF PULMONARY FUNCTION TEST IN PRIMARY MEDICAL AND HEALTH SERVICE INSTITUTIONS

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Background and Aims: To explore the feasibility of pulmonary function test in primary health care institutions.

Methods: SWOT (Strength, Weakness, Opportunity, Treats) is a situation analysis method, used to explore the advantages and disadvantages of pulmonary function test in the screening of airway obstructive pulmonary disease in primary medical and health institutions, and systematically analyzed the current health policy opportunities and the risk of social environment and put forward construction.

Strength analysis: (1) Pulmonary function test is an important item for respiratory diseases. (2) The advantages of Pulmonary function test. (3) A series of technical guidelines for pulmonary function examination have been formulated to provide important guidance for primary medical practice.

Weakness analysis: (1) The accuracy of pulmonary function test results are affected by the instrument itself, environmental interference and so on; (2) large scale pulmonary function equipment is expensive and has limited operation environment. (3) There is no uniform standard for operator qualification of pulmonary function test in China.

Opportunity: (1) the "13th Five-Year" Health Plan (from the government) announced that Pulmonary function test has been included in the routine physical examination category; (2) A quality management system for pulmonary function examination in China has been established. (3) "SMILE" (Screening and Monitoring to Improve Lung diseases, Early Detection) project has been established since 2015.

Threats: (1) Weak awareness of the application of pulmonary function examination in primary medical and health institutions; (2) Weak awareness of the prevention and treatment of chronic respiratory diseases in public; (3) Lack of health promotion support.

Results: (1) Strengthening health promotion. (2) More extensive training and technical quality control on standardized pulmonary function test. (3) To raise the awareness of patients with respiratory diseases and healthy people on pulmonary function test.

Conclusion: It is feasible and practical to popularize lung function examination technology in primary medical field. And it can effectively prevent the early chronic respiratory disease.

AP626

DIFFERENCES BETWEEN THORACIC AND ABDOMINAL RESPIRATION IN MOSTGRAPH ANALYSIS

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Background and Aims: The MostGraph is a forced oscillation method for measuring respiratory resistance. It may detect physiological changes more sensitively than spirometry and its reproducibility is good. Measurement can be performed during quiet breathing, allowing a broad scope of application. However, thoracic respiration is dominant in some patients during quiet breathing, while abdominal respiration is dominant in others.

Methods: In order to investigate the potential influence of the pattern of respiration on MostGraph measurements, MostGraph data were compared between subjects with thoracic respiration and abdominal respiration. The subjects were 12 healthy volunteers (6 males and 6 females with a mean age of 34.8 years). Thoracic respiration and abdominal respiration were each performed for the same duration and MostGraph measurements were obtained. The Wilcoxon matched-pairs signed rank test was conducted for statistical analysis, and $P < 0.05$ was considered significant.

Results: Regarding mean values during inspiration and expiration, and values for expiration only, no significant differences of R5, R20, R5-R20, X5, Fres, and ALX were observed between the two patterns of respiration. Regarding values for inspiration only, there were no significant differences of R5, R20, R5-R20, and X5 between the two patterns of respiration, but Fres and ALX were significantly lower with abdominal than thoracic respiration.

Fres and ALX are indexes of the elastic resistance of the respiratory system. Accordingly, changes of Fres, whether small or large, reflect changes in of respiratory system elastic resistance. In the same subjects, Fres and ALX were significantly different between abdominal and thoracic inspiration. Accordingly, the patient's pattern of respiration should be taken into consideration when assessing MostGraph test results.

Conclusion: The pattern of respiration (abdominal or thoracic) influenced the values of Fres and ALX during inspiration, and the clinical significance of this finding requires further evaluation.

AP627

A 6-WEEK OLD INFANT WITH FIRST EPISODE OF COUGH DIAGNOSED WITH BRONCHUS SUIIS: A CASE REPORT WIVINA BANCORO¹

¹Chong Hua Hospital, Philippines

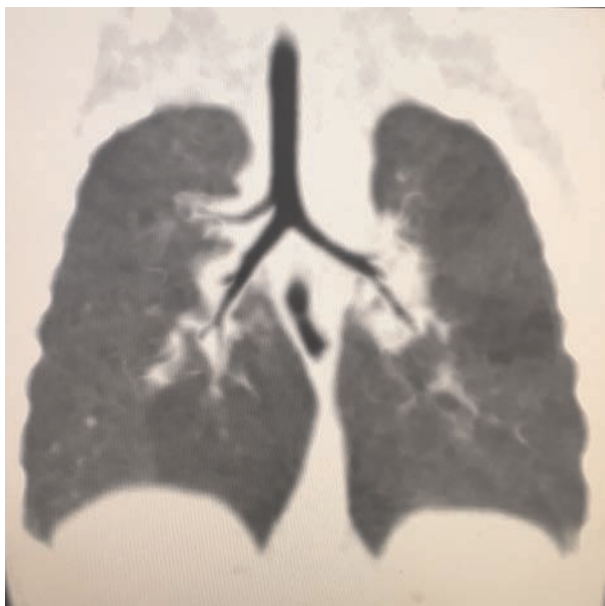
Background and Aims: Bronchus suis is a rare congenital anomaly in children with an incidence rate of less than 2%. It was first described by Sandisfort in 1785 as an aberrant bronchus originating from the lateral wall of the trachea. It is usually suspected in children with recurrent respiratory infection. It is also one of the differential diagnosis in patients who are ventilated yet still presented with persistent respiratory distress or atelectasis of the right upper lobe. Management will be medical treatment for the pulmonary infection. However, in cases of recurrent or persistent pulmonary problems, right upper lobectomy is advised.

This paper aims to present a case of a 6 week old infant who had her first episode of cough which was diagnosed as a case of bronchus suis.

Methods: This is a case report.

Results: I have presented a case of a 6-week old infant with first episode of cough who was eventually diagnosed with bronchus suis by chest computed tomography scan.

Conclusion: Bronchus suis is a rare congenital anomaly which we should consider not only in patients with recurrent cough but also in patients who will have persistent cough or severe respiratory distress despite adequate management.



AP628

SHORT-TERM INSPIRATORY MUSCLE TRAINING IN HOSPITALIZED HEART FAILURE PATIENTS IS SAFE AND EFFECTIVE FOR IMPROVING INSPIRATORY MUSCLE STRENGTH AND DYSPNOEA ON EXERTION

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Background and Aims: Some studies have indicated that inspiratory muscle training (IMT) in chronic heart failure patients improves inspiratory muscle strength, exercise tolerance and quality of life. However the effect and safety of IMT in heart failure patients during the subacute phase has not been established. The aim of this study was to investigate the effect and safety of short-term IMT in hospitalized patients with heart failure.

Methods: A total of 24 hospitalized patients were allocated to intervention group or control group. Intervention consists of IMT loaded with 40% of maximal inspiratory pressure (P_{Imax}). Control sham intervention consists of loaded with 10% of maximal inspiratory pressure. IMT was supervised by a physical therapist. The patients performed IMT in sets of 30, 2 times a day, 5 times a week, for 2 weeks. Before and after intervention, the following measures were obtained: P_{Imax}, knee extensor muscle strength (KEMS), six-minute walk distance (6MWD), Borg Scale after six-minute walk test, and the signs of heart failure exacerbation (Body weight, LVEF, BNP, and CTR). The effect of intervention between groups, the effect of time, and the effect of group × time interactions were evaluated using split-plot-factorial analysis of variance.

Results: Short-term IMT resulted in a significantly higher benefit in P_{Imax} ($P < .05$), dyspnoea ($P < .05$). In both intervention and control groups, heart failure didn't exacerbated by 2-week IMT.

Conclusion: These results suggest that IMT in patients with heart failure during the subacute phase is safe and effective for improving inspiratory muscle strength and dyspnoea on exertion.

DECREASED LUNG FUNCTION IS ASSOCIATED WITH INCREASED RISK OF DEVELOPING NON-ALCOHOLIC FATTY LIVER DISEASE: A LONGITUDINAL COHORT STUDY

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Background and Aims: Decreased lung function is associated with an increased risk of many adverse outcomes, but its association with the risk of developing non-alcoholic fatty liver disease (NAFLD) is unclear. Our aim was to investigate whether baseline lung function is associated with incident NAFLD in middle-aged healthy Koreans.

Methods: A cohort study was undertaken in 96,104 healthy subjects (mean age: 35.7 years) without NAFLD. Subjects were followed up annually or biennially from 2002 to 2015. The presence of fatty liver at baseline and at follow-up was determined using ultrasound. Baseline percent predicted forced expiratory volume in one second (FEV1%) and forced vital capacity (FVC%) were categorized in quartiles. Adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) (using the highest quartile as reference) were calculated for incident NAFLD at follow-up, controlling for covariates and potential confounders.

Results: During 579,714.5 person-years of follow-up, 24,450 participants developed NAFLD (incidence rate, 42.2 per 1,000 person-years). The mean follow-up period was 5.9 ± 3.4 years. Regardless of smoking history, the risk for incident NAFLD increased with decreasing quartiles of FEV1 (%) and FVC (%) in a dose-response manner (P for trend < 0.001). In never smokers, the aHRs (95% CIs) for incident NAFLD were 1.15 (1.08–1.21), 1.11 (1.05–1.18), and 1.08 (1.02–1.14) in quartiles 1–3 for FEV1 (%) and 1.12 (1.06–1.18), 1.11 (1.05–1.18), and 1.09 (1.03–1.15) in quartiles 1–3 for FVC (%), compared with the highest quartile reference.

Conclusion: Reduced lung function was a risk factor for incident NAFLD in a large middle-aged Korean cohort with over half a million person-years of follow-up, regardless of smoking history, measures of obesity/central obesity, and other potential confounders.

Tuberculosis 2

AP630

ANALYSIS OF AGE-SPECIFIC BACKGROUND OF ACTIVE TUBERCULOSIS IN AIZU MEDICAL CENTER, JAPAN

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Background and Aims: Tuberculosis (TB) morbidity in Japan is now 13.9 per 100,000 person year, which is still in a moderate epidemic situation. Reasons of this phenomenon are thought to be aging population and increase of immunosuppressed patients. Patients' and doctors' delay are also seen as problems of epidemiological features in new TB patients.

Methods: To grasp the current situation of TB, 159 of active TB-patients in Aizu Medical Center from March 2009 to February 2018, were looked into by their age, gender, lifestyle, chief complaints, patients' delay, doctors' delay, complications, performance status (PS), and laboratory data. Furthermore, these data were weighed in 3 age groups:

36 patients of group A are younger than 65 years old; 48 patients of group B are between 65 and 80; 75 patients of group C are older than 80.

Results: Approximately 20% patients were asymptomatic, and patients without typical respiratory symptoms tended to increase with age. Mean patient's delay in days was 124 in group A, 36 in group B, and 15 in group C, and it was significantly longer in group A. Doctor's delay was about 30 days in all 3 groups. In group A, which included many medical workers and heavy labourers, only a few had complications. The merger rate of diabetes mellitus (DM) was high in group B and C. In group C there were many dementia and cerebral infarction sequelae patients with low PS. The number of lymphocytes and the albumin value were significantly lower in group B and C than in group A. There was no HIV patient.

Conclusion: Group A had many medical workers, and patient's delay of this group was remarkable, whereas it was not noticeable in groups B and C. Immunosuppressed cases with complications like DM and low PS cases tended to increase with age.

AP631

REDUCING TUBERCULOSIS BUT CONTRACTING SHINGLES IN PATIENTS WITH TYPE 2 DIABETES RECEIVING STATIN VS NONSTATIN LIPID LOWERING AGENTS

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Background and Aims: Type 2 diabetes mellitus (T2DM) patients are at increased risk of tuberculosis (TB) and shingles. Statins and non-statin lipid lowering agents (NsLLA) are commonly used in T2DM patients, the former has demonstrated anti-TB effect in animal studies but is associated with increasing risk of shingles in observational studies. The double-edged sword effects of statin vs NsLLA on infection risk in T2DM patients remains uncertain.

Methods: In this cohort study of patients with T2DM diagnosed during 2001–2013, subjects without prior statin or NsLLA use were identified from the Taiwan National Health Insurance Research Database. After excluding combined initiator of statin and NsLLA, patients were classified as statin-user, NsLLA-user and those without LLA (LLA-free). Patients were observed for TB development (the primary outcome) from T2DM diagnosis date until treatment crossover or December 2013. The secondary outcomes included shingles and liver abscess. Cox regression was used, and statin-user and NsLLA-user were time-dependent variables.

Results: During a 240,782 person-years of follow-up, TB incidences were 115, 182, and 279 per 100,000 person-years in statin-user ($n = 17,696$), NsLLA-user ($n = 5,327$), and LLA-free group ($n = 22,316$), respectively. In a multivariate analysis, statin-users had a 34% reduced risk of TB compared with NsLLA-users (aHR, 0.66; 95% CI, 0.44–0.99) after adjustment for age, sex, income levels, rural residence, metformin dose and comorbidities. This association was further confirmed in an age-, sex-, calendar-year-matched subcohort. In contrast, the incidence of shingles was higher in statin-user than in NsLLA-user and LLA-free groups (957, 690, and 812 per 100,000 person-years). The statin-users had a 23% increased risk of shingles compared with NsLLA-users (aHR, 1.23; 95% CI, 1.01–1.50). Notably, the risk of TB and shingles were not statistically different between NsLLA-user and LLA-free groups. There was no association between statin-user and the risk of liver abscess.

Conclusion: T2DM patients treated with statin had a decreased risk of TB but an increased risk of shingles compared to those with NsLLA.

INCIDENCE OF ACTIVE TUBERCULOSIS WITHIN 1 YEAR AFTER TUMOR NECROSIS FACTOR INHIBITOR TREATMENT ACCORDING TO LTBI STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background and Aims: We investigated the incidence of active tuberculosis among patients with inflammatory bowel disease (IBD) treated with tumour necrosis factor (TNF) inhibitors, with or without latent tuberculosis infection (LTBI).

Methods: The study was performed at a South Korean tertiary referral centre between January 2011 and June 2017. In total, 740 patients with IBD who underwent LTBI screening tests and were followed-up for ≥ 1 year after TNF inhibitor treatment initiation were enrolled. LTBI was detected on the basis of tuberculin skin test results, interferon-gamma release assay results, chest X-ray findings, and previous tuberculosis treatment history. The patients were classified into LTBI ($n = 84$) or non-LTBI ($n = 656$) group. The risk of developing tuberculosis in each group was assessed on the basis of standardized incidence ratio (SIR) and 95% confidence interval (CI) for active tuberculosis.

Results: Mean patient age was 33.1 years, and patients with Crohn's disease were predominant (80.7%). Within 1 year after the initiation of TNF inhibitor treatment, 1 patient in the LTBI group (1/84; 1.2%) and 7 patients in the non-LTBI group (7/656; 1.1%) developed active tuberculosis. The overall 1-year incidence of tuberculosis among the patients was significantly higher than that among the general population (SIR 14.0, 95% CI 7.0–28.0), and SIR was not affected by LTBI status (LTBI group: 14.5, 95% CI 2.0–102.6; non-LTBI group: 14.0, 95% CI 6.7–29.4).

Conclusion: Patients with IBD undergoing TNF inhibitor treatment showed a higher 1-year incidence of tuberculosis than the general population irrespective of LTBI status.

AP633

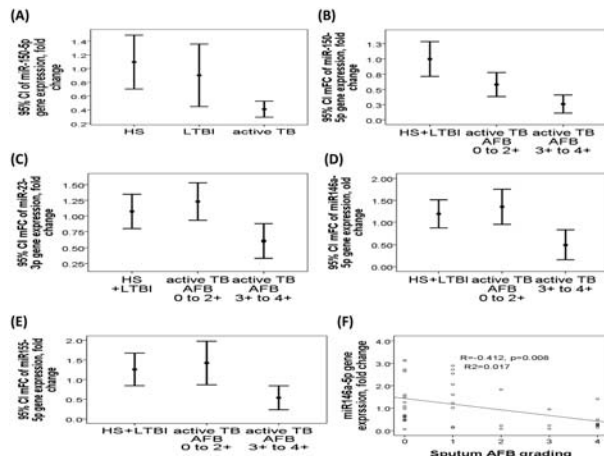
DECREASED MIR-150-5P EXPRESSION IN PATIENTS WITH ACTIVE PULMONARY TUBERCULOSIS (TB) DISEASE

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Background and Aims: The aim of this study is to explore the role of microRNAs (miR)-21/23/146a/150/155 targeting the toll-like receptor pathway in host immune response to active pulmonary tuberculosis (TB) disease and in response to 6-month anti-TB drugs treatment.

Methods: Gene expression levels of the five miRs, TLR2, and their down-stream mediators were assessed by quantitative RT-PCR method in peripheral blood mononuclear cells from 40 patients with active pulmonary TB, 16 matched-subjects with latent TB infection (LTBI), and 16 non-infected healthy subjects (HS). Human monocytic THP-1 cells were transfected with miR mimics or inhibitors under the stimuli with mycobacterium TB-specific antigen, ESAT-6 and CFP-10.



Results: Gene expression levels of miR-150-5p were significantly decreased in patients with active pulmonary TB disease as compared with either LTBI subjects ($P = 0.021$) or non-infected HS ($P = 0.001$). Subgroup analysis showed that gene expression levels of miR-23-3p, miR-146a-5p, miR-150-5p, and miR-155-5p were all decreased (all P values < 0.05) in active TB patients with high bacterial burden (defined as sputum acid fast bacilli 3+ to 4+ at diagnosis) as compared with that in those with low bacterial burden (defined as sputum AFB 0 to 2+) or HS, and negatively correlated with sputum AFB gradings.

Conclusion: MiR-150-5p was down-regulated in active pulmonary TB patients, while miR-150-5p, miR-23-3p, miR-146a-5p, and miR-155-5p were all down-regulated in those with high bacterial burden. These findings provide biological insight into mechanisms by which *Mycobacterium TB*-suppressed miRs modulate human immunity, and indicate that over-expression of the miR-150 gene may be a new host-directed immunotherapy for active TB.

AP634

CORRELATION BETWEEN MATRIX METALLOPROTEINASE-9 AND THE SEVERITY DEGREE OF CHEST X-RAY IN PULMONARY TUBERCULOSIS PATIENTS

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Background and Aims: According to mechanism of extracellular matrix damage in patient with Pulmonary Tuberculosis is still poorly understood. The damage of the lung parenchyma is caused by production of metalloproteinase-9 which produced by *Mycobacterium Tuberculosis*. We hypothesized that there was correlation between MMP-9 and degree of severity chest X-Ray of pulmonary tuberculosis patient.

Methods: We studied 30 subjects with minimal lesion and advanced lesion. MMP-9 level was examined and measured by Enzyme-linked assay (ELISA) and expressed with pg/mL. This research is an observational analytic with cross sectional design. Chi-square statistical analysis is used to analyzed the correlation between the two variables

Results: Characteristics of the samples consist of 16 men and 10 women. Advanced lesions obtained 26 (86.7%) and minimal lesions obtained 4 (13.3%). The averaged levels of MMP-9 was higher significantly in advanced lesion compared to the minimal lesions ($P < 0.000$). Chi-square statistical analysis (P value: 0.048; $P < 0.05$), has a medium strength (coeff. contingency: 0.394) which is a significantly positive correlation (unidirectional)

Conclusion: There is significantly positive correlation between the levels of MMP-9 and the severity degree of chest x-ray in patients with

pulmonary tuberculosis at Dr. Soetomo General Hospital Surabaya with $P = 0.048$ ($P < 0.05$) which shown the medium strength of the correlation (0.394)

AP635

DIFFERENTIATION BETWEEN LYMPHOMA ASSOCIATED EFFUSIONS AND TUBERCULOUS PLEURAL EFFUSION

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Background and Aims: Lymphoma-associated effusions (LE) usually mimic tuberculous pleural effusion (TPE) characterized by lymphocytic exudate with high adenosine deaminase (ADA) levels. Furthermore, low cytological yield of LE makes differentiation between LE and TPE more challenging. However, there is little data regarding differential diagnosis of these difficult situations.

Methods: This retrospective study included all consecutive patients who were diagnosed with LE and TPE, respectively, between January 2011 and December 2016 at Kyungpook National University Hospital. Clinical, laboratory, and pleural fluid characteristics were analyzed to find the independent variables that could discriminate between LE and TPE.

Results: Nineteen patients with LE and 216 patients with TPE were included in this study. Median age was 63 years in both LE and TPE groups. Fever was significantly more frequent in patients with TPE compared to those with LE (48% vs 11%, $P = 0.001$). Serum LDH levels were significantly higher in patients with LE than those with TPE (881 vs 371 U/L, $P < 0.001$). Pleural fluid ADA levels were commonly elevated in both groups with LE and TPE (66 vs 84 IU/L). In the multivariate analysis, fever was negatively associated with LE (Odds ratio [OR], 0.150; 95% confidence interval [CI], 0.028–0.813; $P = 0.028$), while S-LDH levels were positively associated with LE (OR, 1.005; 95% CI, 1.003–1.007; $P < 0.001$). S-LDH > 460 U/L provided a high negative predictive value (98%), with a sensitivity of 79% and specificity of 81% to distinguish LE and TPE. In addition, S-LDH > 460 U/L without fever increased the specificity into 89%.

Conclusion: Patients with LE and TPE present very similar clinical and pleural fluid characteristics. Fever and S-LDH levels may be helpful in the differential diagnosis of LE and TPE. Lymphoma should be kept in mind in the differential diagnosis in patients with lymphocytic pleural effusion and high ADA levels.

AP636

ANALYSIS OF TB SURVEILLANCE DATA ON FOREIGN-BORN PERSONS "TRANSFERRING OUT" IN JAPAN - IMPLICATIONS FOR CROSS-BORDER COLLABORATION FOR TB CARE AND PREVENTION

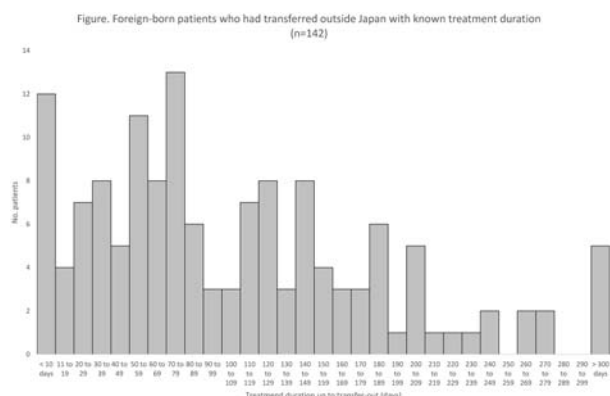
LISA KAWATSU^{1*}, AKIHIRO OHKADO¹, KAZUHIRO UCHIMURA¹, KIYOHICO IZUMI¹

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Background and Aims: Cross-border referral of TB patients is important both for the patients themselves, and from the perspective of preventing antimicrobial resistance. In Japan, despite a sizeable proportion of TB patients moving out of Japan while still on treatment, there is currently no standardized system of cross-border referral. Their treatment outcome is often not followed-up, and are recorded as "transferred out". We thus aimed to investigate those foreign-born patients who have transferred out and provide basic evidence which may be assist establishment of such referral system.

Methods: We analyzed the cohort data of pulmonary TB patients notified to the JTBS between 1st January 2011 and 31st December 2015. The foreign-born patients whose treatment outcome were recorded as "transferred out" were examined in terms of occupational status in Japan, county of birth, year of entry to Japan, and duration of treatment in Japan.

Results: Treatment outcome of 4,179 foreign-born patients, whose cohort data was available for the study period, was analyzed.



16.0% ($n = 668$) had transferred out, of which 51.3% to outside Japan. The largest category of occupational status among the 343 international transfers was students (44.3%), followed by full-time workers (16.0%), however, the transfer-out rate was the highest among the latter (72.3%). Although patients from China and the Philippines constituted 33.5% and 19.0% of the international transfers, the transfer-out rate was the highest among patients from Indonesia (76.0%). Of the 221 international transfers whose year of entry to Japan was known, 40.7% had entered Japan in the same year they were diagnosed with TB. Figure shows that 24.6% had moved during the intensive phase.

Conclusion: Our results strongly point to the need for a systematic cross-border referral. A more detailed study is needed to examine the reasons why patients travel while on treatment, as well as identify issues in referring foreign-born patients to medical institutions outside Japan.

AP637

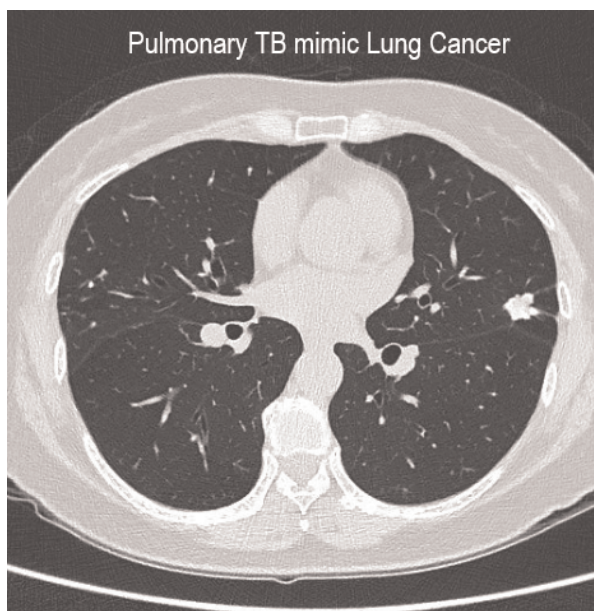
THE ROLE OF SURGERY FOR THE TREATMENT OF INCIDENTAL PULMONARY TUBERCULOSIS FINDING IN A TUBERCULOSIS-ENDEMIC COUNTRY

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Background and Aims: The indication of surgery is limited to the management of complicated forms of tuberculosis (TB) and mostly to cases in which medical treatment is failing. There is however limited good quality data about the effectiveness of using surgery alongside drug treatment for TB. This study investigated the prognosis of patients with incidental pulmonary TB finding after surgical resection.

Methods: The study enrolled patients received video-assisted thoracic surgery (VATS) wedge resection or lobectomy for lung lesions from 2013 to 2017. Pulmonary TB diagnosis was based on pathological examination with acid-fast stain or mycobacterial culture result of surgical specimens. Medical records were reviewed and clinical data, including age, gender, surgical type, pathological reports, microbiological cultures, treatment and follow-up duration were analyzed. Major adverse cardiovascular events occurring after long-acting bronchodilators inhalation were recorded.



Results: A total of 443 patients were included from National Taiwan University Hospital Yunlin Branch, Yunlin County, Taiwan. 200 patients (45.1%) were primary lung cancer, 31 (7.0%) were metastatic cancer, 20 patients (4.5%) were diagnosed as mycobacterial infection and 11 patients (2.5%) had Cryptococcosis. 13 of 20 patients (65.0%) with mycobacterial infection received anti-TB treatment and the other 7 patients (35.0%) were followed at clinic without any therapeutic medication prescription. The median of tracking duration was 57 days (range: 9 to 1610 days). All of these patients were stable after lung lesions resection without evidence of pulmonary TB recurrence.

Conclusion: Anti-TB treatment may not be essential after complete surgical resection with incidental diagnosis of pulmonary tuberculosis. There is a need for well designed trials to provide more information about the effectiveness of surgery.

AP638

THE GREAT MIMICKER: PULMONARY TUBERCULOSIS WITH AXILLARY MASS

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Background and Aims **Background:** Tuberculosis and malignancy such as lymphoma are commonly being misdiagnosed due to the similarities in presentation of constitutional symptoms which can subject patients to delay diagnosis and incorrect treatment. We reported a case with simultaneous dual pathology, tuberculosis and lymphoma.

Aims: To share experience in managing patient who was diagnosed of pulmonary tuberculosis concurrent with right axillary mass secondary to lymphoma in Hospital Raja Perempuan Zainab 2.

Methods: Medical record review. All results were analyzed including the laboratory and radiographic findings.

Results: A 54-year-old man active smoker and diabetes presented with chronic cough for five months with whitish sputum, low grade and associated with right axilla swelling for three months which progressive in size. He had history of admission and treated as axillary abscess. Ultrasound done suggestive of abscess formation. Antibiotic was given but no significant improvement. His physical examination revealed right axillary mass with skin hyperpigmentation, oedematous and present of serous discharge. CXR revealed left apical opacities. Bronchoscopy done with

bronchoalveolar lavage AFB isolated and MTB complex detected. He was started on antituberculosis drugs. He was treated as pulmonary tuberculosis with possible right axilla abscess secondary to TB. He refused biopsy for right axillary mass initially. After two weeks on treatment, clinically the mass not reduced in size. CT thorax done revealed large lobulated soft tissue mass over right axilla ($15 \times 10 \times 15.4 \text{ cm}^3$) with muscle involvement suggestive of infiltration and present of cavitating lesion over apicoposterior segments of left upper lobe with multiple lymphadenopathies. Wedge biopsy done revealed the tissue histopathology features suggestive of lymphoma.

Conclusion: Diagnostic biopsy is very important to confirmed final pathology.

AP639

A RARE CASE OF ANTERIOR MEDIASTINAL MASS IN A 12 MONTH OLD: TUBERCULOSIS

MARY ANN ENTERIA^{1*}, MA. DULCE REQUIRON-SY¹

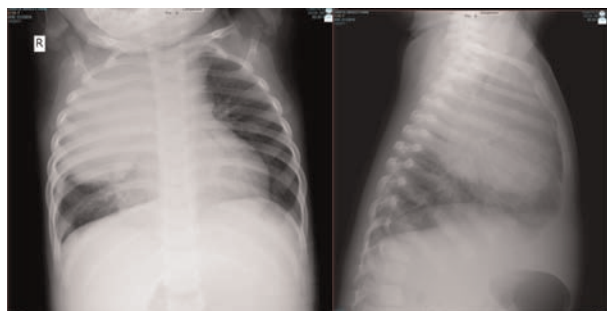
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Background and Aims: Tuberculosis (TB) is one of the world's top health challenges. The aim of this report is to present a rare case of anterior mediastinal mass in a relatively immunocompetent infant.

Methods: This is a case of a twelve month old child with cough for 5 months without relief on antibiotics (Amoxicillin, Co-amoxiclav and Clarithromycin). She was exposed to an aunt who has not completed TB treatment. She was comfortable, afebrile and without weight loss. There were cervical lymphadenopathy and crackles on both lung fields. Chest X-ray (CXR) showed right upper to mid hemithorax dense opacity, rule out massive consolidation vs mass with obstructive pneumonia and or atelectasis (Figure 1). Mantoux test was positive. Chest CT scan revealed a calcified heterogeneously enhancing anterior mediastinal mass lesion, more on the right (consider lymphoma, teratoma, germ cell tumour); subcentimeter to marginal sized axillary lymph nodes; right middle to right lower lobe obstructive pneumonia. CBC showed anaemia. Tumour markers such as alpha fetoprotein and lactate dehydrogenase were elevated while beta HCG was within normal limit. CT scan guided core needle aspiration biopsy showed cytomorphic features consistent with a chronic granulomatous inflammation with extensive necrosis favour TB in nature; stain for acid fast bacilli was positive. Ampicillin-Sulbactam and anti TB medications such as Isoniazid, Rifampicin, Pyrazinamide and Ethambutol were started. Close follow up and repeat CT scan were advised.

Results: The location of the mediastinal mass gives a clue to its diagnosis. Differential diagnosis includes lymphoma, thyroid, thymoma, teratoma. TB is common in endemic countries such as the Philippines. Contrast CT of the thorax and biopsy of the mass were helpful in differentiating the mass. Mantoux test was also positive which warrants treatment while waiting for the TB culture result.

Conclusion: This case has shown a consideration of infectious cause of an anterior mediastinal mass in an infant.



AP640

VITAMIN D, SERUM IL-15 AND SERUM IP-10 ARE POTENTIAL BIOMARKERS TO DIFFERENTIATE ACTIVE TB AND LATENT TB

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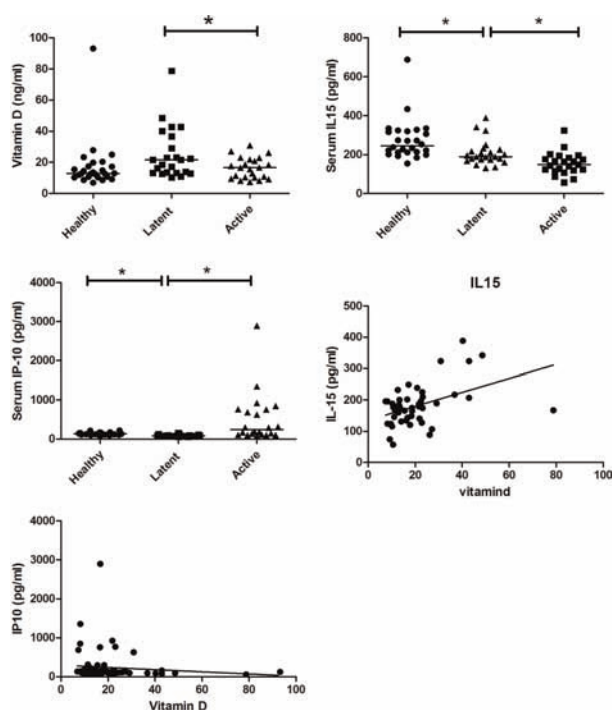
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Background and Aims: Vitamin D levels are known to be associated with mycobacterial activity. IL-15 plays a role in vitamin D-defense mechanism. Serum IP-10 is affected on vitamin D status. This study evaluated the ability of vitamin D and related cytokines to distinguish between active TB and latent TB infection.

Methods: 25 healthy controls, 23 active TB patients and 23 latent TB patients were enrolled in tuberculosis outbreaks in a high school. We assessed the levels of serum vitamin D, serum IL-15, Serum IP-10 and TB antigen dependent IL-15/ IP-10 at the time of diagnosis.

Results: Vitamin D level and serum IL-15 levels were lower in active TB patients than latent TB patients (Vitamin D: 16.64 ng/mL vs 21.6 ng/mL, $P = 0.031$; IL-15 148.9 pg/mL vs 189.8 pg/mL, $P = 0.013$). Serum IP-10 were higher in active TB patients than latent TB patients (246.0 pg/mL vs 85.57 pg/mL, $P < 0.001$). TB antigen-dependent IL-15 secretion and TB antigen-dependent IP-10 secretion were not significantly different between active TB patients and latent TB patients. Vitamin D and IL-15 showed significant positive correlation ($r = 0.389$, $P = 0.007$). Vitamin D and IP-10 showed negative positive correlation ($r = -0.217$, $P = 0.06$).

Conclusion: Serum vitamin D, IL-15, IP-10 may constitute specific biomarkers to distinguish between active TB and LTBI.



AP641

RISK FACTORS OF TIME ADVERSE EFFECTS OF KANAMISIN ON TUBERCULOSIS DRUG RESISTANT

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Background and Aims: Kanamycin is a tuberculosis drug resistant therapy. Kanamycin can cause adverse effects of hearing loss, impaired kidney function, and electrolyte disorders especially hypokalemia. The objectives of this study was to analyze the survival time of adverse events caused by kanamycin in drug resistant TB patients and effects of age risk factors, previous history of streptomycin therapy and body weight of time adverse effects.

Methods: A retrospective cohort study. We reviewed medical records of TB patient's from January 2011 to December 2017 at Dr. Moewardi hospital Surakarta. Analysis of survival by the method of Kaplan-Meier and cox regression had test for the effects of risk factors on the emergence of adverse effects.

Results: Of 238 TB patients 143 (survival rate 39.96%) was hearing loss, renal function impairment occurred in 147 patients (survival rate 38.2%) and hypokalaemia was 169 patients (survival rate 29.0%) . Age over 40 years hazard ratio (HR) 2,419 (95% CI: 1716–3409; $P = 0.000$) and female gender HR: 1.549 (95% CI: 1.089–2.202; $P = 0.015$) at risk of hearing loss. Age over 40 years HR: 1892 (95% CI: 1353–2646; $P = 0.000$) and female gender HR: 1,667 (95% CI: 1179–2357; $P = 0.004$) risk of impaired renal function. Previous history of streptomycin and body mass index (BMI) were not at risk of adverse effects due to kanamycin.

Conclusion: Strict supervision of the adverse effects of hearing loss and renal dysfunction of patients aged over 40 years and women on TB treatment.

AP642

THE GREAT MASQUERADER: A CASE REPORT ON PULMONARY TUBERCULOSIS AND LUNG CANCER

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Background and Aims: Tuberculosis remains the most common pulmonary infection and most common cause of morbidity and mortality from any infectious disease around the world, especially in developing countries. It is also considered as one of the great mimickers of other pulmonary disease, making diagnosis sometimes elusive to the clinician despite advances in imaging and microbiological studies. There is also controversy with regards to it being a risk factor in developing lung malignancy, with lung malignancy being the third most common cause of cancer death and morbidity around the world.

Methods: We present a case of a 72 year old man with significant smoking history who has been having recurrent left upper lobe infiltrates. He has been repeatedly worked up for both granulomatous disease and malignancy, treated twice for pulmonary tuberculosis and later on developed Squamous Cell Carcinoma of the lung.

Results: When faced with a diagnostic dilemma regarding the aetiology of a mass, one must obtain tissue for a definitive diagnosis if non-invasive work up are equivocal.

Conclusion: In correlation to our case, due to the high incidence rate of TB and cancer in the country, the patient's clinical profile (age, smoking history, PTB exposure, symptoms), radiologic findings and sputum studies may be equivocal and pose a diagnostic dilemma in managing the case. The clinician must be judicious in choosing the appropriate route for tissue biopsy for a more definitive diagnosis, as to prevent delay in management.

AP643

'TENNIS RACKET' SIGN: AN OBLIVION PREDICTOR OF ACTIVE TUBERCULOSIS

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Background and Aims: Tuberculosis has higher prevalence among cavitory lesions on chest radiograph. Up to 45% of chest radiograph changes in tuberculosis depict cavitory lesions.

Methods: Case Series. We present 3 cases of patients who presented to us with various symptoms of on and off fever, cough, and loss of appetite and weight. We noted typical 'Tennis Racket' signs in chest radiograph of these patients. Immediate treatment for tuberculosis commenced while awaiting the sputum results. Sputum AFB for all 3 patients was positive. They showed remarkable improvement with antituberculosis treatment.

Results: The cavity is the "hallmark" of the active and highly contagious tuberculosis, and it is widely recognized in both primary and reactivation tuberculosis. The draining bronchus of most of the tuberculous cavities leads to tennis racket appearance. This infamous sign rarely has been described as predictor of active tuberculosis. In this study, we confirmed a higher grade of bacteriological yield in all these cases.

Conclusion: This case series illustrates the significance of 'Tennis Racket' sign as it can be used as predictor of active tuberculosis and each radiograph with such sign should be investigated thoroughly for tuberculosis.

AP644

ANALYSIS OF AGE-SPECIFIC CT FINDINGS OF ACTIVE TUBERCULOSIS IN AIZU MEDICAL CENTER, JAPAN

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Background and Aims: Tuberculosis (TB) morbidity in Japan is now 13.9 per 100,000 person-year, which is still in a moderate epidemic situation. The main reason of this phenomenon is considered to be aging. The characteristic CT images of elderly TB patients have been reported to have pneumonia pattern without cavity formation. The aim of this study is to analyze pulmonary CT findings in TB patients.

Methods: Thin-section CT scans obtained from 159 patients with active pulmonary TB in Aizu medical center, Japan between March 2009 and February 2018 were retrospectively evaluated. These data were weighed in 3 age groups: 36 patients of group A are younger than 65 years old; 48 patients of group B are between 65 and 80; 75 patients of group C are older than 80.

Results: In group A, cavity lesions were mainly detected, whereas in groups B and C, tree in bud and infiltrative lesions were mainly found. Bronchial stenosis were rarely seen in group A but found more in groups B and C. Pleural effusions were significantly more seen in groups B and C than in group A. While apical segment lesions were more common in group A, lower basal segments lesions were characteristically more found in groups B and C.

Conclusion: It was revealed that in elderly TB patients infiltrative shadows were more common than cavities as indicated by previous reports. Also, lower basal segment lesions were characteristic in elderly TB patients.

AP645

KNOWLEDGE, ATTITUDES AND BEHAVIOUR PATIENT SUSPECT MDR-TB AT PULMONARY HEALTH CENTER (BKPM) IN MALUKU-INDONESIA

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Background and Aims: Indonesia is one of the 27 MDR-TB high burden countries worldwide, with estimated 6,800 new cases every year. In Maluku, although there is no data on MDR TB cases but suspected cases of MDR TB already exist and there are increasing number of suspected MDR-TB at pulmonary health centre in Maluku. The aim of this study is to know the knowledge, attitude and behaviour of patient suspect MDR-TB in BKPM Maluku.

Methods: We used cross sectional study with accidental sampling method from January 2010 to December 2012 at BKPM Maluku- Indonesia with total sampling was 50 patients.

Results: The study included 29 (58%) males and 21 (42%) females with highest education backgrounds was senior high school 29 (58%). There were twenty-six (52%) patients have the monthly income salary less than USD74. Half of them (58%) had normal IMT. There were 6 (12.5%) patients with DM, and 17 (34%) patients were alcoholic or smokers. Moreover, there were 13 (26%) patients had received the injection TB drug program.

Patients were diagnosed with suspected MDR-TB (62%) having less knowledge about TB and mostly do not know the aetiology of TB and MDR-TB as well.

Thirty respondents (60%) had the moderate attitude about TB. Most of them had followed the recommendation to take regular TB medication 38 (76%). Unfortunately, they dropped out from the treatment program. Only 4 (8%) patients adhered the standard TB treatment. Regarding the attitude of coughing, side effects and quitting smoking/alcohol, there were 1 (2%), 1 (2%), 1 (2%) patients had better attitude respectively.

Conclusion: The lack of knowledge about the causes of TB and MDR-TB is the greatest finding that affected the attitude and behaviour of TB patients.

AP646

CLINICAL FACTORS ASSOCIATED WITH INITIATION OF LTBI TREATMENT AMONG HEALTH CARE WORKERS IN A REFERRAL HOSPITAL IN KOREA

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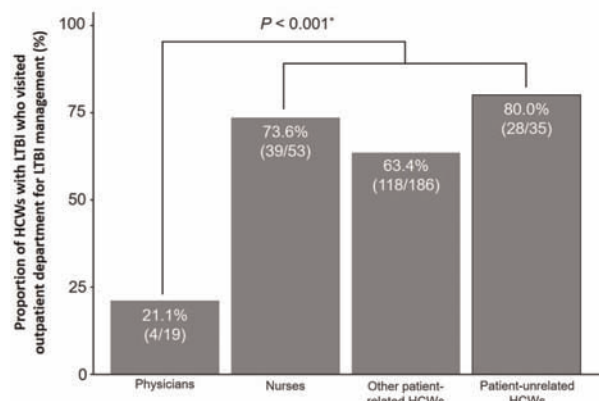
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Background and Aims: Despite wide use of interferon-gamma releasing assay for the diagnosis of latent tuberculosis infection (LTBI), the initiation rate of and factors associated with LTBI treatment among health care workers (HCWs) have not been well elucidated. The aim of this study was to evaluate the initiation rate of LTBI treatment and find factors associated with non-initiation of LTBI treatment among HCWs.

Table 4. Unadjusted and adjusted odds ratios of clinical variables associated with not receiving LTBI treatment among the HCWs with positive QFT-GIT

	Total (N = 293)	LTBI treatment		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
		Yes (n = 128)	No (n = 165)		
Age					
Twenties	25 (8.5)	15 (10)	10 (6)	Ref	Ref
Thirties	40 (13.6)	17 (13.4)	23 (14.4)	2.74 (1.05-7.40)	1.36 (0.37-5.06)
Forties	131 (44.7)	62 (47.3)	69 (52.7)	1.67 (0.73-3.99)	0.64 (0.18-2.30)
Over Fifties	89 (30.4)	34 (26.2)	55 (33.8)	2.43 (0.98-6.01)	0.80 (0.21-3.04)
Sex					
Male	113 (38.6)	45 (39.8)	68 (60.2)	Ref	Ref
Female	180 (61.4)	83 (46.1)	97 (53.9)	0.77 (0.48-1.25)	0.72 (0.42-1.24)
Occupation					
Physician	35 (11.9)	20 (15.1)	15 (12.9)	Ref	Ref
Nurse	19 (6.3)	3 (15.8)	16 (84.2)	7.11 (1.75-28.93)	12.87 (2.78-59.54)
Other patient-related HCWs ^a	93 (31.7)	27 (29.1)	66 (70.9)	1.28 (0.54-3.03)	2.04 (0.73-5.68)
Other patient-unrelated HCWs ^a	146 (50.1)	78 (53.1)	68 (46.9)	1.85 (0.89-3.83)	2.35 (1.06-5.21)
Years of employment					
< 10 years	57 (19.5)	33 (25.8)	24 (42.1)	Ref	Ref
10-20 years	47 (15.9)	32 (42.7)	15 (31.3)	1.59 (0.74-3.06)	1.96 (0.74-5.21)
> 20 years	169 (57.7)	63 (49.3)	106 (62.7)	2.31 (1.28-4.20)	4.54 (1.76-11.74)
History of working at TB associated department					
No	192 (65.5)	87 (67.2)	105 (64.8)	Ref	Ref
Yes	101 (34.5)	41 (31.8)	60 (59.2)	1.21 (0.74-1.95)	1.09 (0.62-1.93)

^aPatients included laboratory staff, cleaners, and other staff.



Methods: A cross-sectional study of 293 HCWs with LTBI was performed in a teaching hospital in Korea. LTBI was diagnosed with QuantiFERON-TB Gold In-Tube tests (Cellestis Ltd., Carnegie, VIC, Australia).

Results: Of the 293 HCWs with LTBI, 189 HCWs (64.5%) visited outpatient department to receive medical consultation for LTBI treatment. Of these, 128 subjects (67.7%) agreed with LTBI treatment with an overall 43.6% of LTBI treatment initiation rate. In multivariate analysis, being physicians (adjusted odds ratio [OR] = 12.87, 95% confidence interval [CI] = 2.78–59.54) and years of employment ≥ 20 years (adjusted OR = 4.54, 95% CI = 1.76–11.74) were independent factors associated with non-initiation of LTBI treatment. Among the subjects who visited outpatient department, those with the years of employment ≥ 20 years (adjusted OR = 7.05, 95% CI = 1.59–31.31) and having chronic liver diseases or taking potential hepatotoxic drugs (adjusted OR = 10.51, 95% CI = 2.15–51.36) were independently associated with refusal of LTBI treatment.

Conclusion: The overall initiation rate of LTBI treatment was suboptimal in HCWs with LTBI diagnosed with interferon-gamma releasing assay. An augmented LTBI treatment strategies which can improve the participation rate of medical consultation and encouraging acceptance rate of LTBI treatment are needed to effectively control LTBI in HCWs.

AP647

SPECTRUM OF TUBERCULOSIS IN ADVANCED CHRONIC KIDNEY DISEASE (aCKD)

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Background and Aims: Patients with aCKD carry a higher risk for both pulmonary and extrapulmonary tuberculosis due to multi-factorial immunosuppression. Anuradhapura is the highest CKD prevalent District in Sri Lanka. We performed a retrospective descriptive study to assess spectrum of tuberculosis in aCKD.

Methods: We reviewed clinic records of all patients above 16 years of age with advanced CKD (Cockcroft-Gault stage III-V), who were diagnosed with tuberculosis from January 2015 to December 2016, at District Chest Clinic, Anuradhapura.

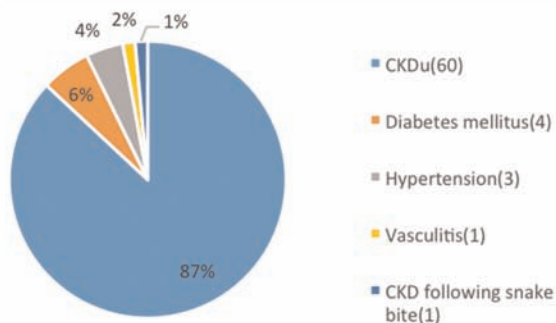
Results: Out of total 475 patients registered in tuberculosis clinic during the study period, 69 (15%) were found to have aCKD. Majority of them were male ($n = 63$, 91.3%) with mean serum creatinine 458.04 $\mu\text{mol/L}$. CKD of unknown aetiology endemic to the region (CKDu) was the commonest causative factor among the CKD population studied ($n = 60$, 87.67%: Figure 1).

Out of 69 patients with aCKD, 51 patients were presented with Pulmonary TB ($n = 51$, 73.91%), and 17 patients presented with EPTB (26.09%). In non-aCKD population too, majority presented with Pulmonary TB ($n = 282$, 69.46%). Commonest extrapulmonary site in aCKD population was central nervous system (CNS) ($n = 5$, 7.2%) followed by pleural effusion ($n = 3$, 4.34%), skin ($n = 2$, 2.9%) and uveitis ($n = 2$, 2.9%). TB lymphadenitis was the commonest extra-pulmonary site in non-aCKD population ($n = 37$). (Table. 02)

Out of 69 aCKD patients, Tuberculin Skin Test (TST) results were available for 43 patients, which was positive in 19 (44.19%) and negative in 24 (55.81%). In non-aCKD patients, TST results were available for 256 patients, where 153 (59.76%) gave positive results, and 103 (40.23%) gave negative results. Fisher's Exact Test revealed a statistical significance of TST negativity in the presence of aCKD in this study population ($P = 0.05$).

Conclusion: Pulmonary tuberculosis was commoner than extra-pulmonary tuberculosis in all categories. CNS was the common extra-pulmonary site in aCKD, compared to lymph node involvement in non-aCKD. TST was significantly negative in aCKD.

Site of TB	CKD patients	Non patients	CKD X2	p
Pulmonary	51	282	0.5585	0.4548
Extra pulmonary				
TB pleural effusion	3	23	0.1978	0.6565
TB lymphadenitis	1	37	4.7067	0.0300
TB spine	0	14	NA	
CNS TB	5	11	3.7297	0.0534
Skin TB	2	6	0.7189	0.3965
Abdominal TB	1	4	0.1219	0.7269
TB uveitis	2	7	0.4376	0.5082
Skeletal TB	1	3	0.3564	0.5505
GI TB	1	6	0.0003	0.9854
Renal TB	1	1	2.0356	0.1536
Milliary TB	1	9	0.1686	0.6814
Scrotal TB	0	3	NA	
total	69	406		



PULMONARY TUBERCULOSIS IN ADVANCED CHRONIC KIDNEY DISEASE; A DESCRIPTIVE STUDY ON DISEASE PATTERN AND TREATMENT OUTCOME IN A HIGH CKD PREVALENT SETTING

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Background and Aims: Advanced CKD (aCKD) is a risk factor for lung infections including pulmonary tuberculosis (PTB). Anuradhapura District has a high prevalence of CKD, mostly due to endemic CKD of unknown origin (CKDu).

Methods: We reviewed clinic records of all patients above 16 years of age with aCKD (Cockcroft-Gault stage III-V), who were diagnosed with PTB from January 2015 to December 2016, at District Chest Clinic, Anuradhapura.

Results: Out of total 475 patients registered in tuberculosis clinic during the study period, 333 (70%) had PTB. aCKD was noted in 51 (15%) of them (41(80%) bacteriologically confirmed; 10 clinically diagnosed), while 282 (250 (89%) bacteriologically confirmed; 32 clinically diagnosed) did not have aCKD. Sputum direct smear positivity in relation to aCKD was statistically not significant ($X^2 = 2.674$, $P = 0.102$).

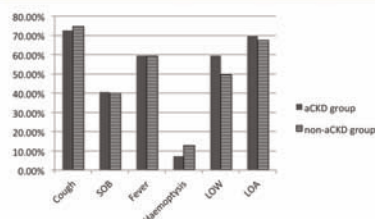
Cough and loss of appetite were the commonest symptoms in both groups, who showed a similar symptom profile (Figure 1). Mean CXR severity score (Ralph AP, et al. BMJ 2010), in aCKD was 55.3, compared to 25.1 in non-aCKD ($t = 14.8$, $P = 0.469$).

In bacteriologically confirmed PTB in aCKD, 16 (39.02%) had sputum grade +1 positivity and 7 (17.07%) had scanty positivity on direct examination for acid fast bacilli (AFB). In contrast, in non-aCKD group 97 (38.8%) had +3 positivity and 68 (27.2%) had +2. Significantly low sputum positivity is noted in aCKD ($X^2 = 6.9247$, 0.008).

Cure rate of PTB was 90% in aCKD, compared to 98% in non-aCKD. Death rates were significantly high in aCKD in relation to both bacteriologically confirmed PTB (3 each; $X^2 = 6.1588$, $P = 0.013$) and clinically diagnosed PTB (2 each; $X^2 = 4.0884$, $P = 0.043$). (Table 1)

Conclusion: Symptomatology in PTB was not different in aCKD, compared to non-aCKD group. However sputum AFB direct examination revealed significantly low mycobacterial load in aCKD patients. PTB in aCKD had a comparatively lower cure rate (90% vs 98%) with significantly higher death rates.

Treatment outcome	Patients with CKD (n=69)			Non CKD (n=406)		
	PTB(+)	PTB(-)	EPTB	PTB(+)	PTB(-)	EPTB
Cured (n)	37	0	0	244	0	0
(% of total)	53.62%	0%	0%	60.09%	0%	0%
Treatment completed(n)	0	8	17	0	30	121
(% of total)	0%	11.59%	24.64%	0%	7.4%	29.8%
Treatment failed (n)	1	0	0	3	0	0
(% of total)	1.45%	0%	0%	0.74%	0%	0%
Died (n)	3	2	1	3	2	3
(% of total)	4.35%	2.9%	1.45%	0.74%	0.49%	0.74%
Total	41	10	18	250	32	124
	59.42%	14.5%	26.08%	61.58%	7.88%	30.54%



AP649

THE IMPORTANT OF RAPID MOLECULAR TEST IN TB DIAGNOSIS AND PROMPT TREATMENT

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Background and Aims: MDR TB was the most difficult case in TB management. In this study, we evaluate all TB patient were treated in our setting as tertiary referral hospital. The interim result try to evaluate characteristic among subjects with drug resistance and susceptible.

Methods: Design of this study was cohort prospective, we screen all TB patient who diagnose and treat in our hospital. Subjects will be examined with smear, rapid test, culture, and demographic as well clinical diagnostic. Ethical clearance were evaluated by Persahabatan Hospital Ethics Committee.

Results: Since November 2017 until May 2018, we evaluate subjects with complete the data and there were 12 susceptible TB case and 6 drug resistant treated diagnoses with xpert MTB/ RIF either smear, chest x-ray, and clinically. Both group showed more male 77% than female, both have history to come to public either private health service, and more cases with cavities (susceptible 58% and 66% resistance). All resistant group have smear positive and previously treated, as the risk MDR TB was high among previously treated cases.

Conclusion: There were no difference characteristic among susceptible and resistant TB cases, there for it is important to diagnose TB using rapid molecular test that could distinguished susceptible and resistant cases specifically to initiate prompt treatment rapidly.

AP650

THE TREND OF TUBERCULOSIS RESEARCH IN NORTH KOREA BASED ON A REVIEW OF LITERATURE

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Background and Aims: Tuberculosis (Tb) is one of the most prevalent diseases and multidrug-resistant tuberculosis (MDR-Tb) is a serious public health problem in North Korea. However, there is little information on tuberculosis and its treatment in North Korea.

Methods: We analyzed articles on Tb published in The Internal Medicine Journal, one of the nine medical journals published in North Korea between 2006 and 2015.

Results: Of the total 2092 articles, 200 were related to respiratory medicine and 37 to Tb. All articles began by citing the teachings of the supreme leader as the aim of the study and were one or two pages in length, similar to an abstract. They typically had two authors, and less than five references. Twenty-two articles were based on experimental research, 8 were observational studies, 5 were reviews, and 2 were case reports. There were 26 studies on treatment, 9 on diagnosis, and 2 on other topics. Pleural effusions were treated as Tb pleurisy; however, no article provided information regarding the basis on which the diagnosis had been made. Streptomycin and isoniazid were the standard treatment regimen for Tb. Rifampin, isoniazid, and pyrazinamide combination therapy was described in only one case report. Thirteen articles described the treatment duration (over 6 months in only 4 studies). Other articles did not include the treatment duration or reported it as 1 to 3 months. There were only 3 articles that described the negative conversion of sputum culture. In other studies, the responses to treatment were the improvement of symptoms, such as cough and sputum quantity, and resolution of fever.

Conclusion: These findings suggest that the increase of MDR-Tb in North Korea results from the inappropriate combination of drugs and the short treatment duration.

AP651

A FILIPINO WITH MULTIPLE SACCULAR ANEURYSMS CAUSED BY MYCOBACTERIUM TUBERCULOSIS

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Background and Aims: Tuberculous aortitis is an unusual presentation of a common disease in the Philippines. The majority of tuberculous aortic aneurysms are saccular (98%) and false (88%) with abdominal and descending aorta as preferential sites. We report a case infectious aortitis with no previous history of pulmonary tuberculosis.

Methods: A 58-year old Filipino male presented with severe abdominal pain. There was no cough, haemoptysis or afternoon fever. His past history was negative for connective tissue diseases, tuberculosis or vasculitis. CT aortography revealed an atheromatous aorta with a partially thrombosed saccular aneurysm arising from the aberrant right subclavian artery (Figure 1) and segmental partially thrombosed dissections at the distal abdominal aorta (Figure 2). He was referred to thoraco-cardiovascular surgery service and underwent total arch replacement. Surgeon noted aortitis with external inflammatory adhesion during surgery. Histologic examination of aortic wall revealed granulomatous aortitis and showed acid-fast bacilli on staining. Patient was started with fixed dose anti-tuberculous therapy.

Results: Tuberculous aortitis is a very rare form of extra-pulmonary tuberculosis. Mycobacterium infection of the aorta usually occurs as a result of direct extension from an adjacent focus or via haematogenous spread. A primary tuberculous infection in the lung spreads into the peri-aortic structures subsequently invading the aortic wall. Clinically, a patient with a tuberculous aneurysm may initially present pain related to the location of the aneurysm. Medical treatment is not sufficient, and once tuberculous aortic aneurysm is suspected, surgery should not be delayed because of the high probability of aneurysmal rupture.

Conclusion: Tuberculous aortitis, albeit rare, should be suspected in any patient presenting with aortic aneurysm. A combination of surgical treatment and long term anti-tuberculous therapy is the best treatment option.

Figure 1. Aneurysm at the distal abdominal aorta



AP652

THE INFLUENCE OF COMPLICATION OF INTERSTITIAL LUNG DISEASE TO MORTALITY AND LENGTH OF STAY IN WARD FOR THE PATIENTS WITH PULMONARY TUBERCULOSIS

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Background and Aims: Although we sometimes experienced patients with pulmonary tuberculosis complicated with interstitial lung disease (ILD), there are only limited information about the influence of complication of ILD to mortality and length of stay in ward for the patients with pulmonary tuberculosis.

Methods: The information of the patients who admitted to the tuberculosis care unit of our hospital since 2015 to 2017 were reviewed with clinical chart. Patients were divided into two groups, one is ILD group and the other is non-ILD group. Mortality and length of stay in ward were compared in the two groups. Fisher's exact test and Mann-Whitney test were used.

Results: 371 patients were enrolled and the percentage of the patients with ILD was 7.3% (27/371). The mortality of the ILD group and non-ILD group were 22.2% and 11.9%, respectively ($P = 0.132$). The length of stay in ward of the two groups were $67. \pm 0.3$ and $55. \pm 1.9$ days respectively ($P = 0.480$).

Conclusion: Complication of ILD for the patients with pulmonary tuberculosis resulted in the trend of higher mortality and longer stay in ward, but they were not significant.

AP653

DIAGNOSTIC DISCREPANCY, A DRUG SENSITIVE OR MDR-TB : CASE REPORT

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Background and Aims: Tuberculosis is still a high burden problem in Indonesia. The problem increased by MDR case since we are in the top ten rank. The most important thing of MDR is diagnosis. The faster and more accurate the diagnosis of MDR TB, expected higher treatment rate. That's why we use rapid molecular test (GeneXpert MTB/RIF Assay) and DST test. The sensitivity and specificity of GeneXpert MTB/RIF assay for the diagnosis of MDR-TB was found to be comparable to gold standard, conventional DST. In this case we discussed about the difference result between culture and rapid molecular test.

Methods: A 35 year old previously treated female presented with cough more than 2 weeks, weight loss, loss of appetite, shortness of breath, night sweating and fatigue. Chest X-Ray showed opacity at the upper and mid-zone of right lung and cavity at the apex of the lung. From hospital examination, the smear showed 1+ and Gene Xpert MTB Assay showed MTB positive rifampicin susceptible. From research sputum specimen, it was 1+ smear and MTB positive rifampicin susceptible. Patient received DS-TB line 1 treatment. Three months later, Drug Sensitivity Test (DST) from hospital showed Rifampicin, Streptomycin and Isoniazid Resistance. Meanwhile, DST from research sputum showed Mycobacterium other Than TB (MoTT). Patient was diagnosed as MDR-TB and has got Short Term Regimen. Investigators confirm the diagnosis by GenoscholarTM test and it was found that the DNA was susceptible for Rifampicin and Isoniazid.

Results: The patient was returned to continue DS-TB Line 1 treatment. Patient's condition clinically improved

Conclusion: There are discrepancy among smear, Gene Xpert MTB/RIF Assay and DST. Even in previously treated patient, we have to confirm the diagnosis carefully. In our case, we confirm the difference result by GenoscholarTM.

AP654

QUALITY OF LIFE OF PATIENTS WITH MULTI-DRUG RESISTANT TUBERCULOSIS AT PROGRAMMATIC MANAGEMENT OF DRUG-RESISTANT TUBERCULOSIS WESTERN VISAYAS MEDICAL CENTER JANUARY 2013 TO APRIL 2015 PHILIPPINES

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¹Western Visayas Medical Centre, Philippines

Background and Aims: Besides clinical impact, the disease affects the quality of life (QOL) as well. With the rise of 21st century, multi-drug-resistant TB (MDR-TB) has risen as a significant public health problem due to emergence of resistance to anti-tuberculosis therapy drugs.

Methods: A cross sectional descriptive study conducted from January 2013 to April 2015 in (PMDT) WVMC using the World Health Organization Quality of Life Instrument Brief version (WHOQOL-BREF).

Results: Data was collected from 62 patients. Domain scores were generally better in males, younger (<50 yr. old) patients, patients with higher incomes, single, college graduates, and patients with a shorter course of treatment.

The most affected was the physical health domain which assesses the impact of disease on the level of independence, activities of daily living, pain and discomfort, dependence on medicinal substance, lack of energy, sleep and rest, mobility and capacity to work on the other hand.

Followed closely by the psychological domain which assesses the impact of self-esteem, positive and negative feelings, bodily appearance and spirituality, then the social relationships domain which assesses social support, personal relationship and sexuality.

Environmental health domain was least affected.

Conclusion: MDR-TB affects quality of life both directly and indirectly.

This study suggests to design an applicable, reliable and valid TB/MDR-TB-specific HRQL instrument, which can better address quality of life issues methodologically.

This would further enable the health care professionals and management to devise relevant interventions to improve the quality of the patients, as well as the programme.

AP655

SUCCESSFUL DESENSITIZATION FOR ANTI-TUBERCULOSIS HYPERSENSITIVITY DRUG REACTION: A CASE SERIES

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Background and Aims: Hypersensitivity reaction to anti-tuberculosis medications poses a great challenge. Its incidence ranges from 4–6% of cases (Siripassorn et al. 2018). Normally second-line drugs would be given once reaction developed however, desensitization to the offending drug is an alternative strategy.

Methods: We report three cases of hypersensitivity reaction to anti-tuberculosis drug with successful desensitization. They had allergic skin rash while on fixed-dose combination or loose tablet. The culprit drug

were identified during sequential re-challenged of anti-TB drug. Rapid desensitization were done by prescribing small incremental dosage on the first day, split dosage on the second to third day and full dose once daily on the fourth day.

Results: Case 1: 17 year-old lady with underlying overlap syndrome (SLE and systemic sclerosis) on hydroxychloroquine and prednisolone 10 mg presented with 3 weeks history of fever. CT thorax showed matted necrotic mediastinal and hilar lymph nodes with lingular focal consolidation. Patient was then treated as smear negative PTB with Akurit-4 but developed DILI. Culpit drugs identified were rifampicin, isoniazid and levofloxacin. The levofloxacin desensitization failed but she was successfully desensitized to rifampicin and isoniazid.

Case 2 : 64 year-old lady with underlying overlap syndrome (SLE, Sjogren's syndrome and dermatomyositis) on hydroxychloroquine and prednisolone 10 mg OD was diagnosed as smear positive pulmonary tuberculosis (PTB) and was started on Akurit-4. She had urticaria on Day 7. She was then re-challenged with anti-TB and culprit drug identified was pyrazinamide. She was then successfully desensitized with pyrazinamide.

Case 3: 32-year-old lady presented with chronic cough and was diagnosed as smear negative culture-positive tuberculosis. She developed generalised maculopapular rash at day 3 of Akurit-4 treatment and culprit drug identified during rechallange was isoniazid and rifampicin. She was then successfully desensitized to both drugs.

Conclusion: These case series highlights that desensitization can be a successful strategy for drug hypersensitivity reaction.

AP656

ABDOMINAL TUBERCULOSIS MANAGED SURGICALLY IN THE LATE PHASE: A CASE REPORT KEN HUI FU¹

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Background and Aims: Abdominal tuberculosis (TB) is an uncommon presentation that complicates pulmonary TB in 1-5 % of cases, affecting primarily young adults. The clinical diagnosis is challenging and often delayed due to the symptoms being non-specific and may be confused with other inflammatory bowel diseases, therefore resulting in significant morbidity and mortality.

Methods: A 27-year-old man attended our Emergency Department complaining a fever of 38.4°C and acute abdomen, in addition to suspicious pulmonary TB. Abdominal TB associated intestinal obstruction, ascites and lymphadenopathy were found by imaging and exploratory laparotomy. He was treated surgically by segmental resection, however passed away due to severe bleeding caused by recurrence of perforation of the small intestine and state of immunocompromised with sepsis.

Conclusion: Aggressive promotion of TB education could be suggested for both medical personnel and general population, which might improve the early diagnosis and timely treatment.

APL016

LATENT TUBERCULOSIS INFECTION ON HEALTHCARE WORKER IN WEST SUMATERA PULMONARY HOSPITAL FENTY ANGGRAINY¹*, IRVAN MEDISON¹, SABRINA ERMAYANTI¹, YESSY SABRI¹

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Background and Aims: A third of the world's population is infected with Mycobacterium tuberculosis (M.tb). Certain individual exposed to M. tb, such as healthcare worker that contact with tuberculosis patient, would be in latent condition and could be reactivated to tuberculosis disease.

Identified the population with risk of latent tuberculosis is the important part in controlling tuberculosis.

Methods: Study design is cross-sectional design in healthcare worker in West Sumatera Pulmonary Hospital on March-May 2016 with data based and IGRA test (Quantiferon-Gold).

Results: There is 42 respondent; there were woman (71.4%), mean age 37.7 years old, bachelor (47.6). The most common occupation is nurse (40.5%), duration of working for 1-≤5 years (40.5%). There is non-smoker healthcare worker (73.3%), without comorbid (97.6%). History of BCG vaccination were 64.3% and never perform tuberculin test (83.3%). LTBI prevalence were 38.1%. Many of man and age ≤35 years old with latent tuberculosis infection. But not statistically significant (41.7% vs 36.7%, $P = 1$, CI 95% dan 42.3% vs 31.2%, $P = 0.5$, CI 95%). Direct tuberculosis contact occupation and duration of work >10 years more often with latent tuberculosis infection. But not statistically significant (50% vs 35.3%, $P = 0.45$, CI 95% dan 44.4% vs 26.7%, $P = 0.4$, CI 95%).

Conclusion: Incidence of latent tuberculosis in West Sumatera Pulmonary Hospital are not affected by direct tuberculosis contact occupation and duration of work.

Karakteristik	Prevalensi	N
Jenis Kelamin		n=42
Pria	12	28.6
Wanita	30	71.4
Status Pendidikan		
SMP	34	81
Tinggi Sekolah	8	19
Pendidikan		
SDA	1	2.4
Diploma	13	31.2
Sarjana	28	67.4
Usia (tahun)		(22-65)
< 25 tahun	34	81.0
25-35 tahun	12	28.6
35-45 tahun	30	71.4
> 45 tahun	8	19.0

Pekerjaan	Prevalensi	N
Pegawai Samping		
Dokter	6	14.3
Paramedis	17	40.5
Laboran	3	7.1
Ruangrawan	3	7.1
Ayatan	2	4.8
Guru	3	7.1
Supervisor	1	2.4
Pegawai tidak Samping		
Tanah Ulat	6	14.3
Lama Bekerja		
< 1 tahun	4	9.5
1-5 tahun	17	40.5
5-10 tahun	6	14.3
> 10 tahun	15	35.7

Karakteristik	IGRA +	IGRA -	P-value	PR
Jenis Kelamin				
Pria	12	16.6		
Wanita	26	35.4		
Status Pendidikan				
SMP	34	45.7		
Tinggi Sekolah	8	10.5		
Pendidikan				
SDA	1	1.3		
Diploma	13	17.4		
Sarjana	28	37.1		
Usia (tahun)				
< 25 tahun	34	45.7		
25-35 tahun	12	16.6		
35-45 tahun	30	40.5		
> 45 tahun	8	10.5		

Karakteristik	IGRA +	IGRA -	P-value	PR
Jenis Kelamin				
Pria	12	16.6	0.69	1.8 (0.4-8.0)
Wanita	26	35.4		
Status Pendidikan				
SMP	34	45.7	0.69	1.8 (0.4-8.0)
Tinggi Sekolah	8	10.5		
Pendidikan				
SDA	1	1.3		
Diploma	13	17.4		
Sarjana	28	37.1		
Usia (tahun)				
< 25 tahun	34	45.7	0.69	1.8 (0.4-8.0)
25-35 tahun	12	16.6		
35-45 tahun	30	40.5		
> 45 tahun	8	10.5		

APL017

STATIN TREATMENT MAY PREVENT DEVELOPMENT OF ACTIVE TUBERCULOSIS IN DIABETIC STATE: AN ANALYSIS OF A NATIONALLY REPRESENTATIVE COHORT HUI-YUAN HSIAO¹*, KWONG-LEUNG YU¹, LONG-CHUNG CHANG¹, LI-HSIANG CHEN¹

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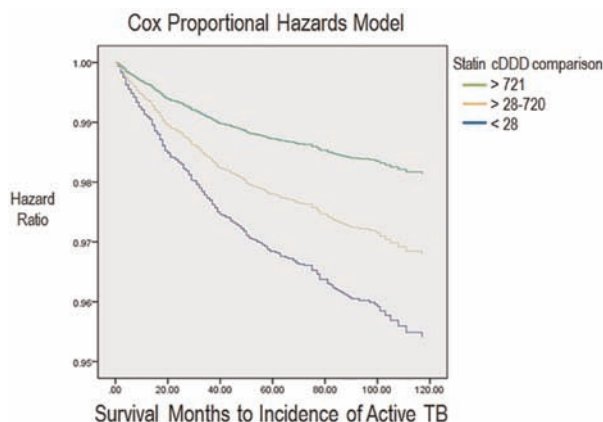
Background and Aims: Diabetes mellitus (DM) triples the risk of tuberculosis and increases the likelihood of adverse tuberculosis outcome, such as treatment failure, death and recurrence. Epidemiological data suggest that statin improve the clinical outcome of respiratory infections and reduce the risk of active tuberculosis (TB). We sought to

examine whether statin therapy decreases the incidence of active TB in diabetic patients.

Methods: We conducted a nested case-control study on data obtained from a national health insurance claims database between 2004 and 2013. Pairwise (1:1) propensity score method was carried out to match statin and non-statin samples for each TB patient in a diabetic population. Logistic regression was then used to calculate the incidence of TB among matched groups. To observe the survival of diabetic patients to the incidence of TB between the number of months as a time variable, according to gender, age, co-morbidities (CCI) and statin cumulative definite daily dose (cDDD, low <28 vs medium 28–720 vs high dose >720) variables were divided into different groups and the Cox proportional hazards model was used to construct a survival regression model of diabetes.

Results: Matching of 11,998 diabetic patients yielded two cohort of 5999 patients, statin users and non-users. During the study period, 403 individuals were diagnosed with active TB. In comparison to non-TB patients, statin users were less frequent among TB patients (42.7% vs 57.3%, $P < 0.001$). Active TB protection increased with increasing dose of statin prescription. High dose statin users was associated with the lower risk of TB than medium dose (HR 0.643; 95% CI 0.614 to 0.744, $P = 0.033$). The effects estimates obtained for medium and low dose statin users were similar (HR 1.063; 95% CI 0.989 to 1.108, $P = 0.606$).

Conclusion: Statin therapy among diabetic patients was associated with a protective effect on TB incidence, especially high dose.



Respiratory Infections (Non-Tuberculous) 2

AP657

THE DIAGNOSIS VALUE OF BRONCHOALVEOLAR LAVAGE DETECTION BY HIGH-THROUGHPUT SEQUENCING FOR PULMONARY INFECTIOUS DISEASES

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Background and Aims: High-throughput sequencing technology is widely used to find the unknown pathogens in cerebrospinal fluid, blood and so on. But it is controversial in bronchoalveolar lavage for pulmonary infectious diseases. The aim of this study was to investigate the diagnosis

value of bronchoalveolar lavage detection by high-throughput sequencing for pulmonary infectious diseases.

Methods: We included patients with pulmonary infectious diseases or as control group from November 2017 to December 2017 in the department of respiratory disease, the third affiliated hospital of Sun Yat-sen University. High-throughput sequencing and culture of bronchoalveolar lavage fluid were used to evaluate the pathogens.

Results: We included 14 patients, 12 cases were pulmonary infectious diseases and 2 cases were without pulmonary infectious diseases. High-throughput sequencing was fast (24h-48h) and expensive. The pathogens of 10 cases (71.4%) were confirmed by high-throughput sequencing, consistent with culture. At the same time, 9 cases (64.3%) showed not only one pathogen, which seemed lung microbiome detected by high-throughput sequencing. Some rare pathogens were found, containing some were difficult cultured, such as *neurospora crassa* OR74A, *prevotella*, *treponema*, human herpesvirus 5 and *spirometra mansonii*.

Conclusion: High-throughput sequencing was fast and expensive. The bronchoalveolar lavage detection by high-throughput sequencing for pulmonary infectious diseases can help confirm the common pathogens, unknown pathogens or rare pathogens. It also helped to know the lung microbiome change of pulmonary infectious diseases.

AP658

HOSPITAL-ACQUIRED PNEUMONIA RATE IN A HOSPITAL AFFILIATED UNIVERSITY IN CHINA: A CROSS-SECTIONAL SURVEY INVOLVING 210417 INPATIENTS

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Background and Aims: This study aimed at evaluating the hospital-acquired pneumonia (HAP) rate and the risk factors and prognosis associated with HAP caused by multidrug-resistant organisms (MDROs) in a hospital affiliated university in China.

Methods: Data were collected relating to all episodes of HAP occurred in the third affiliated hospital of Sun Yat-sen University between January of 2014 and December of 2017. Variables of interest included age, gender, comorbidities, central venous catheter use, prior treatment, diagnosed department, 30-day mortality. The study was approved by the Institutional Review Board of the hospital.

Results: Out of 210417 inpatients, there were 1472 (0.7%) HAP cases. 1158 cases were eventually included. The most common organisms were *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*. 188 cases were MDROs. The first logistic regression analysis identified the independent risk factors of MDROs-HAP included age, gender, encephalorrhagia, cerebral infarction, prior endotracheal tracheostomy, antibiotics therapy in the preceding 90 days, stomach tube intubation or gastrostomy, central venous catheterization, clinical pulmonary infection score >6, multi-lobular infiltration. In the second multivariable analysis that encephalorrhagia, cerebral infarction, prior endotracheal tracheostomy, antibiotics therapy in the preceding 90 days, stomach tube intubation, clinical pulmonary infection score >6, multi-lobular infiltration were still associated with MDROs-HAP. The therapy of MDROs was obviously with compliance to the guideline. The hospital stays were longer and 30-day mortality was worse with MDROs-HAP.

Conclusion: The overall prevalence rate of HAP was 0.7% among 210417 inpatients surveyed. The most common organisms were *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*. Encephalorrhagia, cerebral infarction, prior endotracheal tracheostomy, antibiotics therapy in the preceding 90 days, stomach tube intubation, clinical pulmonary infection score >6, multi-lobular infiltration were

associated with MDROs-HAP. The therapy of MDROs was obviously with compliance to the guideline. The hospital stays were longer and 30-day mortality was worse with MDROs-HAP.

Critical Care Medicine 1

AP659

INFLUENZA A PANDEMIC (H1N1) 2009 VIRUS INFECTION WITH DEATH LIMB EXTREMITIES INFERIOR AND ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS): A CASE REPORT

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Background and Aims: Influenza A pandemic (H1N1) 2009 virus has created a major worldwide health problem within a short time after its emergence. This infection is often self limited, but sometimes can cause severe and fatal complication. In adults, patients typically present with fever and respiratory symptoms, and may develop ARDS and sepsis. In recent years, there has been an emergence of clinical data suggesting that H1N1 infection may also predispose patients to the development of thromboembolic complications.

Methods: Case Report

Results: A 66-year old female was admitted to the hospital with shortness of breath, dry cough, fever, sore throat, myalgia, malaise, nasal congestion since 4 days prior admission. The first we assessed patient with suspected MERS- CoV infection because she had travelled to Saudi Arabia one week before admission. The patient had a history of hyperthyroidism for 36 years.

On general examination, she was severe cardiovascular instability with hypotension, tachycardia, tachypnea, hyperthermia, respiratory failure, along with oligouria and altered mental status. On Physical examination rhonchi were detected in the lower lung fields. We found absent of her right lower extremity pulses, along with other signs of acute arterial insufficiency (cold right lower extremity). Chest radiograph showed patchy air-space disease consistent with multifocal pneumonia. On laboratory examination were as follow leukopenia, lymphopenia, thrombocytopenia, elevated levels of creatine kinase and hepatic aminotransferase. Polymerase chain reaction determination of nasopharyngeal swab for MERS-CoV was negative and Influenza A pandemic (H1N1) 2009 virus was positive. Culture of specimens of blood, urine, and sputum were steril.

The patient was administered oseltamivir and supportive treatment, including wide-spectrum antibiotics, thyrozol, intravenous unfractionated heparin, vasopressor, and mechanical ventilation.

Conclusion: Although rapidly progressive pneumonia and respiratory failure are severe complications, clinicians should be aware that Influenza A pandemic (H1N1) 2009 virus may be complicated with death limb extremities.

Interstitial Lung Disease 1

AP660

CLINICAL COURSES AND TREATMENT EFFECTS IN SYSTEMIC SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE

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Background and Aims: Interstitial lung disease (ILD) coexists with systemic scleroderma (SSc). However, ILD also coexists with patients who do not fully match the diagnostic criteria of SSc. The clinical courses of SSc patients and the ILD patients without SSc features have not been clarified. It is unclear that whether ILD patients with SSc is regarded in the same as ILD patients with clinical features of SSc but do not meet the diagnostic criteria.

Methods: We retrospectively reviewed 42 ILD patients' clinical records in our hospital from October 2002 to March 2017. We defined the SSc group as patients with Classification Criteria for SSc (ACR/EULAR 2013) and the SSc-like group as patients without it. We compared each groups about clinical backgrounds, treatment effects and prognosis.

Results: The rate of anti-topoisomerase 1 antibody positive patient in SSc-group was higher than SSc-like group. The short-term effect of treatment in SSc group may be better than SSc-like group, and the progression of ILD in SSc group may be slower than SSc-like group in long-term treatment.

Conclusion: SSc-like group is different from SSc-group about clinical backgrounds, treatment effects, and so on. We need to consider SSc-ILD and SSc-like ILD separately.

COPD 2

AP661

PERCEPTION OF SYMPTOMS AND PATIENT'S VIEW IN COPD- MARKERS OF CHANGING NEEDS CAN OZTURK¹

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Background and Aims: It is not too easy to explain individual differences in presentation of COPD among people with the same disease severity. Influence of symptoms and patient's behaviour due to these symptoms may be very different. A meta analysis showed that illness perceptions explained %21–30 of the variance of HRQoL results. This study aims to explore the experiences and perceptions of patients. Results may serve as a stimuli for their physicians to collaborate better with their patients if they consider these markers of perceptions.

Methods: 30 patients met the following criteria; >50 years old with a diagnosis of COPD and receiving maintenance therapy for at least 12 months and including LABA's, LAMA's; ICS's or their combinations. Exclusion criteria for participation included NIV requirement at least once and cognitive impairment.

Results: A total of 30 patients were recruited. All subjects had moderate to severe COPD. The majority of patients were male.

23 patients complained from their restrictions for their hobbies such as shopping, gardening, being together with his/her friends, walking long distances. 25 patients suffer from reduced activity levels.

14 patients complained about experiencing self-care duties such as having a bath, helping to his wife for household chores, helping to her

husband for houseworks. Most of them were anxious about maintaining their dignity. 28 of 30 patients expressed frustration and disappointment for their inability for sexual activities.

24 patients expressed confidence for their "outpatient follow-up" programmes. They declared that they believed for admission to the hospital when they could not have been managed at home. This belief cleared away their anxiety for acute episodes.

Conclusion: Our survey suggests that although optimal care has been given by physicians there are significant gaps between the perception of patients and their doctors. More open discussions between patients and their doctors are needed.

Respiratory Infections (Non-Tuberculous) 1

AP662

CHARACTERISTICS OF HOSPITAL-ACQUIRED PNEUMONIA PATIENTS WITH MULTIDRUG-RESISTANT BACTERIAL INFECTION IN DR.CIPTO MANGUNKUSUMO GENERAL HOSPITAL INDONESIA

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Background and Aims: To describe the epidemiology and possible risk factors for the development of multidrug-resistant (MDR) Hospital-acquired Pneumonia (HAP) in Indonesia.

Methods: Using medical records, we conducted a descriptive cohort retrospective study among patients diagnosed with HAP hospitalized in 2015–2016. Cases were defined as patients with qualified sputum Gram stain according to Murray & Washington classification, culture-confirmed MDR HAP according to Magiorakos classification. Data were analyzed using Microsoft Excel.

Results: Out of 68 HAP patients with positive sputum culture during 2015–2016, 63 patients were infected with MDR bacteria while 5 cases were infected with non MDR bacteria. Proportion of HAP during 2015 and 2016 respectively were 6.12 per 1000 admission and 6.15 per 1000 admission. Proportion of MDR bacteria in 2015 and 2016 were 95% and 82.1% respectively. Patients infected with MDR bacteria were more likely to have been previously treated with antibiotic 90 days before diagnosis and had albumin level <2.5 g/dL. Statistical analyses could not be applied due to proportion discrepancy between MDR and non MDR group. The most common MDR isolates found were *K. pneumoniae* (27.1%), *A. baumannii* 923.4%) and *A. Iwoffii* (7.4%) respectively.

Conclusion: High proportion of MDR bacterial infection were found among HAP patients hospitalized in 2015–2016. Patients infected with MDR bacteria were more likely to have been previously treated with antibiotic 90 days before diagnosis and albumin level <2.5 g/dL. Most common MDR isolates found was *K. pneumoniae*.

Respiratory Infections (Non-Tuberculous) 2

AP663

IDENTIFYING OF RISK FACTORS OF MULTI-DRUG RESISTANT BACTERIA IN HOSPITALIZED ACQUIRED PNEUMONIA

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Background and Aims: Hospital-acquired pneumonia (HAP) infection by multidrug-resistant (MDR) bacteria leads to high mortality, length of stay and high maintenance costs. Institution based risk factor identification can be used to identify patient with high risk condition to have MDR bacteria and it is essential in determining appropriate location based empirical antibiotic therapy. Therefore it is important to know factors associated with MDR bacteria infection in HAP.

Methods: We conducted a retrospective cohort study attained from medical records of HAP patients hospitalized at Dr. Cipto Mangunkusumo General Hospital Jakarta in January 2015 - December 2016. The data obtained from medical records only patients diagnosed with HAP and presenting with positive bacterial cultures. It was classified as MDR bacteria and non-MDR bacteria. Chi-square was used to compare categorical variables. Logistic regression was used to identify risk factors for MDR bacteria in HAP.

Results: The proportion of HAP with MDR bacteria during 2015–2016 was 63 patients (61.6%). The three most common microorganisms found in HAP with MDR bacteria were *Klebsiella pneumoniae* (27.1%), *Acinetobacter baumannii* (23.4%) and *Pseudomonas aeruginosa* (6.1%). Univariate analysis showed that the risk factors for MDR bacteria infection were: age >60 years; prior ICU/HCU hospitalization in the last 90 days; Charlson Comorbidity Index ≥3; and history of nasogastric tube (NGT) insertion. Multivariate analysis showed that prior ICU/HCU hospitalization in the last 90 days was the only independent predictor of infection with MDR bacteria (OR = 0.015; 95% CI: 0.001–0.202; *P* = 0.002).

Conclusion: Prior ICU/HCU hospitalization in the last 90 days before diagnosis of HAP was the only independent predictor of infection with MDR bacteria in patients with HAP.

AP664

ASSOCIATION OF SERUM URIC ACID LEVELS AND OUTCOMES OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A PROSPECTIVE COHORT STUDY

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¹Philippine Heart Center, Philippines

Background and Aims: Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of morbidity and mortality with increasing prevalence worldwide. Changes in oxygen tension such as hypoxia, has been found to modulate the release of purine metabolites such as uric acid which increases significantly during hypoxia. Elevated uric acid levels could serve as a non-invasive indicator for COPD severity.

Methods: This is a prospective cohort analytic study among COPD in exacerbation patients at Philippine Heart Center. Serum uric acid level determination was done as part of the routine blood tests obtained during admission. Patients were followed-up until discharge and through a telephone conversation 30 days after discharge to determine mortality.

Fisher's exact analysis used to determine the association between elevated serum uric acid level and mortality and independent t-test was used to determine the length of hospitalization, ICU stay and NIV use between patients with low and high serum uric acid levels. A p-value of ≤ 0.05 was considered significant.

Results: A total of 159 patients were included in the study. Fifty-seven patients (57 %) were males and forty-three (43 %) were females. The mean age of the study population was 69 years old. Majority of the patients (91 %) were smoker, with mean average pack-year-smoker of 25.57 ± 9.03 pack-year. Majority of the patients (66%) were hypertensive with GOLD Classification C (55 %). Patients with high serum uric acid levels required more prolonged hospitalization with a mean average hospital stay was 16.38 ± 6.58 days and presented higher rates of 30-day mortality. Moreover, patients with high serum uric acid levels required noninvasive ventilation (NIV) which were both statistically significant ($p = 0.005$ and $p < 0.001$ respectively).

Conclusion: Elevated serum uric acid levels on admission among patients with COPD in exacerbation are associated with increased 30-day mortality and increased risk of NIV use.

Table 1. Baseline Characteristics of the Study Population

Characteristics	Normal Uric Acid (2.5-6.9 mg/dL) n=69	High Uric Acid (>6.9mg/dL) n=90	p-value
Age (years)	71 $\pm$ 9.1	69 $\pm$ 7.3	0.055
Gender (male)	31 (34.44)	59 (65.56)	0.865
Smoking history	57 (82.61)	88 (7.78)	0.001
Pack-year smoker	16.6 $\pm$ 11.1	25.6 $\pm$ 9.0	<0.001
PTB treatment history	8 (11.59)	7 (7.78)	0.427
Cardiovascular disease			0.059
a. Hypertension	52 (75.36)	53 (58.89)	
b. Congestive heart failure	4 (5.80)	14 (15.56)	
c. Arrhythmias	0	0	
COPD GOLD Classification			<0.001
A	0	0	
B	44 (63.77)	12 (13.33)	
C	25 (36.23)	62 (68.89)	
D	0	16 (17.78)	

Table 2. Association between Uric Acid level and COPD Outcomes

Outcomes	Normal Uric Acid (2.5-6.9 mg/dL) n=69	High Uric Acid (>6.9mg/dL) n=90	p-value
Length of hospital stay	14.48 $\pm$ 7.24	16.38 $\pm$ 6.58	0.9535
Death within 30 days	0	9 (10.0)	0.005
ICU admission	8 (11.59)	9 (10.0)	0.799
Non-invasive ventilation			<0.001
Use of NIV	0	18 (20.0)	
No NIV use	61 (88.41)	63 (70.0)	
Intubated	8 (11.59)	9 (10.0)	

Table 3. Association between Uric Acid level and Mortality

Mortality	Alive n=150	Dead n=9	p-value
Normal Uric Acid (2.5-6.9 mg/dL)	69 (46.0)	0	
High Uric Acid (>6.9mg/dL)	81 (54.0)	9 (100.0)	0.005

AP665

A META-ANALYSIS ON INDWELLING PLEURAL CATHETERS VERSUS PLEURODESIS IN THE MANAGEMENT OF MALIGNANT PLEURAL EFFUSIONS: A MODERN DILEMMA

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Background and Aims: Recently, studies have shown that indwelling pleural catheters (IPC) can also be done even to patients who fit the criteria for pleurodesis as a paradigm shift revolutionized the goal of

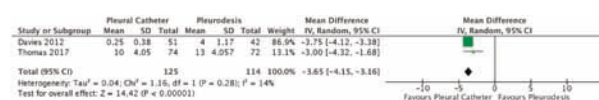
treating recurrent malignant pleural effusions (MPE) shifted from treating the patient by radiologic evidence of pleural effusion to patient symptoms and quality of life. The choice between pleurodesis and IPC for the management of) has been a controversial topic because not one of the two interventions has conclusively shown to be superior to each other.

The primary was control of effusion. The secondary outcomes were length of hospital stay (LOS), dyspnea, quality of life (QOL), chest pain and complication rates.

Methods: We conducted an extensive search for published studies that compare pleurodesis with IPC for MPE. Eligibility and bias assessments were done.

Results: 24 studies were screened. Only four studies (N=472) met the inclusion criteria. A homogenous population ($I^2 = 14$, $P = 0.28$) who underwent IPC insertion had significantly decreased length of hospital stay by 3.63 days (95% CI -4.15, -3.16) compared to those who underwent pleurodesis. IPC also showed less loculations or effusions by 45% (CI 95%, 0.23, 1.31) that lead to reintervention by 40% (95% CI -1.78, 0.59), and better survival but it did not establish clinical significance. Pleurodesis, although not statistically significant, showed a trend towards better QOL with a mean difference of 2.02 (CI 95% -5.41, 9.45). It also had reduced complication rates with RR of 1.61 (CI 95% 0.85, 3.05), empyema of 2% (versus 5% in patients who had pleurodesis) and chest pain with RR of 1.57 (95% CI 0.53, 4.66).

Conclusion: Compared to pleurodesis, IPC significantly decreased the LOS and showed a trend towards less recurrence and improved survival. Pleurodesis had a trend towards favorable results in terms of QOL, complication rates, empyema and chest pain.



AP666

ACCURACY OF GAS EXCHANGE MEASUREMENTS AS PREDICTORS OF EARLY SUCCESSFUL WEANING AMONG ICU PATIENTS OF PHILIPPINE HEART CENTER: A PROSPECTIVE COHORT STUDY

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Background and Aims: Rapid weaning and extubation is essential to fast-track recovery of the critically-ill patients. Gas exchange measurements such as inspired – expired oxygen concentration difference (I-E) O₂ and end-tidal carbon dioxide concentration (PETCO₂) are useful in identifying patients who are likely to succeed in liberation from mechanical ventilation. Study aims to determine the accuracy of (I-E)O₂ and PETCO₂ that will greatly aid the physicians in the ventilator management and weaning.

Methods: This is a prospective cohort study done at the ICU of our Institution. Patients who were intubated and mechanically ventilated were included in the study. Both standard and study weaning assessment protocols were done on a daily basis. Weaning were classified as successful if the patient was able to maintain spontaneous breathing for 48 hours after extubation. Sensitivity, Specificity, PPV and NPV were used to determine the diagnostic accuracy of gas exchange measurement in predicting optimal outcome.

Results: There were 290 patients enrolled in the study. A total of 210 patients who were successfully weaned from the mechanical ventilator, 142 (67.6%) males and 68 (32.3%) females. The mean age for both groups ranges from 48-51 years old. The probability of detecting weaning success using (I-E)O₂ and PETCO₂ is 92.92% and 90.35% respectively, while the probability of detecting weaning failure is 100% and 93.55% respectively. The ability of these measurements to detect weaning success in the general population were 80% in (I-E)O₂ and 72.5% in PETCO₂. Based on the sensitivity and specificity of these gas exchange measurements, a cut-off value of $\geq 4.6\%$ in (I-E)O₂ and $\geq 4\text{kPa}$ in PETCO₂ were determined.

Conclusion: Capnography is a non-invasive monitoring technique that allows fast and reliable insight into ventilation and it is useful in the weaning of patients from mechanical ventilation. According to our results, (I-E)O₂ and PETCO₂ measurement provides an accurate predictor of weaning in mechanically ventilated patients.

Table 1. Baseline Characteristics of the Study Population

Variables	Successful n=210 Mean $\pm$ SD or n (%)	Failure n=80 Mean $\pm$ SD or n (%)	p-value
Gender:			0.854
Male	142 (67.62)	55 (68.75)	
Female	68 (32.38)	25 (31.25)	
Age (years)	50.98 $\pm$ 15.17	48.50 $\pm$ 15.92	0.219
Height (cm)	163.25 $\pm$ 7.64	164.87 $\pm$ 9.08	0.126
Weight (kg)	70.11 $\pm$ 11.59	71.10 $\pm$ 12.00	0.520
BMI (kg/m²)	26.33 $\pm$ 3.79	25.82 $\pm$ 3.91	0.310
Medical History:			
Cardiac			
Hypertension	182 (86.67)	74 (92.5)	0.168
CHD/VHD	147 (70)	66 (82.50)	0.031
CHF	37 (17.62)	20 (25)	0.157
CAD	31 (14.76)	19 (23.75)	0.070
CAD	53 (25.24)	19 (23.75)	0.793
ACS/MI	11 (5.24)	1 (1.25)	0.127
COPD	15 (7.14)	9 (11.25)	0.257
Bronchial Asthma	4 (1.90)	4 (5)	0.150
PTB	9 (4.29)	3 (3.75)	0.838
Stroke/CVD	11 (5.24)	9 (11.25)	0.116
Diabetes Mellitus	106 (50.48)	26 (32.50)	0.006
CKD	2 (0.95)	2 (2.50)	0.313
Smoking History:			<0.001
Non-smoker	118 (56.19)	22 (27.50)	
Smoker	92 (43.81)	58 (72.50)	
APACHE II Score	7.36 $\pm$ 2.24	7.46 $\pm$ 2.44	0.751
Duration of MV (hours)	3.66 $\pm$ 1.56	3.38 $\pm$ 1.54	0.177
Internal Diameter of ETT			0.166
7 mm	6 (2.86)	0	
7.5 mm	31 (14.76)	17 (21.25)	
8 mm	173 (82.38)	63 (78.75)	
Mode of Ventilation prior to weaning:			
AC Mode	146 (69.52)	56 (70)	0.937
SIMV- PS	3 (1.43)	1 (1.25)	1.000
ASV	18 (8.57)	18 (22.50)	0.102
PSV	43 (20.48)	5 (6.25)	0.104
Hemoglobin (g/L)	129.92 $\pm$ 18.4	134.28 $\pm$ 17.7	0.0697

Table 2. Respiratory and ventilatory parameters during weaning

Variables	Successful n=210 Mean $\pm$ SD or n (%)	Failure n=80 Mean $\pm$ SD or n (%)	p - value
Initial lung compliances:			
Cstat (ml/cmH ₂ O)	41.81 $\pm$ 13.21	42.43 $\pm$ 11.54	0.710
Cdyn (ml/cmH ₂ O)	36.06 $\pm$ 11.96	34.95 $\pm$ 32.87	0.452
RSBI	58.15 $\pm$ 19.65	53.41 $\pm$ 17.42	0.059
ABG (before weaning):			
pH	7.45 $\pm$ 0.03	7.38 $\pm$ 0.07	<0.001
pCO ₂ (mmHg)	35.08 $\pm$ 5.40	38.78 $\pm$ 7.55	<0.001
pO ₂ (mmHg)	163.19 $\pm$ 47.89	168.22 $\pm$ 60.39	0.459
HCO ₃ (mmol/L)	24.33 $\pm$ 2.64	23.65 $\pm$ 2.92	0.058
O ₂ Sat (%)	98.50 $\pm$ 1.14	98.52 $\pm$ 1.29	0.906
ABG (before extubation):			
pH	7.42 $\pm$ 0.05	7.40 $\pm$ 0.04	0.003
pCO ₂ (mmHg)	37.46 $\pm$ 6.17	39.10 $\pm$ 5.49	0.037
pO ₂ (mmHg)	136.37 $\pm$ 40.50	143.08 $\pm$ 48.47	0.233
HCO ₃ (mmol/L)	24.33 $\pm$ 2.70	24.26 $\pm$ 2.92	0.851
O ₂ Sat (%)	98.09 $\pm$ 1.52	97.98 $\pm$ 1.52	0.570

Table 3. Gas exchange measurements during weaning

Variables	Successful n=210 Mean $\pm$ SD or n (%)	Failure n=80 Mean $\pm$ SD or n (%)	p - value
Inspired - expired oxygen concentration difference (I-E)O ₂	5.63 $\pm$ 0.37 kPa (42.23 $\pm$ 2.63 mmHg)	3.79 $\pm$ 0.88 kPa (28.43 $\pm$ 6.6 mmHg)	<0.001
End-tidal carbon dioxide concentration (PETCO ₂)	4.51 $\pm$ 0.40 kPa (33.83 $\pm$ 3 mmHg)	3.84 $\pm$ 0.81 kPa (28.8 $\pm$ 6.08 mmHg)	<0.001

Table 4. Accuracy of gas exchange measurements

Variables	Specificity	Sensitivity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)	Overall Accuracy
Inspired - expired oxygen concentration difference (I-E)O ₂	80%	100%	92.92%	100%	94.48%
End-tidal carbon dioxide concentration (PETCO ₂)	72.50%	98.10%	90.35%	93.55%	91.03%
Combined (I-E)O ₂ difference and PETCO ₂	70%	100%	89.74%	100%	91.72%

AP667

ASSESSMENT OF QUALITY OF SLEEP IN PATIENTS RECOVERING FROM CRITICAL CARE ILLNESS AND FACTORS AFFECTING IT

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Background and Aims: Sleep in ICU is disturbed, distorted and fragmented. Both patient centric and environmental factors (light, noise, mechanical ventilation, drugs etc) are responsible for affecting the sleep architecture in ICU.

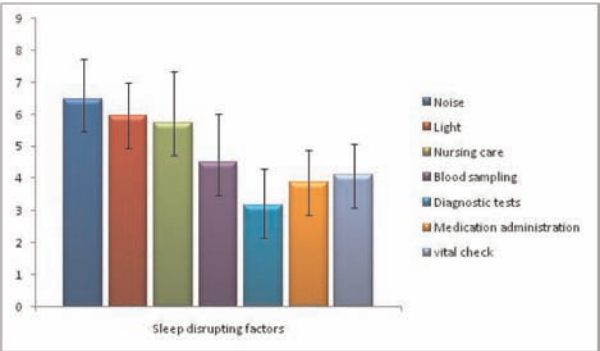
Methods: It was an observational study. Prehospital insomnia was assessed by using insomnia severity index (ISI) and daytime somnolence was assessed using Epworth sleepiness scale (ESS) Quality of sleep of patients recovering from their critical care illness was assessed using Richard Campbell sleep questionnaire (RCSQ) and sleep in ICU questionnaire (SICQ). Light intensity and noise in ICU were recorded using luxmeter and soundlevel meter. Nursing care activities were also recorded.

Results: 26 patients completed the study. The mean ISI score was 6.88 $\pm$ 2.58 and mean ESS was found to be 4.92 $\pm$ 1.99. Mean RCSQ score in ICU was 54.65 $\pm$ 7.6960. Prehospital sleep of the study group was quite normal (8.26 $\pm$ 1.16). Perceived sleep quality in the ICU was very poor with mean score of 4.19 $\pm$ 1.16 and the difference was statistically significant (<0.0001) when compared to prehospital sleep. Sleep disrupting factors were also assessed by SICQ in which nursing interventions and noise were important disrupting factors. Important disruptive noises were ventilator alarms and staff conversations (table 1). Mean illuminance in the ICU was 55.06 $\pm$ 4.68 lux. During night it was lower (14.98 $\pm$ 2.04 lux) than during the day time (77.09 $\pm$ 3.66 lux).

Sound levels were high in the ICU and the mean Sound level ('A'-weighted) was 59.17±1.69 dB.

Conclusion: Quality of Sleep in ICU perceived by patients was very poor. Light, noise and nursing care activities are the major factors which affects the sleep in patients recovering from their illness.

	ICU
RCSQ	54.65 ± 7.69
SQC	
Prehospital sleep	8.26 ± 1.16
ICU sleep	4.19 ± 1.16
Daytime sleepiness in ICU	5.96 ± 1.21
Sleep disrupting factors	
Noise	6.86 ± 1.27
Light	5.96 ± 1.09
Nursing interventions	5.79 ± 1.61
Blood samples	4.5 ± 1.5
Diagnostic test	3.15 ± 1.15
Medications administration	3.88 ± 0.99
Vital signs	4.11 ± 0.95
Causes of disruptive noise in ICU	
Vent alarm	5.92 ± 0.79
Monitor alarm	4.9 ± 0.93
Staff talking	6.07 ± 1.26
IV set alarm	4.15 ± 1.22
Finger probes	3 ± 1.01



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