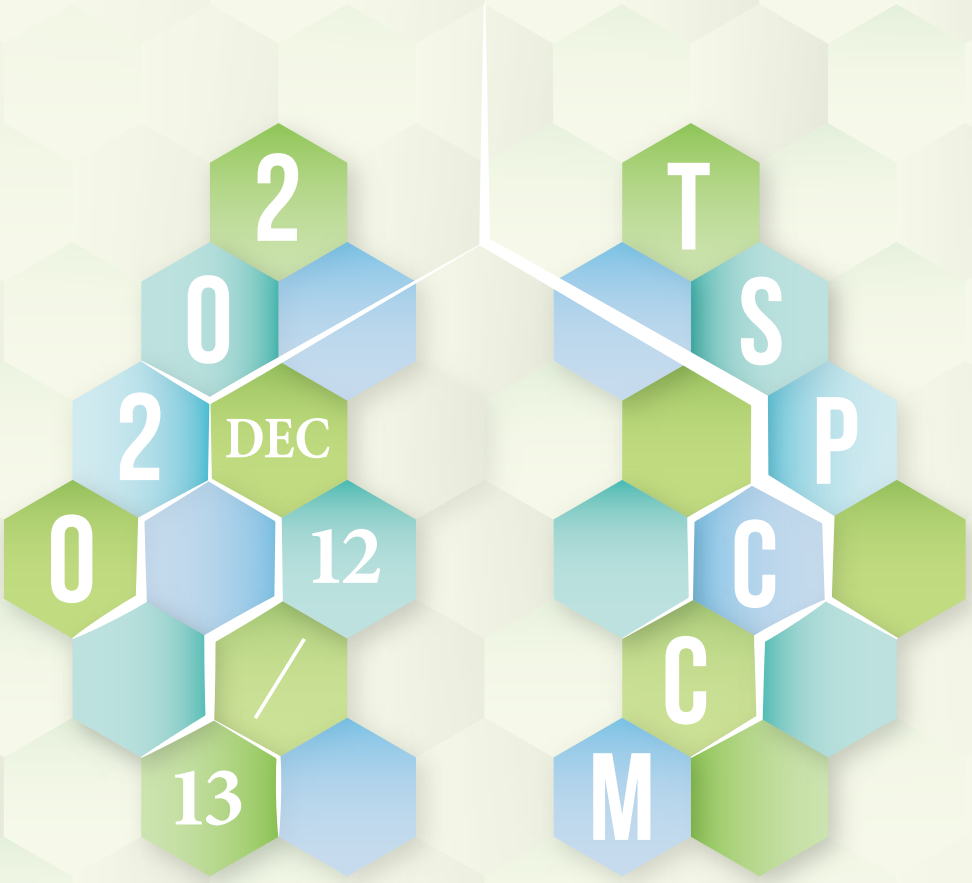
2020 台灣胸腔暨重症加護醫學會年會

暨台灣胸腔外科醫學會、台灣胸腔及心臟血管外科學會聯合會議
暨台灣胸腔暨重症加護醫學會第18屆第1次會員大會

2020 Annual Congress of Taiwan Society of Pulmonary and Critical Care Medicine
And Taiwan Society of Thoracic Surgeons, Taiwan Association of Thoracic & Cardiovascular Surgery Joint Conference



日期 — 2020. **12/12** (Sat) - **12/13** (Sun)

地點 — **臺大醫院國際會議中心**
(台北市中正區徐州路2號)

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12 / 13 (Sun)

TIME	101	301	401	202	203
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09:20-10:00	Moderator: **林恒毅** 院長 Speaker: **高國晉** 教授 **The application of AI in critical care**	Moderator: **林慶雄** 副院長 Speaker: **蘇一峰** 醫師 **Climate change and lung health**	Moderator: **陳育民** 教授 Speaker: **魏裕峰** 主任 **Update of EGFRm in Lung Cancer**		台灣胸腔外科醫學會 **09:30-10:00** Moderator: **徐紹勛** 主任、**趙盈凱** 主任 Speaker: **柳晨** 副院長 **Percutaneous lung ablation therapy : Chinese experience**
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10:30-11:10	Moderator: **曹昌堯** 教授 Speaker: **詹明澄** 主任 **Recent evidences in influenza-related ARDS (TSIRC study)**	Moderator: **李岡遠** 副院長 Speaker: **Prof. Edmund Lau** **Differentiating WHO Group I from Group II Pulmonary hypertension**	Moderator: **施金元** 教授 Speaker: **張基晟** 教授 **Update of ALK/ROS1m in Lung Cancer**	台灣胸腔及心臟血管外科學會 **09:40-10:30** Moderator: **李章銘** 主任 Speaker: **Prof. Calvin S.H.Ng** **Transbronchial abrasion of pulmonary nodules in HYBRID OR**	台灣胸腔外科醫學會 **10:30-10:45** Moderator: **黃文傑** 主任、**黃培銘** 主任 Speaker: **莫麗雯** 醫師 **Navigation System in one-stop Lung Cancer solution with Hybrid OR** **10:45-11:00** Moderator: **黃文傑** 主任、**黃培銘** 主任 Speaker: **楊順貿** 醫師 **Cone-beam CT augmented fluoroscopy-guided endobronchial procedures for small pulmonary lesions** **11:00-11:15** Moderator: **馮瑤** 主任、**湯恩魁** 主任 Speaker: **鄭雅夫** 醫師 **Extended segmentectomy for small lung nodule with iVATS**
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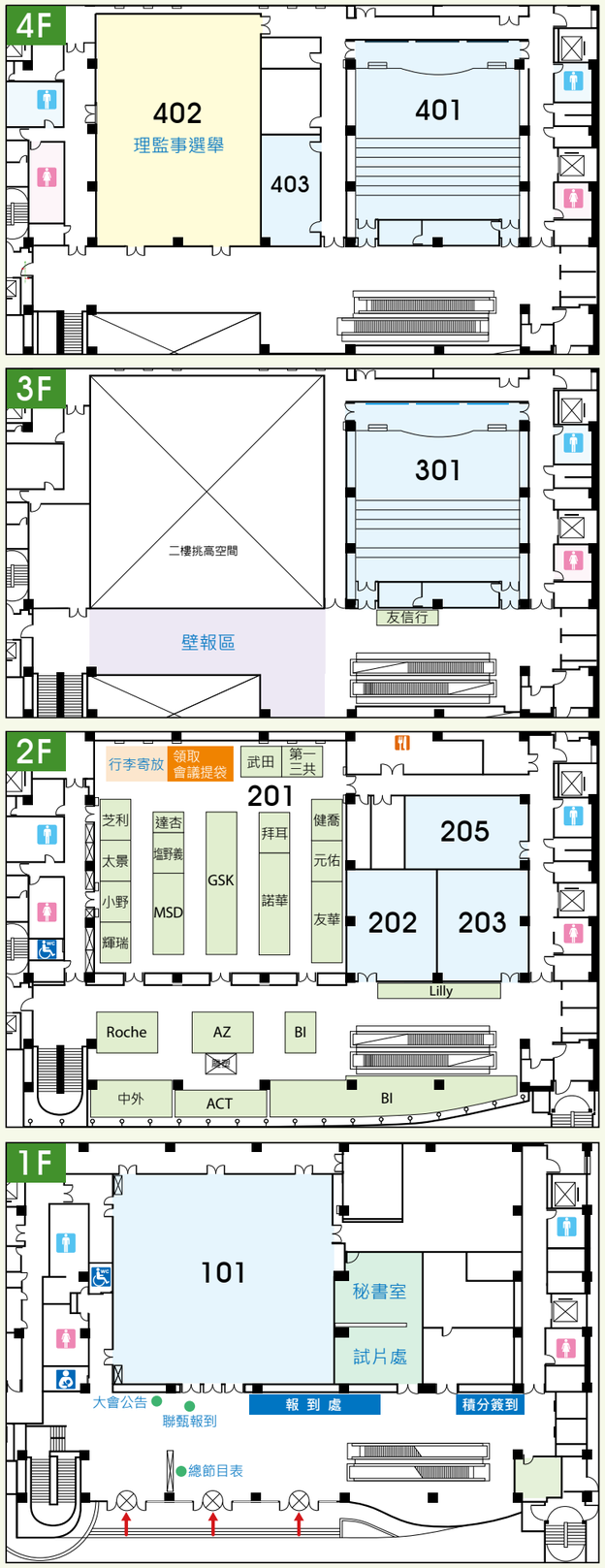
				台灣塩野義製藥 股份有限公司贊助 *Infection*	臺灣阿斯特捷利康 股份有限公司贊助 *Airway disease*		台灣武田藥品工業 股份有限公司贊助 *Lung cancer*

會場平面圖



演講摘要

- 台灣胸腔暨重症加護醫學會
- APSR Joint Symposium
- 台灣胸腔外科醫學會
- 台灣胸腔及心臟血管外科學會
- Satellite Symposium

台灣胸腔暨重症加護醫學會

101 會議室

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Consensus for diagnosis and treatment of COPD and CHF in Taiwan

鄭世隆 / Shih-Lung Cheng, M.D., Ph.D.
Chief, The Center of Evidence-Based Medicine, Far Eastern Memorial Hospital
Professor, Yuen Ze University and Chest Division Far Eastern Memorial Hospital

Chronic obstructive pulmonary disease (COPD) and heart failure (HF) both are global epidemics with substantial burden on morbidity and mortality. They present major challenges to healthcare providers and often coexsist. Heart failure (HF) and chronic obstructive pulmonary disease (COPD) represent the most important differential diagnoses of dyspnea in elderly people. Heart failure is the inability of the heart to pump sufficient amounts of blood through the cardiovascular system. Pump failure is caused by compromised contractility and/or filling of the ventricles leading to forward and backward failure and subsequently to dyspnea. In COPD, the destruction and remodeling processes of the bronchiolar architecture inhibit proper exhalation of air, thereby leading to exhaustion of the thoracic muscles, insufficient oxygen diffusion, and dyspnea. Despite these fundamental differences in the pathophysiology of both disorders, their clinical presentation may be very similar. This renders accurate and timely diagnosis and therapy, especially in patients with coexisting disease, difficult. Multiple interactions exist between these conditions. COPD is often responsible for delayed diagnosis of HF and vice versa, since both conditions have similar symptoms such as dyspnea and poor exercise tolerance based on the skeletal myopathic response rather than the primary organ failure. Patients with COPD also have an increased risk of developing HF and higher hospitalization and death rates compared with HF patients without COPD. Echocardiography and pulmonary function tests along with natriuretic peptides should be performed and carefully interpreted. Diagnostic assessment of both conditions present in the same patient is often difficult, but therapeutic approach is also often non-adherent to current guidelines. Closer collaboration between cardiologists and pulmonologists is required for better identification and management of concurrent COPD and HF. Currently, a consensus has been established for COPD and HF diagnosis and treatment from TSPCCM and TSOC two societies. This presentation will review typical problems in the diagnosis of COPD, HF, and coincident disease, and describes strategies that help avoid misdiagnosis and ineffective treatment.

Pulmonary rehabilitation at the post pandemic era

李岡遠 / Kang-Yun Lee, M.D., Ph.D.
Professor of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University
Vice Superintendent, Taipei Medical University-Shuang Ho Hospital, New Taipei City, Taiwan
Attending physician (V.S.), Division of Pulmonary Medicine, Department of Internal Medicine, Taipei Medical University-Shuang Ho Hospital, New Taipei City, Taiwan

Pulmonary rehabilitation has long been recognized as a core component of the management of patients with chronic respiratory disease, which has been recommended in treatment guidelines worldwide. For example, in COPD, pulmonary rehabilitation has been concluded to have substantial effects in improving all aspects of quality of life and exercise capacity. This improvement is significant enough, exceeding the well accepted minimal clinically important difference (MCID). Recently, community-based programmes have been developed, which have shown promising results compared with the conventional hospital-based programmes. To provide a comprehensive care of patients with complex nature, integrated care principles including action plan, education, self-management, and personalized pulmonary rehabilitation, are being adopted. In the post pandemic era, application of digital technology and big data science will be accelerated. New care system, such as telecare or even Internet of Things (IoT) will be introduced. This talk will review the current state of art and progress in pulmonary rehabilitation, focusing on the future changes the COVID-19 pandemic will make.

COPD control program in Taiwan

林慶雄 / Ching-Hsiung Lin, M.D., Ph.D
Superintendent of Han-Ming Hospital, Changhua Christian Hospital
Deputy Superintendent of Changhua Christian Hospital
Attending doctor of Division of Chest Medicine, Changhua Christian Hospital

The impact of chronic obstructive pulmonary disease (COPD) is substantial worldwide. In Taiwan, it is currently the seventh leading cause of death. Furthermore, the prevalence rate of COPD is now projected to be 6.1 % in a nationwide telephone survey study. With the cumulative exposure to risk factors and increasing percentage of elderly predicted for the next few decades, the COPD prevalence is expected to grow, and will incurs huge healthcare system burden. Moreover, underdiagnosis of COPD leads to failure to prescribe appropriate pharmaceutical and nonpharmaceutical therapies which also results in reduction of overall health outcome.

In this section, we provide a comprehensive review of COPD prevention and disease management in Taiwan. Since 2016, there are important revolution for COPD care implemented by National Health Insurance Administration and The Health Promotion Administration, including Taiwan COPD guideline, Taiwan COPD pay-for-performance program and COPD early detection program,

developing feasible nationwide COPD screening strategy and providing standard and comprehensive COPD care bundle to achieve the goal of early detection, timely intervention and high quality care of COPD. For Taiwan COPD pay-for-performance (P4P) program, the rate of decline in COPD-related hospitalization and emergency visit is higher in the P4P group compared to non-P4P group. Moreover, the higher COPD-related hospitalization, emergency visit and ICU admission in non-P4P group were attributed to lower patient compliance. For COPD early detection program, we developed a feasible tool for COPD case-finding using APP-based portable spirometer with AUROC of 0.903 (95% CI, 0.860-0.947) under the best cut-off point at 0.74. It proved to be a simple and reliable tool for early detection of COPD in outpatient clinics. These result indicated that these national action plans have positive influence on COPD management and achieving high quality of care.

Update of severe asthma - systemic assessment and individualized treatment

詹明澄 / Ming-Cheng Chan, M.D., Ph.D.
Director, Section of Critical Care and Respiratory Therapy, Taichung Veterans General Hospital
Attending Physician, Section of Chest Medicine, Taichung Veterans General Hospital

Severe asthma refers to asthma that is uncontrolled despite adherence to maximal optimized therapy and treatment of contributory factors, or that worsens when high dose treatment is decreased. Severe asthma is often refractory to high dose inhaled therapy and most patients with severe asthma remains symptomatic and repeatedly experience acute exacerbation. However, with the advent of biologic therapies, treatment results are much improved. Diagnosis of severe asthma is a retrospective label by combination of asthma control status and therapies used. With the advancement of knowledge about basic pathophysiological of asthma, pharmacological treatment also gains substantial progress in the past few years. But economic burden should also be taken into consideration in real life practice. Based on these considerations, the TSPCCM Airway Disease Committee organized a task force aiming at establishing a consensus of management of severe asthma. We focused at important issues regarding diagnosis and management of severe asthma in real life practice in Taiwan. By collecting opinions from key experts in this field in Taiwan, we finally give recommendations based on currently available evidence and pragmatic considerations, including patient-physician behavior and national health insurance reimbursement. This documents also include real life cases for education and reference. The publication of this document is not the end of the work. But, as the emerging medical evidence, progress of concepts and available pharmacological and non-pharmacological treatments in the coming years. It serves as the first step of the beginning of a new era in the management of severe asthma.

How to manage MDR-GNB pneumonia in ICU?

彭忠衍 / Chung-Kan Peng, M.D., Ph.D.
Director of TingJhou Campus, Tri-Service General Hospital
Director of Division of Pulmonary Medicine and Critical Care Medicine, Department of Internal Medicine, Tri- Service General Hospital
Director of Sleep Medicine Center, Tri-Service General Hospital
Associate professor, The school of Medicine, National Defense Medical Center

Infections due to multidrug-resistant Gram-negative bacilli (MDR-GNB) are increasing globally. Acutely ill patients assisted in the intensive care units (ICUs) are at high risk of both colonization and infection with multidrug resistant organisms which might cause high mortality rate. MDR-GNB causes an increasing burden of infection in ICUs. Among MDR-GNB, extended-spectrum beta-lactamases (ESBL) organisms, carbapenemase producing enterobacteriaceae, carbapenem-resistant Acinetobacter species, multidrug-resistant Pseudomonas aeruginosa are the major culprits. The treatment of MDR-GNB infections in critically ill patients presents many challenges. The lack of new antibiotics active against these pathogens and few new antimicrobials are in the pipelines of the pharmaceutical industry.
Colistin is a bactericidal drug which belongs to polymyxin group of antibiotics. Limited therapeutic options have forced infectious disease clinicians and microbiologists to reappraise the clinical application of colistin. Colistin appears to be a safe and efficacious drug for treating MDR-GNB infections. We summarize recent progress in understanding the pharmacodynamics of colistin, and their effect on the clinical use of this important antibiotic. Physicians should know the local resistance and risk factors of patients for MDR-GNB to prescribe appropriate antimicrobial therapy and prevent further resistant strains developed.

The application of AI in critical care

高國晉 / Kuo-Chin Kao, M.D.
Professor, Department of Thoracic Medicine, Chung Gung Memorial Hospital, Linkou
Vice Director, Department of Internal Medicine, Chang Gung Memorial Hospital, Linkou
Professor, College of Medicine, Chung Gung University

According to the Encyclopedia Britannica, artificial intelligence (AI) is defined as a system "endowed with the intellectual processes characteristic of humans, such as the ability to reason, discover meaning, generalize, or learn from past experience." AI computer systems are able to perform tasks normally requiring human intelligence and that are considered "smart" by humans. AI systems act on information, such as controlling a self-driving automobile or influencing consumer shopping decisions. In the application of medicine, AI has been performed in personalized diagnostics and therapeutics, bioinformatics, molecular biology, medical imaging and drug discovery. AI applications are also capable of discerning patterns of disease by scrutinizing and analyzing massive amounts of digital

information stored in electronic medical records (EMR). In a recent proposal aimed at regulating AI software in medical devices, the U.S. Food and Drug Administration states that "Artificial intelligence-based technologies have the potential to transform healthcare by deriving new and important insights from the vast amount of data generated during the delivery of healthcare every day".
In this lecture, I would like to introduce the recent AI application in the area of critical care medicine and propose the possible direction of AI application in the ICU in the near future.

Recent evidences in influenza-related ARDS (TSIRC study)

詹明澄 / Ming-Cheng Chan, M.D., Ph.D.
Director of Respiratory Intensive Care Unit, Taichung Veterans General Hospital
Attending Physician, Section of Chest Medicine, Taichung Veterans General Hospital

Acute respiratory distress syndrome (ARDS) remains an important disease for critically ill patients in the intensive care unit (ICU) due to high incidence and mortality. Although there are many impressive advances about pathophysiology and management of ARDS in the past few years, including ventilatory strategy and adjunctive intervention, the mortality remains high. In the past few decades, global health was threatened by pandemics from emerged and re-emerged transmission viral respiratory disease, including influenza, severe acute respiratory disease (SARS) and corona virus disease (COVID-19). These illnesses may cause severe pulmonary infection, often leading to the development of ARDS and ultimately death. Thus successful management ARDS is important issue both for individual patient and public health. In 2016, we experienced a local epidemic of influenza pneumonia in Taiwan. Hundreds of patients with acute respiratory failure needing mechanical ventilation were admitted to ICUs. We thus organized a group called Taiwan Severe Influenza Research Group (TSIRC), including 8 major medical centers from north to south. The purposes of this organization are to exchange patient care information and collection of domestic data for research. These data are valuable because it not only provides important information about influenza-related ARDS management in Taiwan. In the past 4 years, we published a couple of papers regarding ventilator management, corticosteroid use, prone position ventilation, fluid management and nosocomial infection in severe influenza patients. It also serves as a foundation for preparedness of intensive care while facing challenge from COVID-19 from this January. Finally, we established a model of corporation in research among critical care physicians in Taiwan. Hopefully this can improve quality of research in this field and also benefits out patients.

Oxygen saturation targets in critically ill patients

許超群 / Chau-Chyun Sheu, M.D.

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Acute hypoxemia is one of the most common reasons that patients require intensive care, and is generally managed with supplementation of oxygen in inspired gas. The targets of oxygen saturation were usually set to balance adequate oxygen delivery vs. oxygen toxicity. The traditional strategy of oxygen therapy is using the lowest oxygen supplementation to keep the patient on the plateau region of the hemoglobin-oxygen dissociation cure, based on the concept that additional increments in PaO_2 or SaO_2 provide little increments in O_2 content, and may bring up harmful effects of hyperoxia. Recently, two large randomized-controlled trial showed that conservative oxygen therapy is no better than usual (liberal) oxygen therapy in clinical outcomes (ICU-ROX trial and $LOCO_2$ trial). Conservative oxygen therapy may even result in a higher 90-day mortality and more mesenteric ischemic events ($LOCO_2$ trial). In addition, a retrospective analysis using two large databases (eICU-CRD and MIMIC) found that the optimal range of SpO_2 was 94% to 98%. In this lecture, we will review the fundamental knowledge about oxygen therapy, oxygenation goals recommended by each guidelines, previous studies, and recent evidence.

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Progressive fibrosing interstitial lung diseases: current practice in diagnosis and management

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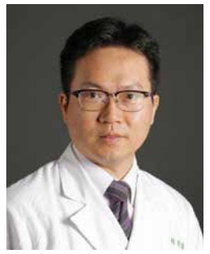
Honors:
National Research Service Award, "Parthogenesis of Pulmonary Fibrosis," National Institutes of Health (1983-1985)
National Research Service Award, National Institutes of Health (1981-1983)

A milestone of ILD Treatment in Taiwan: from IPF to PF-ILD



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Abstract
Interstitial lung diseases (ILDs) are a group of rare respiratory, non-malignant disorders, characterized by varying degrees of damage to the lung parenchyma via inflammation and fibrosis. Clinically, the heterogenous diseases can be classified as idiopathic interstitial pneumonia (IIP), autoimmune ILD, hypersensitivity pneumonitis, sarcoidosis, and other ILDs. The diagnostic approach and MDD, especially for idiopathic pulmonary fibrosis (IPF), was introduced by TSPCCM 3 years ago, and anti-fibrotic agents can be applied to IPF treatment in Taiwan since March 2017.
Patients with certain types of fibrosing interstitial lung disease (ILD) are at risk of developing a progressive phenotype characterized by self-sustaining fibrosis, decline in lung function, worsening quality of life, and early mortality. Terminology recently used to describe these patients with a progressive phenotype as “progressive-fibrosing ILD (PF-ILD)”. The literature report that ILDs at high risk developing a progressive-fibrosing phenotype are idiopathic nonspecific interstitial pneumonia, unclassifiable idiopathic interstitial pneumonia, connective tissue disease-associated ILDs (e.g. rheumatoid arthritis-related ILD), fibrotic chronic hypersensitivity pneumonitis, fibrotic chronic sarcoidosis and ILDs related to other occupational exposures. The anti-fibrotic agent, nintedanib, has been approved for systemic sclerosis (March 2020) and PF-ILD (October 2020) by TFDA. This is a milestone of ILD treatment in Taiwan to improve cooperation between pulmonologist and rheumatologist to manage PF-ILD.

Interventional bronchology in COPD treatment

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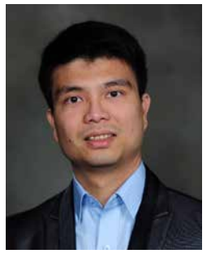
Abstract
Patients with severe emphysema often have limited response to maximal medical therapy for their disease which has led to the development of minimally invasive lung volume reduction procedures. These techniques were derived from the early learnings of lung volume reduction surgery and now have matured to the extent that they are recommended interventions in the latest COPD GOLD Guidelines. This presentation will cover current available options for patients with severe emphysema including endobronchial valves, bronchoscopic thermal vapor ablation, endobronchial coils, and chemical sclerosis.

Current and new challenge in occupational lung diseases



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Abstract
Occupational lung diseases are thought preventable but keep threatening labors’ health and leading disease burden globally today. In recent decades, the industrial structure, workforce, and society have transformed very dramatically. The diagnosis of occupational lung disease has become increasingly challenging. A definite diagnosis is helpful for the following patient caring and industrial preventive strategy. However, under-diagnosis is never a new topic on this issue. Occupational exposure is the key to the diagnosis of occupational diseases. Knowledge about occupational respiratory hazards is essential to clarify the patients’ exposure. The aging population with pre-existing respiratory disease may also distract physicians from evaluating potential occupational exposure. Physicians should also know the benefit of the diagnosis of occupational disease, both for the patients and the public health strategy. The present overview focused on the challenge in the diagnosis of occupational lung disease in Taiwan currently, proposed to build up a coping strategy for caring for occupational lung disease in the future.

Climate change and lung health

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Abstract
Climate change has many consequences with global impact. Two of the planet's main environmental problems, climate change and air pollution, are closely linked. Climate change can impact air quality and, conversely, air quality can impact climate change. Emissions of pollutants into the air can result in changes to the climate. Ozone in the atmosphere warms the climate, while different components of particulate matter (PM) can have either warming or cooling effects on the climate. These climate change impacts endanger our health by affecting our food and water sources, the air we breathe, the weather we experience, and our interactions with the built and natural environments. As the climate continues to change, the risks to human health continue to grow. Climate change can therefore affect human health in two main ways: first, by changing the severity or frequency of health problems that are already affected by climate or weather factors; and second, by creating unprecedented or unanticipated health problems or health threats in places where they have not previously occurred. The global level of air pollution could increase fivefold over the next half-century if the situation is not remedied. Accelerating climate change poses a particular threat to people living with chronic disease, including respiratory issues like asthma, chronic obstructive pulmonary disease (COPD), allergies, emphysema, and lung cancer. Climate change factors affecting respiratory illness include more extreme weather events, more wildfires, higher levels of allergens, increased insect and water-borne diseases, and higher levels of air pollution.

Differentiating WHO Group 2 from Group 1 Pulmonary Hypertension

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Abstract
The epidemiology of Group 1 PAH has changed over the past decade, and this condition is increasingly diagnosed in older patients with cardiovascular risk factors. Distinguishing Group 1 PAH from Group 2 PH due to left heart disease can be difficult in clinical practice, but critically important in terms of therapeutic approach.

Surgical treatment of pulmonary hypertension

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Abstract
With development of new targeted therapies and new treatment strategies in the past 20 years or so, outcomes of most pulmonary hypertension (PH) patients have improved. However, in some, due to possible delay in diagnosis and treatment initiation, the resultant irreversible pathological changes in pulmonary arteries may require surgical intervention to treat. For patients with secondary PH due to congenital heart disease, medical treatment could only maintain, but not cure, the patient's underlying disease. Bilateral lung transplant (BLTx) with intraoperative cardiac defect repair could resolve the cause of PH and improved the quality of life. Although heart-lung transplant could also be one of the transplant choices, BLTx with cardiac repair has some benefits. First, this procedure can spare the heart for another patient who needs heart transplant. Second, with single type of organ transplant, risks of having two organs rejected (heart and lung) in the future is nil. For patient with pulmonary crisis due to end stage idiopathic pulmonary arterial hypertension (iPAH), peripheral or central extracorporeal membrane oxygenation (ECMO) could be a life-saving bridge procedure before donor organ available.

Taiwan Cohort - Registry of Chronic Thromboembolic Pulmonary Hypertension (TREC): A Preliminary Study

劉景隆 / Ching-Lung Liu, M.D., Ph.D.

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Abstract

Chronic thromboembolic pulmonary hypertension (CTEPH) is rare and associated with significant morbidity and mortality. The clinical features and prognosis of the condition is not well-known in Taiwan. By means of registry of diagnosed CTEPH patients, this study aim to investigate the prevalence, clinical characteristics, and management of CTEPH in a Taiwanese cohort. This is a non-interventional, retrospective registry and prospective follow-up to document the data from patients with CTEPH in 6 tertiary referral hospitals in Taiwan. Diagnosis of CTEPH was confirmed by echocardiography, computerized tomography (CT), ventilation/perfusion (V/Q) lung scan, right heart catheterization, and/or pulmonary angiography. From Jan 2018 to Jan 2020, 107 patients had been enrolled. The average age was 61.4 ± 16.5 yrs, and female predominance (32 males and 75 females, female to male ratio of 2.34) was observed. A history of acute pulmonary embolism and deep vein thrombosis was reported for 81.3% and 22.4 % of patients, respectively. Progressive exertional dyspnea (90.7%) and exercise intolerance (52.3%) were most common initial presentations in these patients. Echocardiography (98.1%) was usually used as the initial testing tool when pulmonary hypertension was suspected; in addition, V/Q lung scan, right heart catheterization, and contrast chest CT/chest CT angiography were done respectively in 94.4%, 100.0%, and 96.3% of patients to confirm the diagnosis. Among these patients, 25 (23.4%) underwent surgical pulmonary endarterectomy (PEA), and 38 (35.5%) received balloon pulmonary angioplasty (BPA). At the time of CTEPH diagnosis, 92 patients initiated at least 1 pulmonary artery hypertension-targeted therapy, including sGC stimulator (n=75), PDE-5 inhibitor (n=35), ERA (n=6), and prostacyclins (n=2). The TREC study will contribute to improve our understanding of the diseases and conditions in CTEPH patients over time in Taiwan.

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Consensus Statement of Nontuberculous Mycobacterial Lung Disease in Taiwan

Over the past two decades, there has been explosive awareness of nontuberculous mycobacteria (NTM) as important pathogens. Among various NTM diseases in human, NTM-lung disease (NTM-LD) is the most common disease entity and can lead insidious lung destruction and function decline. The incidence of NTM-LD is increasing, both globally and in Taiwan. Given that, President of Taiwan Society of Pulmonary and Critical Care Medicine, Professor Meng-Chih Lin, has launched an NTM workgroup of panel experts and collaborated with the Taiwan Society of Tuberculosis and Lung Diseases, led by President Yi-Wen Huang. Besides educational seminars, this NTM workgroup drafted a series of review articles which have been published in the Journal of the Formosan Medical Association (JFMA) as a special issue. This special issue covers nine important topics of NTM-LD, starting from NTM-LD epidemiology in Taiwan, followed by host factors associated with NTM-LD development, clinical relevance and diagnosis of NTM-LD, species identification and susceptibility testing, and non-pharmacologic treatment. Then, treatment for NTM-LD caused by 3 most common NTM species, i.e.Mycobacterium kansasii, M. abscessus complex, and M. avium intracellulare complex (MAC), is discussed. Lastly, surgical management for NTM-LD is reviewed. Though the consensus statements of NTM-LD are not intended to be clinical guidelines for physicians to follow, we believe that physicians who could possibly encounter NTM-LD in clinical practice will benefit a lot from reading this series of review articles.

Epidemiology of NTM-LD in Taiwan

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Risk population of NTM-LD

樹金忠 / Chin-Chung Shu, M.D. Ph.D.
Assistant Professor, School of Medicine, College of Medicine, National Taiwan University
Attending Physician, Department of Internal Medicine, National Taiwan University Hospital

Clinical Relevance and Diagnostic Criteria

馮嘉毅 / Jia-Yih Feng, M.D., Ph.D.
Assistant Professor, College of Medicine, National Yang-Ming University
Attending Physician, Department of Chest Medicine, Taipei Veterans General Hospital

Identification and drug susceptibility testing for nontuberculous mycobacteria

黃偉彰 / Wei-Chang Huang, M.D., Ph.D.
Assistant Professor, Department of Industrial Engineering and Enterprise Information, Tunghai University
Attending Physician, Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital

Non-pharmacologic management of pulmonary rehabilitation

藍胄進 / Chou-Chin Lan, M.D., Ph.D.
Chief, Division of Pulmonary Medicine, Buddhist Tzu-Chi General Hospital
Associate Professor, School of Medicine, Tzu-Chi University, Hualien

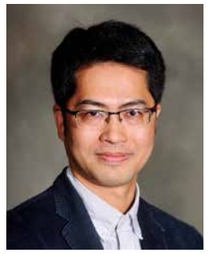
Mycobacterium kansasii-Lung Disease

黃虹綾 / Hung-Ling Huang, M.D.
Attending Physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine. Kaohsiung Municipal Ta-Tung Hospital

Treatment of *Mycobacterium abscessus* complex lung disease

李欣蓉 / Susan Shin-Jung Lee, M.D., Ph.D.
Associate Professor, School of Medicine, National Yang-Ming University
Attending Physician, Division of Infectious Disease, Department of Internal Medicine, Kaohsiung Veterans General Hospital

Mycobacterium avium complex-Lung Disease



潘聖衛 / Sheng-Wei Pan, M.D., Ph.D.
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Recent Advances and Controversies in Surgical Intervention of Nontuberculous Mycobacterial Lung Disease: A Literature Review

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Attending Physician, Department of Surgery, National Taiwan University Hospital

The way towards precision medicine for obstructive sleep apnea: from phenotype to artificial intelligence

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Director, Center of Sleep Disorder, National Taiwan University Hospital
Attending physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, NTUH

Obstructive sleep apnea (OSA) is characterized by repeated episodes of upper airway obstruction that results in cessation of airflow during sleep. OSA is a common disease with a prevalence of 9-38% in the general population. Risk factors for OSA included age, male, obesity, smoking, anomalies of craniofacial features, and menopause in women Symptoms suggestive of OSA included habitual snore, witnessed apnea, choking or gasping, frequent awakening, nocturia, unrefreshed sleep, and daytime sleepiness. Early diagnosis of OSA is essential because untreated OSA may increase the probability of developing cardiovascular diseases, metabolic disorders, and neurocognitive dysfunctions.

Polysomnography (PSG) is the gold standard for the diagnosis of OSA, and the OSA severity is commonly determined by apnea-hypopnea index (AHI). PSG is costly and the access is often limited. As a result, prioritizing patients with high risk for moderate-severe OSA for PSG can be crucial for many sleep labs. The prediction models for identifying patients with high probability of OSA reported in previous studies tend to have high sensitivity but low specificity which may lead to over-prescription of PSG.

Despite AHI is well accepted as criteria for OSA diagnosis, it is poorly correlated with the clinical outcomes. The long-term CPAP treatment based on AHI fails to lower the risk of major cardiovascular events. Recently, the emerging evidences suggest the phenotype of OSA is associated with long-term outcomes. Traits to phenotype patients include respiratory indices, symptoms, and polysomnographic parameters. However, the complexity of phenotype needs an efficient and robust modality to discover and cluster traits of the certain phenotype.

In our previous works. we investigated the sequel of OSA. First, we identified that among 6-12-year-old Down syndrome children, OSA and % REM were associated with their language function. Second, we have showed that OSA is associated with metabolic dysregulation including lower intra-extra-muscular lipid, and higher C-reactive protein, insulin resistance, dyslipidemia, and metabolic syndrome. Moreover, we identified the temporal sequence and the time interval between sleep apnea diagnosis and incident myocardial infarction was associated with the cardiovascular events after myocardial infarction, especially within one year after myocardial infarction.

We also investigated the CPAP effect for treating OSA. We have demonstrated that combining mandibular advancement device and CPAP showed additive effects on reducing apnea-hypopnea index
and oxygen desaturation index, and lowered the therapeutic pressures. Our meta-analysis validates the observation that CPAP can reduce lipid profiles in patients with OSA.

Recently, we proposed a data-mining driven study proposed an SVM-based prediction model built with two, six, and six features commonly collected at clinic visits to identify patients with AHI. Moreover, we developed a single-channel frontal electroencephalography (F4-M1) based automatic sleep staging system which had a good overall validity compared with expert scoring using full-channel polysomnography. We also developed an ultra-low-power dual-mode automatic sleep staging processor design using a neural-network-based decision tree classifier to enable real-time, long- term, and flexible sleep monitoring. Our works showed AI may be the modality to discover phenotype and its linkage to long-term outcomes which may discover the new insight beyond expertise' knowledge.

Management of adult obstructive sleep apnea: challenges and prospectives

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Clinical Associate Professor, Department of Medicine, MacKay Medical College
Attending Physician, Division of Chest Medicine, Department of Internal Medicine, MacKay Memorial Hospital

Obstructive sleep apnea (OSA) is a chronic condition in which the upper airway frequently collapses, resulting in repeated cessation of breathing and intermittent hypoxia during sleep. OSA can cause severe symptoms, such as excessive daytime sleepiness, and increase the risk for cardiovascular, cerebrovascular and metabolic disorders. If not treated, it will very likely lead to death. Different treatment options are now available for effectively manage this disease. Continuous positive airway pressure (CPAP) can provide positive airflow to keep the airway open, and is still regarded as the standard treatment for moderate to severe OSA. It is very effective in controlling symptoms, improving quality of life and reducing the clinical sequelae of sleep apnea. Mandibular advancement device (MAD) can increase airway diameter by displacing the soft tissue through the protrusion of the mandibular. It is effective for mild to moderate OSA and provide an alternative for patients intolerant to CPAP therapy. Oral pressure therapy (OPT) uses negative pressure in the mouth to move the soft palate and tongue forward, which can effectively treat OSA. It shows the potential as a clinically useful new alternative for the treatment of OSA. The role of surgery is still controversial. Uvulopalatoparyngoplasty (UPPP) is a well-established procedure that removes excess tissue in the throat to make the airway wider, and in selected cases can reduce apnea-hypopnea. Maxillary-mandibular surgery can be recommended to patients with craniofacial abnormalities. Weight loss can improve the symptoms and morbidity in all obese patients, and bariatric surgery is an option for severe obesity. For physicians and healthcare systems, OSA is a major challenge. In addition to the apnea-hypopnea index (AHI), management decisions should be linked to the underlying phenotypes and the outcomes. For optimal management of OSA, a multidisciplinary approach is necessary.

Update of immunotherapy in Lung Cancer

何肇基 / Chao-Chi Ho, M.B., Ph.D.
Clinical professor, Department of Internal Medicine, College of Medicine, National Taiwan University
Attending physician (Pulmonologist), Department of Internal Medicine, National Taiwan University Hospital

Lung cancer is the leading cause of death in Taiwan. In the past two decades, chemotherapy and targeted therapy have significantly improved the survival of non-small cell lung cancer (NSCLC). But almost all the patients are inevitably confer drug resistance and relapse. The

immunotherapy brings a breakthrough treatment in a subset of cancer patients. After the development of immunotherapy, immune checkpoint inhibitors (ICIs) have made a breakthrough in NSCLC patients. ICIs targeting the programmed death 1 receptor (PD-1), programmed cell death receptor ligand 1 (PD-L1) and cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) showed significantly antitumor efficacy, produced durable clinical responses, and prolonged survival by regulating T cell-mediated immunologic responses in patients with advanced/refractory and metastatic NSCLC in clinical trials. But not all the patients benefit from immunotherapy. There remains a large portion of NSCLC patients who fail to benefit from the treatment. Combination with chemotherapy, anti-angiogenesis or other immunotherapy showed a promising option to enhance the anti-cancer efficacy of PD-1/PD-L1 immunotherapy. This year had a lot of updated data including KEYNOTE-189 final analysis, CHECKMATE 227, CHEKMATE 9LA... Some interesting results will be highlight and try to find the best way to implement into our clinical practice.

Update of EGFRm in Lung Cancer

魏裕峰 / Yu-Feng Wei, M.D.
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The development of EGFR-tyrosine kinase inhibitors (EGFR-TKIs), including third-generation TKIs, has revolutionized the treatment of non-small cell lung cancer (NSCLC), but new strategies are needed to overcome resistance mechanisms and prolong overall survival.
The key consideration of EGFR-TKI treatment strategy in EGFR-mutated NSCLC patients is how to use the best sequential EGFR TKI regimens. The third-generation TKI osimertinib has demonstrated impressive efficacy and tolerability in a first-line setting, especially in patients with Exon 19 deletion. However, there are currently no standard treatment options following disease progression. There is an uncertainty, therefore, weather to reserving osimertinib for second-line use in patients who acquire the T790M resistance mutation after first- or second-generation TKIs.
In addition, several studies demonstrated that EGFR-TKI plus anti-angiogenic therapy would be a promising treatment strategy in EGFR-mutated lung adenocarcinoma patients. However, these evidences were from the first-generation EGFR-TKI. 2020 ESMO reported the efficacy and safety of osimertinib in combination with bevacizumab among advanced lung adenocarcinoma patients.
This talk will update the current evidence on the treatment strategy in EGFR-mutated NSCLC. Also focus on the resistance mechanisms of EGFR mutant NSCLC treatment and provide further treatment options after EGFR-TKI treatment failure.

Update of ALK/ROS1m in Lung Cancer

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Rearrangements of the anaplastic lymphoma kinase (ALK) and ROS1 genes are present in 5%, and 2% of lung adenocarcinoma, respectively. Mutations of these two genes typically occur in younger patients who have never smoked or have a history of light smoking. Crizotinib is the pivotal ALK inhibitor that also inhibits ROS1 and MET receptor tyrosine kinases. In phase I-II trials, crizotinib demonstrated good tolerability and showed an ORR of 59.8% (95% CI 53.6–65.9), and a median PFS of 8.1 months (95% CI 6.8–9.7). In phase III trial, the median PFS was significantly longer for crizotinib compared to chemotherapy (7.7 versus 3 months, HR 0.49; 95% CI 0.37 to 0.64; p < 0.0001) and ORR was strikingly in favor of crizotinib (65% vs. 20%; p < 0.001). Second generation of ALK inhibitors, such as certinib, alectinib, and brigatinib, are ATP competitive, highly selective ALK inhibitors. Lorlatinib is a novel, selective and potent ATP-competitive ALK and ROS1 inhibitor, with very high activity against EML4-ALK and all the recognized mutations driving resistance to crizotinib, ceritinib, and alectinib, especially ALK G1202R/del. Although these drugs have changed the prognosis of this setting of disease, clinical outcomes in these patients vary. The presence of various breakpoints in the context of EML4-gene causes the formation of different variants of translocated EML4-ALK fusion proteins. These variants may be associated with the development of ALK resistance mutations, particularly G1202R, and provide a molecular link between variant and clinical outcome. The kinase domains of ALK and ROS1 share 77% amino acid identity within the ATP-binding sites. The resulting ROS1 fusion kinases are constitutively activated and drive cellular transformation. Crizotinib showed marked antitumor activity in patients with advanced ROS1-rearranged NSCLC (ORR 72%, with a disease control rate equal to 90% and a median PFS of 19.2 months). In phase 1–2 trials, ceritinib and lorlatinib demonstrated efficacy in this setting of disease (ORR 62% for both TKIs) with a great intracranial response rate (63% and 54%, respectively) and acceptable safety profile. Entrectinib achieved high response rates (ORR 77%; CI 95% 64–88) and durable responses (median duration of response 24.6 months; 95% CI 11.4–34.8) in phase 1–2 trials, including in patients with brain metastases. Repotrectinib was the only ROS1 inhibitor to show a potential to overcome TKI resistance mutations, notably G2032R, which is the most common ROS1 resistance mutation after crizotinib treatment.

Update of Rare genes mutation in Lung Cancer

廖唯昱/ Wei-Yu Liao, M.D., Ph.D.
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Attending Physician, Department of Internal Medicine, National Taiwan University Hospital

Implementation of molecular therapies targeting epidermal growth factor receptors (EGFR), anaplastic lymphoma kinase (ALK) and ROS1 fusions using small molecular tyrosine kinase inhibitors (TKIs) are shown to improve survival of non-small-cell lung cancer (NSCLC) patient to a certain degree. However, the prognosis of these NSCLC patients remains unfavorable because of the occurrence of either intrinsic or acquired resistance to TKIs. Besides, the other oncogenic drivers among NSCLC, other than EGFR, ALK and ROS1, has been discovered namely mutations in the BRAF, MET, HER2 and KRAS, as well as RET and NTRK rearrangements. A substantial number of clinical trials are currently underway to evaluate agents specifically designed to target these alterations. Some of the targeted therapies for these oncogenic drivers have received regulatory approval for clinical use, while others have modest clinical benefit. In this session, clinical features, potential targeted therapies and resistant mechanisms for these oncogenic drivers will be discussed.

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Laboratory diagnosis for COVID-19 : development and challenge

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Medical Director, Clinical Virology Laboratory, Chang Gung Memorial Hospital
Professor, Department of Medical Biotechnology and Laboratory Science/Graduate Program of Biomedical Science, CGU

Abstract
The novel human coronavirus disease COVID-19 has become the fifth documented pandemic since the 1918 flu pandemic. The coronavirus was officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses based on phylogenetic analysis. Because the virus is highly contagious, it rapidly spreads and continuously evolves in the human population. This talk will discuss laboratory diagnosis of SARS-CoV-2, including culture-based virus isolation for evaluation of potential infectivity of clinical specimens and viral genomic surveillance in Taiwan. Our results revealed that in addition to viral RNA copy numbers, the integrity of the viral genome should be considered when evaluating the infectivity of clinical specimens from COVID-19 patients. Sequence analysis of SARS-CoV-2 in Taiwan reveals novel ORF-8 deletion mutant and clade possibly associated with infections in middle East. Moreover, serology assay for COVID-19 patients will be discussed too. Microneutralization assay, plaque reduction assay, pseudovirus assay as well as binding assay will be compared.

Non-Pharmacological Management of Severe Covid-19 infection in the ICU

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Rapid City, SD
Chief Scientific Officer, Prolung Inc, Salt Lake City, UT
University Adjunct Faculty, Department of Oncology, Johns Hopkins School of Medicine

The arrival and on-going worldwide transmission of the SARS-CoV-2 virus has presented unprecedented challenges to modern critical care resources in the management of this global pandemic. Our knowledge of the transmission and pathophysiology of SARS-CoV-2 infection is changing on a daily basis, and this presentation will summarize the available up-to-date knowledge of the non-pharmacological critical care management of severe Covid-19.

We will cover the topic broadly in the sense of addressing the entire ICU environment and continuum of care rather than simply the critical care management of individual patients.

Management options depend very much on the extent of local resources, both human expertise and technology, and also the pace of local disease spread which may overwhelm even "sophisticated" health care delivery systems (witness Northern Italy and New York City at the height of their local outbreaks). Facing material (PPE) shortages and the threat of a diminished critical work force through nosocomial infection of health care workers, reduced exposure and effective cleaning are several of the key steps to transmission reduction. Two areas of the rapid expansion of existing technologies include: non-contact communication, in the control of patient centric devices (medication delivery and ventilatory support) from a "remote" location; enhanced patient – family / support staff communication via image-enhanced remote monitoring and communication; use of wide space sterilization technologies such as use of UVC (Ultra-violet C) lighting.

Although multi-organ system involvement is recognized early on in Covid-19, need for advanced ventilatory support remains a significant cause for direct admission or transfer into the ICUs. The notion of the "best practice" has rapidly evolved from early adoption of invasive mechanical support with intubation and avoiding "aerosol generating" support measures by various NIPPV (Non-Invasive Positive Pressure Ventilation), to the recognition that intubation and mechanical ventilation both represents very high risk maneuvers to staff and to the patient, and that NIV technologies such as HFHC (High Flow Nasal Canula) oxygen support and NIPPV such as BiPAP (BiLevel Positive Airway Pressure) support may be both less risky to patient and staff than initially thought, and more effective for a subset of patients developing progressive respiratory insufficiency. Greater focus is for NIPPV support for a period when the disease course may be self-limited or when supplemental pharmacologic support may help the patient avoid need for mechanical ventilation.

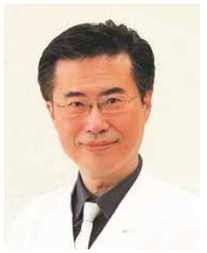
Body positioning, i.e. proning, either prior to intubation and MV or once patients are on mechanical ventilation is widely adopted, as supported by imaging evidence, physiologic reasoning of V/Q matching, and by clinical outcome.

In the most severe cases of ventilatory insufficiency, ECMO (mostly v-v) have been used in those centers with the technical expertise and support. We shall review the outcomes of ECMO in severe SARS-CoV-2 cases as compared to earlier outcome trials such as EOLIA.

Convalescent plasma transfusion, which straddles the pharmacologic (synthetic antibodies) and non-pharmacologic world, will also be considered, and the evidence examined.

While survival in critically ill Covid-19 patients is the parameter most often considered in "outcome", we know that Covid-19 survivors can have a number of long lasting post-critical care illness functional limitations. In addition to avoiding medications that may worsen critical care neuropathies, initiation of rehabilitation while patients are still in the ICU, plus rigorous planning for a post SARS-CoV-2 infection recovery program will be discussed.

Pharmacological treatment for COVID-19: what we learn from clinical trial reports?



陽光耀 / Kuang-Yao Yang, M.D., Ph.D.
Professor, Institute of Emergency and Critical Care Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan
Director, Division of Respiratory Therapy, Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Abstract

Coronavirus disease 19 (COVID-19) is a global health threat and causes significant medical, economic, social and political implications since Jan. 2020. One investigational drug called remdesivir has been authorized by the FDA for emergency use for the treatment of hospitalized patients with severe COVID-19 disease on May 1, 2020. However, many medications have been tested for combating COVID-19 and reported from clinical trials. Researchers are studying other potential treatments for COVID-19, including: (1) Antiviral drugs. In addition to remdesivir, other antiviral drugs being tested include favipiravir and merimepodib. (2) Dexamethasone. (3) Anti-inflammatory therapy. Many anti-inflammatory drugs may treat or prevent dysfunction of several organs and lung injury from infection-associated inflammation. (4) Hydroxychloroquine and chloroquine. (5) Drugs being studied that have uncertain effectiveness. Amlodipine, ivermectin, losartan and famotidine have been studied. But it is not yet known how effective these drugs may be in treating or preventing COVID-19. (6) Drugs to prevent COVID-19. Researchers are studying drugs to prevent COVID-19 before and after exposure to the virus. This presentation will review and summarize the clinical trial reports of pharmacological treatment for COVID-19.

The effect of face covering and social distancing in preventing the transmission of COVID-19.

Yoichi Nakanishi, M.D., Ph.D.
Chairman, Kitakyushu City Hospital Organization
Principal, Kitakyushu Municipal School of Nursing
Professor Emerritus, Kyushu University

Although countermoves against COVID-19 in Taiwan is the most successful in the world, COVID-19 surge is still invading many countries/areas. Under such circumstances, research and development of therapeutic agents are actively push forward. Usefulness of steroid for seriously sick patients with COVID-19 due to cytokine storm was established. However, efficacy of drugs against virus itself, anti-viral agents, has not yet established. Vaccines are expected to be available by the end of this year or early next year, but there are some concerns about their safety and efficacy. Until effective therapeutic drugs and vaccines are launched, the most important and effective preventive measures are to keep social distance and to wear mask. Actually, social distancing measures are the primary strategies used to prevent transmission of the SARS-CoV-2 virus because it is transmitted by droplet or aerosol by way of airway. In addition, wearing mask is today widely recognized as appropriate preventing measure although some investigators and organizations including WHO were not convinced its effect around the beginning of COVID-19 surge. Only recently, simulation using super-computer, Fugaku, has shown that mask composed of a nonwoven fabric almost completely prevent SARS-CoV-2 virus infection, and provided many suggestions in our daily life.

It is true that both social distancing and wearing mask are most easy, cheap and definite measures to prevent from COVID-19. We should keep to pay utmost attention and to 集団免疫take the right action until the day when magic bullet to cure the disease is developed and herd immunity against the virus is acquired.

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203會議室

The Consensus of LDCT Screening in Taiwan: 肺癌早期偵測及健康管理

王英偉 署長 / Ying-Wei Wang, M.D., Dr. P.H.
Director-General,Health Promotion Administration,Ministry of Health and Welfare, Taiwan, R. O. C
Associate Professor, School of Medicine, Tzu Chi University, Taiwan

我國106年肺癌發生數14,282人、標準化發生率為每十萬人有37人，標準化發生率近幾年呈上下震盪趨勢，標準化死亡率近10年(99-108年)自每十萬人口25.8人，逐年降至22.8人，降幅雖達12%，但近10年肺癌仍持續高居國人癌症死因之首，亟需研議有效的防治策略。

低劑量電腦斷層掃描（LDCT）篩檢，是目前唯一具國際實證可早期發現肺癌的篩檢工具，對「重度吸菸族群」(抽菸史超過30包年且戒菸小於15年)可降低2成死亡。衛生福利部自103年起補助台灣肺癌學會「以低劑量電腦斷層掃描台灣不吸菸肺癌高危險群之研究」，評估吸菸以外危險因子以LDCT篩檢之本土資料，初步結果發現，無論男、女，若一等親具肺癌家族史，罹患肺癌的風險較高。

我國刻正研議肺癌早期偵測及健康管理，期待民眾能透過「戒菸益健康、自我須防護、篩檢慎思量、警訊早就醫」等防護，遠離肺癌威脅。

The Consensus of LDCT Screening in Taiwan: 篩檢共識

張基晟 / Gee-Chen Chang, M.D.,Ph.D.
Vice-President of Chung Shan Medical University
Professor of Institute of Medicine, Chung Shan Medical University
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Chief of Lung Cancer Treatment Center, Chung Shan Medical University Hospital
Professor of Medicine, Faculty of Medicine, School of Medicine, National Yang-Ming University
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肺癌是所有癌症死亡的第一名，在臺灣也是，而且發生率高居所有癌症的第二名， 主要是因為發現太晚，有一半以上的病人診斷時，已經有遠處轉移，而肺癌病人若是已經有症狀，大多已經是晚期。

然而臨床第一期前半期(stage IA)病人有八成的五年存活率，因此若能透過低劑量胸部電腦斷層(LDCT)在很早期就有效地將需要治療的病人找 來，這將會大大下降肺癌的死亡率。

但是要如何找到這群病人，就必須從造成肺癌的危險因子與高危險群去做篩檢才比較

容易下降肺癌的死亡率，同時也要符合篩檢的公共衛生原則-具有成本效益、高敏感度及高特異性、安全有效，這就必須從幾方面著手界定肺癌的危險因子與致癌物，針對台灣本土研究，如不抽菸肺癌、肺癌家族史、空氣汙染….等等，從而有台灣自己的高危險群定義，並參考世界對低劑量胸部電腦斷層(LDCT)的作法 (NLST, NELSON trials) 加以修飾改良方可達到真正目標。

目前臺灣有一個低劑量胸部電腦斷層(LDCT)肺癌篩檢臨床試驗，由台灣國民健康署補助，於2014 到2018/10 年間，針對55-75歲、未曾抽菸、且有下列之依危險因子者進行前瞻性低劑量電腦斷層篩檢，主要是由肺癌家族史、易感受基因及二手菸…等環境因素的危險因子加成分數做為篩檢條件，目前初步已經完成收案。

現行利益風險與成本效果評估，都是就吸菸者而言。台灣和日本針對非吸菸者做LDCT 肺癌篩檢試驗，目前結果尚未出爐。所以目前做低劑量胸部電腦斷層(LDCT)肺癌篩檢，其利益可以是有降低肺癌的死亡率、減少晚期肺癌的比例、早期診斷其它疾病、改善生活型態…等。其風險可能有過度診斷、偽陽性、偽陰性、影響生活品質、輻射線暴露等…。

The Consensus of LDCT Screening in Taiwan: 追蹤與處置建議

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Professor and Director, Institute of Emergency and Critical Care Medicine National Yang-Ming University School of Medicine

肺癌一直是全世界死亡率最高的癌症，包括台灣，許多人不管有沒有症狀，常常是被發現的時候，已經有轉移的現象。目前雖然肺癌治療方式都有許多進步，包括內科標靶藥物及外科微創手術的發展，但肺癌死亡率依然居高不下，因此，要提高肺癌的存活率，最重要的就是利用胸腔低劑量電腦斷層，來做肺癌的篩檢及早期發現。的確，根據報告，胸腔低劑量電腦斷層篩檢可以降低肺癌的死亡率。很高興這次可以代表台灣胸腔外科醫學會，與台灣肺癌學會、台灣胸腔暨重症加護醫學會及中華民國放射線醫學會一起來制訂胸腔低劑量電腦斷層肺癌篩檢的共識，藉由這個共識，希望民眾可以知道一般肺結節的處理原則，也讓一般的民眾能夠有所依循，而不會因為低劑量電腦斷層檢查出不同大小的肺結節，導致有恐懼、不知所措的情況，甚至接受了不需要的手術。事實上，有些小的毛玻璃狀結節並不需要立即處理，或者有些只需要定期觀察即可。制定這個共識也是希望讓台灣的各級醫院能夠就這個共識，來提供病患足夠的資訊，給病患適當的建議和處置，進而造福病患。

The adjuvant therapy in lung cancer patients receiving operation-CCH experience

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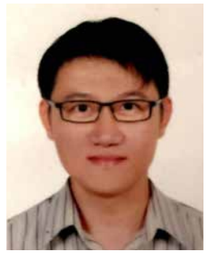
Visiting staff, Division of Thoracic Surgery, Department of Surgery, Changhua Christian Hospital
Chief of Department of Surgery, Changhua Christian Hospital

Lung cancer was also the leading cause of cancer-related death in Taiwan.2 Although medical knowledge and surgical techniques have advanced, the long-term survival of patients with lung cancer is still poor. The high mortality rate is primarily because most patients are diagnosed at an advanced stage, and the response rate to chemotherapy is not satisfactory. According to current guidelines published by the American Society of Clinical Oncology and the National Comprehensive Cancer Network (NCCN), complete surgical resection and mediastinal lymph node dissection provides an opportunity to cure lung cancer, and improve long-term survival in patient with stage I or a subset of stage II (T1-2, N1) disease. Multimodality therapy is suggested for most patients with stage III disease. Systemic therapies, such as chemotherapy or targeted therapies, are recommended for patients with stage IIIB and stage IV disease. When patients receive complete surgical resection, observation is recommended for patients with stage IA disease, and for those with stage IB to IIIA disease adjuvant chemotherapy is suggested after complete surgical resection to decrease the distant recurrent rate and improve survival. The purpose of our study was to investigate the influence of the adjuvant therapy on overall survival in patients receiving surgical resection with lung cancer in Chang-Hua Christin Hospital. We analyzed the perioperative data in all patients and further to investigate the influence impact of adjuvant therapy in Chang-Hua Christin Hospital. Thus, 376 patients with stage IB to IIIA lung cancer who received surgical resection and adjuvant chemotherapy were identified in the database and included in the analysis.

Surgical result of neoadjuvant therapy in non-small cell lung cancer-TCVGH experience



陳顥匀 / Hao-Yun Chen, M.D.
Chief Resident, Division of Thoracic Surgery, Department of Surgery, Taichung Veterans General Hospital

There is good evidence to support the use of chemotherapy in stages II-III. However, whether to use neoadjuvant or adjuvant therapy has been the topic of much debate. With its strong evidence base, adjuvant chemotherapy has been adopted in the European Society of Medical Oncology clinical practice guidelines for early and locally advanced stages II-III non-small-cell lung cancer (NSCLC). There were fewer trials in assessing the benefits of neoadjuvant therapy plus surgery in the management of NSCLC. Here we present our clinical experience of neoadjuvant chemotherapy in a single institutional data about patients with NSCLC. Total of 34 patients with clinical stage of II-IV NSCLC who received neoadjuvant

chemotherapy between 2011 and 2016 were retrospectively identified from chart review. Patients who received sequential resection for second primary lung cancer or loss of follow-up were excluded. Survival curves were estimated by the Kaplan-Meier method and compared by log-rank test. The results showed the 5-year survival rate was 100% (2/2) in stage II, 64.7% in stage III and 80% (4/5) in stage IV. In comparison with the survival rate of variable stages in patients receiving all kinds of treatment strategies within the concurrent time period, the results in the neoadjuvant group were considerably favorable.

Evolving neoadjuvant and adjuvant approaches in early stage resectable NSCLC

Roy S. Herbst, M.D., Ph.D.
Ensign Professor of Medicine
Professor of Pharmacology
Chief of Medical Oncology
Associate Director for Translational Research

Academic Appointments
Chief of Medical Oncology, Yale Cancer Center. 2011-present
Professor of Medicine (Tenure), Yale University. 2011 – present
Professor of Pharmacology, (secondary) Yale University. 2012 – present
Ensign Professor of Medicine (Medical Oncology). 2013-present
Adjunct Professor of Medicine, THNMO, Division of Cancer Medicine, UT-MDACC, Houston, TX. 2013-present
Honorary Professor, University College London (UCL) Cancer Institute. 2015-present

Administrative Appointments/Responsibilities
Editor and Founder, the Protocol Review, THNMO, UT-MDACC, Houston, TX, 2002–present
Associate Cancer Center Director for Translational Research, Yale Cancer Center. 2011-present
Member, Yale COVID Impact Committee Board of Governors, 2020-

Surgery for locally advanced NSCLC after target therapy: a single institute experience

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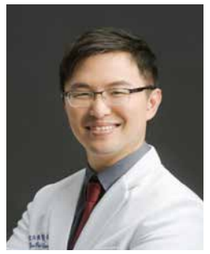
The EGFR-targeting tyrosine kinase inhibitors (TKIs) were used widely in locally advanced non-small-cell lung cancers (NSCLCs) with activating epidermal growth factor receptor (EGFR) mutations. Compare to platinum-based chemotherapy, the progression free survival (PFS) showed significant prolong, and overall survival (OS) was improved for some groups. Lung resection for locally advanced NSCLCs is investigated these years, especially development of target therapy and immunotherapy, and some prognostic factor have been found. We research the data from 2010 to 2019 in Taipei Veterans General Hospital, these patients received pulmonary resection for locally advanced NSCLCs, included neoadjuvant and adjuvant group. Patient with double cancer, loss to follow-up and unclear surgical margin of primary tumor were excluded. The clinical and pathological characteristics were included. The prognostic factors between target therapy and chemotherapy were investigated. The last, we would demonstrate two cases of stage IV adenocarcinoma received target therapy and surgery with pathological complete response.

Neoadjuvant TKI with Thoracic Surgery as the First-Line Treatment for Stage IV Non-Small Cell Lung Cancer with EGFR mutations



陳沛興 / Pei-Hsing Chen, M.D.
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In Taiwan, non-small cell lung cancer (NSCLC) has been the leading cause of cancer death, making a phenomenal impact on the public health. By understanding the oncogenic driver mutations of NSCLC (e.g. EGFR mutation or ALK rearrangement), the target therapy has taken the place of chemotherapy for its effectiveness and specificity, becoming the new standard of care for stage IV NSCLC. Despite the progress of medical treatment, the majority of patients with stage IV NSCLC still underwent disease progression after a period of time. Noticeably, more than half of the progression was restricted to the original sites of tumor. It brings up the hypothesis that combination of local consolidative therapy (e.g. surgery or radial therapy) and medical treatment could be beneficial for these patients.
Therefore we retrospective reviewed our data for the neoadjuvant TKI treatment with thoracic surgery for stage IV NSCLC. 52 patients were enrolled. We used propensity score matching with 1:4 ratio as control. The result showed significant improved in PFS. This result is supposed to establish a new front-line treatment for stage IV NSCLC with EGFR mutation.

The role of TKIs from the perspective of Thoracic Surgeons: TSGH experience sharing

陳穎毅 / Ying-Yi Chen, M.D.
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This study investigated the curative effect of surgical resection combined with molecular target therapy for advanced non-small cell lung cancer (NSCLC).
One hundred and twenty-six female patients with NSCLC with tyrosine-kinase inhibitor (TKI) treatment were enrolled. There were only 16 patients who received curative resection and TKI treatment for stage IIIB to IVB lung cancer patients.
These patients were divided into two groups: 8 patients received the molecular target therapy after surgery (group I); and 8 patients were treated with surgical resection prior to the administration of TKI (group II). We also used propensity score to compare only TKI treatment.
Compared with group I, the rates of partial regression, stabilization of disease and progression of disease were no significant difference in group II. Moreover, the overall survival rate in patients with surgery and TKI treatment was significantly higher than that in patients with only TKI treatment.
This suggests that tumor resection combined with TKI treatment could improve the effects of treatment and the prognosis of patients with advanced NSCLC. There were no significant differences between wedge resection or lobectomy in these advanced lung adenocarcinoma patients with TKIs.

Neoadjuvant therapy in clinical stage IV lung cancer. KMUH experience sharing

姜宏興 / Hung-Hsing Chiang , M.D.
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Almost cases of stage IV lung cancer are non-resectable in time of diagnosis and systemic therapies, including chemotherapy, concurrent chemoradiotherapy, immunotherapy and target therapy are most common treatment options. After above treatment, some cases were become to resectable. We are going to share experience of curative surgical intervention, including decision making, timing, type of surgery, extreme surgical complications and prognosis, in stage IV lung cancer after the systemic therapies from KMUH during in recent 10 years.

Adjuvant Chemotherapy for Completely Resected Non-small Cell Lung cancer: KSVGH Experience Sharing

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Background: Adjuvant chemotherapy (ACT) is now an accepted standard for completely resected stage II and IIIA non–small-cell lung cancer (NSCLC) patients and also recommended in high risks of stage IB patients. Long-term follow-up is important to document its persistent benefit. We report here our hospital's overall survival (OS) data of 14-year experience. Methods: From January 2005 to December 2018, data of 551 patients with pathologic stage IB/II/IIIA non-small cell lung cancer (NSCLC), including 198 of IB patients, 185 of IIA and 168 of IIIA, were obtained from the cancer registered database of Kaohsiung Veterans General Hospital to analyse the effect of adjuvant chemotherapy on survival outcome. Results: A total of 242 patients underwent surgery followed by adjuvant chemotherapy (ACT group) and 309 patients underwent surgery alone (S group). The median survival/5-year overall survival (OS) for ACT and S group was without difference in all patients. In subgroup analysis, the 5-y OS for ACT and S group was 84.0% and 76.8% respectively (P = .202) in stage IB patients. In stage II patients, the median survival/5-year OS for ACT and S group was 86.7 months (95% CI, 72.6-100.8 months)/64.9% and 58.6 months (95% CI, 42.0 to 75.2 months)/49.2%, respectively (P = .024). In IIIA patients, the median survival/5-year OS for ACT and S group was 48.5 months (95% CI, 30.0-66.9 months) /43.3% and 31.2 months (95% CI, 24.1 to 38.3 months)/28.3%, respectively (P = .037). Conclusions: Our retrospective analysis shows a significant survival benefit for adjuvant chemotherapy in stage II to IIIA NSCLC patients.

Percutaneous CT-guided Lung Tumor Ablation-Experiences of a Decade

林巧峯 / Frank Cheau-Feng Lin, M.D., Ph.D., FACS.

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Thoracic Surgery, Chung-Shan Medical University Hospital

CT-guide percutaneous lung tumor ablation was not widespread because of high morbidity in comparison to the liver. Because that 1)the alveolar space is full of air and pneumothorax was easy to happen 2)lots blood are in the lung, easy to bleeding 3)respiratory movement 4) rib may on the way,5) echo cannot be used in the real-time manner 6)adjacent to vital organs 7) ample blood flow makes heat sink effect. Radiofrequency (RF), microwave (MW), and cryotherapy were mainly tools. The principle of RFA is W=IR, and the microwave is water molecular vibration. RF is economical. MW serves a larger ablation volume. The needle we have chosen was a straight needle to avoid complications. We had used cool-tip RFA, big-tip RFA, Jet-tip RFA, and microwaves (Covidien and MedWaves). Double-needle or triple-needle RFA were also tried. Jet-tip is suitable for GGO. Jet-tip, double/tri- needle RFA, and microwave have a larger ablation volume. We had not used cryotherapy for the safety issue that we had not confirmed, and the price was too high.

We started the radiofrequency ablation in 2011. About 300 cases had been performed till 2020. And an animal lab was held in 2013 to verify the safety area of the thoracic cavity and the microwave ablation. We concluded that the esophagus and nerves were fragile to the thermo-ablations and must be avoided.

Our indications of ablation are

1) Early-stage lung cancer with poor patients' condition that surgery is not indicated.
2) Late-stage lung cancer S/P systemic or other local treatment with residual tumors.
3) Cancer reduction therapy.
4) Residual/recurrent multiple GGN with proven malignancy.
5) Metastatic pulmonary cancers.

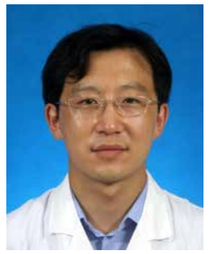
The technic of needle implantation was the same as the pre-operative localization we shared before. Laser Angle guide Assembly was used to guide the puncture angle. The puncture depth was also well controlled. We try our best to make all of the needle punctures in one shot to avoid complications as possible. The ablation of tumors at the danger zone is not impossible for us and will also be presented.

Pre-medication with pain-killer, antibiotics, and anti-cough was used. Local anesthesia, nerve block, artificial pneumothorax, Fentanyl, and Dormicum were also prescribed depending on the situations. IH lidocaine to avoid cough was also tried. IVG is preferred if available.

Complication including pneumothorax, hemothorax, reactive pleural effusion, lung hemorrhage, air emboli, bronchopleural fistula, arterial pseudo-aneurysm, lung cavity, lung abscess, empyema, and skin burn. Dr. Dupuy of Brown University is an expert in it but still report a high complication rate. Survival is inferior to surgery.

The preliminary statistics of ablation data of 2017-2019, complications, and survival will also be shared.

Flexible bronchoscopy-guided ablation therapy in peripheral lung cancer



孫加源 / Jiayuan Sun, M.D., Ph.D.
Chief Physician, Department of Respiratory and Critical Care Medicine
Director, Department of Respiratory Endoscopy
Director, Department of Interventional Pulmonology
Shanghai Chest Hospital, Shanghai Jiao Tong University

手術切除仍然是目前早期周圍型非小細胞肺癌根治方法，但許多高齡或合併症較多的患者無法耐受手術切除。對於這類患者，消融治療是推薦的，目前常用的熱消融治療，如射頻消融、微波消融，多經胸壁方式進行，其氣胸、出血發生率與TTNA相同。隨著引導支氣管鏡技術的發展，導航設備、定位和確認工具的推陳出新為經支氣管方式治療周圍型肺癌提供了可能。 我們中心自2015年開始開展電磁導航引導下經支氣管射頻消融治療周圍型肺癌，聯合企業開發了一系列經支氣管射頻、微波、冷凍消融治療工具，並通過動物實驗驗證了經支氣管微波、冷凍消融的可行性和安全性。我中心2018年4月至2019年7月共納入13例患者，包含14個早期周圍型肺癌，消融後1年局部控制率為85.7%，平均預估無進展生存期18.4月。目前經支氣管消融治療周圍型肺癌這一新興領域還處於探索階段，需要不斷積累經驗、開展大樣本隨機對照多中心研究提供更多循證依據。

Percutaneous lung ablation therapy: Chinese experience

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北京京西腫瘤醫院副院長、影像微創診療中心主任

專業特長：
影像引導下腫瘤介入治療（穿刺活檢、微波消融、射頻消融、放射性粒子植入、椎體成形等）。
擅長病種：胸部腫瘤、脊柱腫瘤、胰腺腫瘤等。

Navigation System in One-Stop Lung Cancer Solution with Hybrid OR

莫麗雯 / Mok Lai-Man, M.D.
Visiting Staff, Department of Thoracic Surgery, Division of Surgery, MacKay Memorial Hospital

隨着民眾健康意識提，以及低劑量電腦掃描技術(Low dose CT)的普及，早期肺癌的偵測率大大提高。針對近年越來越常被發現的細小病灶，傳統的診斷方法診斷性既不高，也無法提供即時治療。在Hybrid OR內應用導航系統及fluoroscopy 可以在real time的狀況下精準定位細小病灶並切片，即時診斷後立刻作相應的治療。

Cone-beam CT augmented fluoroscopy-guided endobronchial procedures for small pulmonary lesions

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Attending Physician, Department of Thoracic Surgery, National Taiwan University Hospital, Biomedical branch

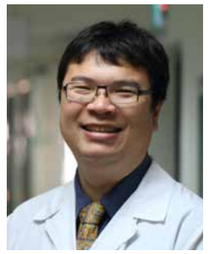
Implementation of low-dose CT for early detection of lung cancers has significantly increased the number of screened small pulmonary nodules. For suspicious malignant nodules, diagnostic biopsy or surgical resection should be performed. Transbronchial localization is an effective alternative for localizing small nodules with fewer complications than CT-guided percutaneous localization. We developed a novel technique, termed augmented fluoroscopic bronchoscopy (AFB), using CBCT with an annotation software, which provides both 2D fluoroscopic view and 3D image data, allowing for real-time guidance during bronchoscopic localization. Our results suggest that AFB could be universally reproducible by using regular bronchoscopy and C-arm CBCT with annotation software, for which most angiography rooms and hybrid operation rooms are suitable.

Extended segmentectomy for small lung nodule with iVATS

鄭雅夫 / YaFu Cheng, M.D.
Resident, division of thoracic surgery, department of surgery, Changhua Christian hospital

Introduction: In these decade, the technique of image-guided video-assisted thoracoscopic surgery (iVATS) grows more and more popular. However, the application of iVATS for intersegmental nodules and segmentectomy have not been explored. Here, we describe a novel technique using iVATS to accomplish extended segmentectomy for intersegmental nodules. This technique helps to overcome the challenges of adequate safe margin for these nodules.
Methods: This is a retrospective study in a single center. The technique of extended segmentectomy with iVATS was described in the study. Patients with lung nodules at intersegmental plane and received extended segmentectomy with iVATS technique between July 2018 to July 2020 were enrolled. Patients with multiple lung nodules or diameter greater than 1 centimeter were excluded. The primary end point were tumor diameter, closest resection margin and adequate resection rate. The adequate resection was defined as margin larger than 2 centimeter or 2 times than tumor diameter.
Results: We successfully performed the extended segmentectomy for intersegmental nodules with iVATS technique in 57 patients. The pathology of 32 patients revealed non-small cell carcinoma (NSCLC) at T1a stage. The mean tumor diameter was 7.53 +- 1.81 millimeter. The mean closest resection margin was 18.65 +- 8.58 millimeter. There were 24 patients (75%) received adequate resection.
Conclusion: The iVATS extended segmentectomy technique is a feasible way to provide adequate resection margin for central and intersegmental lung nodules. Long-term follow-up and outcome are still needed.

Percutaneous Localization of Small Pulmonary Nodules - Chimei Experience



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Teaching Visiting Staff, Chimei Hospital

With the prevalent of low dose computer tomography, more and more asymptomatic pulmonary nodules are found and require management. The sub-centimeter or part-solid pulmonary nodules are difficult to localized in surgery. A cone beam CT in operation theater (or so called hybrid room) is a powerful tool for surgeons to find the nodules.
Chimei Hospital acquired the first Artis Pheno system in Taiwan in 2017. And it brings the thoracic surgery department benefit by percutaneous localization of the small pulmonary nodules. Till the end of Augus, 2020, we have performed 205 cases of it. Most of the cases were small solid or part-solid pulmonary nodules of unknown etiology before surgery. They're not feasible for traditional CT guide biopsy due to it's size or location. In the 205 cases, 130 (63.5%) cancer or precancer lesions were found. Adequate cancer resection were performed after the pathologic impression was made by frozen section. With the experience, we conclude that corn beam CT assisted percutaneous localization in surgery is a efficient and safe therapy for patients with small pulmonary nodules.

Using mobile CT for intraoperative localization to resect small pulmonary lesion: the experience of VGHTPE

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Small pulmonary nodule localization is essential for proper lesion management. Some techniques for pulmonary nodule localization, including preoperative computed tomography (CT)-guided localization and intraoperative electromagnetic navigation, have already been reported. Herein, we report preliminary results of small pulmonary nodule intraoperative localization by using an Airo mobile CT scanner. All lesions were successfully located and resected in a uniportal video-assisted thoracoscopic surgery. We found that intraoperative localization of small pulmonary nodules using a mobile CT scanner is feasible, safe, and provides optimal image quality with potential for more flexible, and cost-effective utilities.

Single-stage localization and removal of small lung nodules using 3D mobile C-arm

周品立 / Pin-Li Chou, M.D.
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Objective: Simultaneous localization and removal of small pulmonary nodules in hybrid operating room (OR) equipped with robotic C-arm cone-beam computed tomography (CT) has gained popularity in recent years. However, the high capital costs of hybrid OR preclude its presence in most hospitals. New generation 3D mobile C-arm offers improved soft tissue image quality with high mobility and more affordable price. So far, its primary applications have been within orthopedic and spinal surgery. This case series illustrates the feasibility of small pulmonary nodules localization using mobile 3D mobile C-arm system.

Material and methods: From 2020/7 to 2020/9 , fourteen patients underwent lung tumor localization by 3D mobile C-arm system in OR. The feasibility and safety of the procedure were assessed through a retrospective review of the patients' clinical charts.

Results: The median tumor size was 7.5 mm (interquartile range [IQR]: 5 to 9.75 mm), whereas the median distance from the pleural surface was 4.2 mm (IQR: 0.5–6.45 mm). All of the lesions were visible on intraoperative CT images and localization was successful in 13 patients with completing thoracoscopic resection subsequently. The median time required for localization was 41.5 min (IQR: 33.75–53.25 min), whereas the median radiation exposure was 143.45 mGy (IQR: 86.1 to 194.6 mGy). Lesion localization was unsuccessful in one case owing to pneumothorax induced by needle puncture. There was no operative mortality and the median length of postoperative stay was 2.5 days (IQR: 2 to 3 days).

Conclusions: The results of our case series support the feasibility of small lung tumor localization using 3D mobile C-arm system.

台灣胸腔及心臟血管外科學會

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The role of surgical resection of advanced non-small cell lung cancer after a response to EGFR-TKI

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INTRODUCTION: The epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) have become the mainstay treatment for advanced EGFR mutation-positive non-small cell lung cancer (NSCLC). Although it provides significant improvement in objective response rate and progression-free survival, disease progression in inevitable and subsequent therapy remains challenge. Recently, there are growing studies focused on the combination treatment strategy to improve the treatment outcome. In current study, we will evaluate the role of residual tumor resection during the use of EGFR-TKI in patients with advanced EGFR-mutant NSCLC.

METHOD: Patients with EGFR mutation-positive advanced NSCLC who visited a tertiary referral center from July 2013 to June 2018 were analyzed retrospectively. They received EGFR-TKI until disease progression, death, or intolerable adverse events. The progression-free survival (EFS) and overall survival (OS) were estimated by the Kaplan–Meier method and compared using the log-rank test.

RESULT: Total 385 NSCLC patients were enrolled, including 43 patients receiving residual tumor resection during the use of EGFR-TKI. Patients receiving surgery were female predominance, better performance status and less brain metastasis. With Cox proportional hazard regression analysis to exclude potential confounders, patients receiving surgery had a significantly better PFS [46.2 vs. 11.5 months, hazard ratio 0.33, $p<0.001$] and OS [not reached vs. 28.5 months, hazard ratio 0.20, $p=0.002$] than patients without surgical resection. In subgroup analysis, patients with contralateral lung metastasis have more benefit from residual tumor resection.

CONCLUSION: In present study, the salvage surgery for residual lesions provide better PFS and OS, it also become an independent good prognostic factor. Further prospective cohort study is warranted to validate the role of surgery in patients with advanced NSCLC harboring EGFR mutations.

Transbronchial abrasion of pulmonary nodules in HYBRID OR

Calvin S. H. Ng, BSc, M.D., FRCS(CTh), FCCP

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Honorary Consultant Surgeon at New Territory East Cluster (NTEC) hospitals in Hong Kong.

With increasing utilization of low-dose computer tomography scans screening and awareness, incidental discovery of lung nodule is becoming more common. Many may harbor pre-malignant or early stage tumours. Local therapies of these lesions may be considered, especially in patients with surgical contraindications. Treatment modalities such as SBRT, percutaneous thermal ablation techniques (for example, RFA, microwave and cryotherapy) can be highly effective and are associated with reasonable local control rates ranging from 64% to 69.8% at 2 years. However, these procedures are also associated with complications: SBRT carries up to 22.3% risk of radiation pneumonitis and pneumonia, while percutaneous ablation techniques carry 11-52% risk of pneumothorax and bronchopleural fistula (BPF). In terms of energy source, radiofrequency relies heavily on electrical conductance of tissues, thus the high impedance of human lung tissue may limit its effectiveness.

Bronchoscopic ablation techniques utilizing radiofrequency energy for eradication of tumor cell have previously been reported, with theoretical advantages of less pneumothorax/BPF due to non-trans-pleural route of entry, being able to reach peri-bronchial tissues easily, and having access to particular locations in lung which are otherwise difficult or impossible to reach. Meanwhile, microwave energy produces a larger and more predictable ablation zone, as it is minimally affected by impedance and has less heat-sink effects. Building upon our institute's experience in lung nodule dye-marking and biopsy via electromagnetic navigation bronchoscopy (ENB) in the hybrid theatre, we identified a selected group of cases which are suitable for bronchoscopic microwave ablation under ENB guidance. We present the indications, technique, experience and early results for our 30 cases.

Lung transplantation in chronic obstructive pulmonary disease

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Attending Staff, Division of Thoracic Surgery, CGMH

Lung transplantation is a well-recognized treatment for patients with a variety of end-stage lung diseases. However, there are still some debates of when to refer, list and offer lung transplant as well as the preferred transplant types. According to the registry of Internal Society for Heart and Lung Transplantation, the 5-year survival of end-stage COPD patients receiving bilateral lung transplantation approaching 60%. Here we review the consensus of referral and listing of COPD patients for Lung transplantation, the preferred procedures of lung transplantation and the impacts on survival and quality of life after lung transplantation. We will also demonstrated our recent achievement of lung transplantation program in Lin-Kou Chang Gung Memorial hospital.

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Evolving treatment landscape in EGFRm stage IV patients

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Lung cancer is the leading cause of cancer death worldwide. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for 80–85% of cases. Epidermal growth factor receptor (EGFR) mutations are observed in approximately 40-60 % in Asian populations. Developing treatment strategies specific for EGFR mutation patients is important and has evolved in recent years.

Guidelines recommend treatment with an EGFR-TKI for EGFR mutated metastatic NSCLC and the clinical practice guidelines of the National Comprehensive Cancer Network (NCCN) recommend osimertinib as the preferred EGFR-TKI option for first line treatment in such patients due to efficacy, safety and CNS effect and potential patient attrition issue. Therefore, resistance management after osimertinib has become an increasingly important clinical issue. Novel combinations with EGFR TKIs to concur potential primary or secondary resistances are being widely examined.

Here we review the evolving treatment landscape in EGFRm stage IV patients and the novel combinations for EGFR-TKIs resistance management.

Step forward to new era of treatment for EGFRm early stage patients

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Attending Physician, Department of Internal Medicine, National Taiwan University Cancer Center

Lung cancer is the leading cause of cancer death worldwide. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for 80–85% of cases. About one-third of them are with resectable disease and surgery is the primary treatment strategy for these patients. Cisplatin-based adjuvant chemotherapy is usually recommended in high-risk populations. Despite applying adjuvant therapy, there are still about 30–55% of patients will develop disease recurrence within the first 5 years of surgery. Therefore, it is important to explore other novel treatment strategies for resected NSCLC patients.

In Asia, the epidermal growth factor receptor (EGFR) mutations are observed in approximately 50% of lung adenocarcinoma patients. Some studies demonstrated increasing risk of metastatic recurrence in resected EGFR mutation-positive patients. In recent years, there are several studies that applied EGFR inhibitor or immune checkpoint inhibitor as one of the neoadjuvant/adjuvant approaches in early-stage NSCLC patients with EGFR mutations. The results of these trials continue to help us understand the role of novel agents and which patients are more likely to benefit.

Here we review the recent treatment development in the management of EGFRm early-stage patients and highlight the major progress in this field.

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Keeping Up-to-Date on COPD Controversies: the foundational therapy of COPD

Jadwiga Anna WEDZICHA, M.D.
Professor of Respiratory Medicine, University College London
Honorary Consultant Physician, Royal Free Hospital NHS Trust, London, UK

Inhaled corticosteroids (ICS) combined with bronchodilators can reduce the frequency of exacerbations in some patients with chronic obstructive pulmonary disease (COPD). There is evidence, however, that ICS are frequently used in patients where their benefit has not been established. Therefore, there is a need for a personalized approach to the use of ICS in COPD and to consider withdrawal of ICS in patients without a clear indication.

An Evolving Algorithm to Select and Sequence Therapies in EGFR Mutation-positive NSCLC

Takashi Ninomiya, M.D., Ph.D.
Medical doctor, Department of Thoracic Oncology and Medicine, National Hospital Organization Shikoku Cancer Center

Non-small-cell lung cancer (NSCLC) is believed as one of the main reasons that cause deaths from cancer worldwide. Three generations of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are now approved in the first-line setting for patients with EGFR mutation-positive non-small-cell lung cancer (NSCLC). Recent randomized trials have demonstrated that afatinib and osimertinib all confer significantly improved progression-free survival versus first-generation TKIs. However, TKI resistance is always a pervasive challenge. While we implement the treatment strategy for our NSCLC patients, how to consider PFS with maximizing overall survival (OS), the most important measure of treatment efficacy, and balance patients' the quality of life, is an important topic in NSCLC.

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The Rationale of Anti-IL5 Treatment: The Clinical Benefits and Real-World Evidence of Mepolizumab

William Walter Busse, M.D.
Professor, Head, Section of Allergy and Clinical Immunology, Department of Medicine, University of Wisconsin Medical School, Madison, WI
Professor of Medicine, Allergy, Pulmonary, and Critical Care Medicine

- Rationale of anti-IL-5
- Benefits and differences of Mepolizumab
- Mepolizumab real world evidence
- Mepolizumab indirect treatment comparison

Once-daily anti-inflammation maintenance treatment for optimal asthma control - an easy way for patient to have better treatment

潘奕宏 / Yi-Hung Pan, M.D.
Attending Physician of Pulmonary Medicine, Antai Tian-Sheng Memorial Hospital

- Rationale of asthma treatment for moderate to severe asthma
- Once daily Benefits and component differences of FF/VI compare to other BID ICS/LABA
- Treatable traits in moderate to severe asthma asthma

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From reactive to proactive for your COPD patients: WHY&WHO&HOW

David Halpin, FRCP, FERS
Consultant Physician and Honorary Professor in Respiratory Medicine at the Royal Devon and Exeter Hospital, Exeter, UK.

- What can we learn from cardiologists treatment strategy?
- The difference between cardiologists and pulmonologists treatment strategy
- The components contributing to COPD death
- How does drug intervention reduce all-cause mortality in COPD patients? What is the potential mechanism behind it?
- What kind of patients potentially can benefit from early intervention treatment through triple therapy?

Taiwan Experts' Clinical Experience Sharing:Once-daily single inhaler triple therapy

張博瑞 / Po-Jui Chang, M.D., Ph.D.
Attending Physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chang Gung Memorial Hospital
Assistant professor, Chang Gung Memorial Hospital, Linkou

分享臨床上使用Trelegy的真實經歷，讓與會醫師了解到如何從學術文獻的結果運用到臨床的使用。在臨床上，如何挑選適合的病患，根據什麼臨床線索，在適合的時機使用上Trelegy。

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Beyond IgE: The role of Mast cell in severe allergic asthma

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Associate Professor in Department of Thoracic Medicine, Lin-Kou Medical Center of Chang Gung Memorial Hospital
Associate Professor of Chang Gung University

Asthma is a heterogenetic disease and affects around 300 million people in worldwide. According to literatures, the proportion of severe asthma is 5-10% and severe allergic asthma is major phenotype, which is over 60% of total severe asthma group. IgE plays a crucial role in allergic inflammation and it can direct interact lots of inflammatory cells as well as structural cells, such as airway smooth muscle (ASM) and epithelial cells.

Furthermore, mast cells (MCs) are key players in the asthmatics response through secretion of a multitude of mediators with pro-inflammatory and airway-constrictive effects. Like most inflammatory cells, MCs express IgE receptors (FcεRI) and it can be activated by several IgE-independent-pathways. Cytokines play an important role in coordinating and maintaining allergic inflammation in asthmatics. MCs have the ability to secrete a broad spectrum of cytokines e.g. IL-1β, IL-2,-3,-4,-5,-6,-9,-10,-11,-12,-13, TNF-α, IFN-γ, GM-CSF, SCF, and TGF-β, as recently reviewed.

In asthma, the number of MCs increases in the airways and infiltration of MCs in a variety of anatomical sites including the epithelium, the submucosal glands, and the smooth muscle bundles occurs. MC localization within the ASM is accompanied with the hypertrophy and hyperplasia of the layer, and smooth muscle dysfunction that is mainly observed in forms of bronchial hyperresponsiveness, and variable airflow obstruction.

Omalizumab, an anti-IgE treatment, was the first humanized biologic for severe allergic asthma (SAA) in the world. In addition, the MoA of Omalizumab are 1) Neutralize free form IgE and 2) down-regulation of Fc RI on inflammatory cells (dendritic cells, eosinophils, and mast cells) as well as structure cells (epithelial cells and airway smooth muscle cells). Therefore, Omalizumab could cover up- and down – stream inflammatory process through previous mechanisms. Alongside this, SAA patients could have benefits, including reduction of asthma exacerbation, health care utilizations (ER and hospitalization) and improving QoL, asthma control as well as lung function. Furthermore, based on a meta-analysis of real world evidences (RWEs), Omalizumab not only demonstrated consistent results between RCTs and RWEs but also showed steroid-sparing effect and decreasing other anti-asthma medications usage. According to GINA guideline, therefore, Omalizumab recommends as a first choice add-on therapy in patients with severe allergic asthma.

Optimal use of inhalers in COPD: focused on peak inspiratory flow

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Dry powder inhalers (DPIs) required patients to generate sufficient inspiratory flow and turbulence in the device to disaggregate the powder into fine particles. Thus, it is advised to inhale with an inspiratory maneuver to generate adequate peak inspiratory flow rate (PIFR) to overcome the internal resistance of the devices. The PIFR is impacted by several factors, such as sex, age, height, the internal resistance of DPIs, inhalation effort, pulmonary function, and even the period following acute exacerbation due to chronic obstructive pulmonary disease (COPD). It is generally suggested that PIFR less than 30 L/min is insufficient and the suggested optimal PIFR is at least 60 L/min for Turbuhaler, Ellipta and Accuhaler, and 50 L/min for Breezhaler. However, compared to optimal PIFR, excessive PIFR also lead to more oropharyngeal deposition and less lung deposition and a PIFR more than 90 L/min was considered excessive. Different DPIs have different internal resistances, which can be categorized to medium-high, medium, medium-low and low internal resistances. The risk of improper PIFRs against different DPIs will impact the clinical outcomes of COPD patients with varying disease severity.

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Mono vs. Combo: 今晚我想來點…

何肇基 / Chao-Chi Ho, M.B., Ph.D.
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Attending physician (Pulmonologist), Department of Internal Medicine, National Taiwan University Hospital

李岡遠 / Kang-Yun Lee, M.D., Ph.D.
Professor of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University
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Lung cancer remains a leading cause of cancer-related mortality worldwide with the poor prognosis. Encouragingly, immune checkpoint blockade targeting programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) has dramatically changed the landscape for treatments in patients with non-small-cell lung cancer (NSCLC). However, only a small proportion of NSCLC patients responded to monotherapy of anti-PD-1/PDL1 agents; together, several companion diagnostic assays for PDL1 expression have been introduced for identifying patients who may benefit the immunotherapy. In addition, results from clinical trials explored combinatory therapeutic strategies with conventional therapy reported a higher efficacy with an acceptable safety profile in NSCLC treatments, as compared to the monotherapy of these agents alone.
Currently, the combinations of immunotherapy are well-established and widely used in NSCLC patients with aggressive disease and potentially improve depth of response. This presentation and discussion will focus on the latest efficacy and safety data of immune checkpoint blockade mono/combo for advanced NSCLC in both the treatment-naïve and pretreated settings. We try to find the way of best strategies on the basis of immune checkpoint blockade in NSCLC.

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Does EGFR mutation type matter?

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Consultant Professor,
Department of Oncology, Taipei Veterans General Hospital
Deaprtment of Chest medicine, Cathay General Hospital
Deaprtment of Chest medicine, Good Liver Health Management Center, Good Liver Clinic

Nearly 85% of primary lung cancers worldwide are of the non-small-cell lung cancer (NSCLC) type, and most patients present with advanced or metastatic disease at diagnosis. Epidermal growth factor receptor (EGFR) mutation-driven NSCLC occurs at frequencies of about 10–20% in white patients and 40–60% in Asian patients. EGFR gene mutations frequently occur in exons 18–21, while deletions in exon 19 and a mutation in exon 21 (specifically the L858R point mutation) occur during EGFR-tyrosine kinase inhibitor (TKI) treatment. The discovery of activating mutations in the EGFR gene and development of TKIs of EGFR have provided a tremendous impact on treatment strategy for advanced NSCLC patients. For advanced NSCLC harboring activating EGFR mutations, an EGFR-TKI is preferably prescribed as it provides a superior survival benefit over platinum-based chemotherapy. In a recent clinical trial, the 3rd generation, an irreversible EGFR-TKI showed a superior survival benefit with lower toxicity profile. The existing literature revealed that the EGFR mutation status (deletions in exon 19 and an exon 21 mutation) was an important index for predicting the effectiveness of the EGFR-TKI in the treatment of NSCLC, which is the current standard first-line treatment. Angiogenesis is an integral process for growth of solid tumors dependent on endothelial cell proliferation and migration. In addition, recent several studies have shown that combination blockade of the epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) pathways leads to synergistic antitumor effects. This talk will review and discuss the current status and future perspectives of treatment for EGFR-mutated NSCLC.

Management of advanced EGFR mutant NSCLC patients-Relaying a better treatment option

邱昭華 / Chao-Hua Chiu, M.D.

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Associate Professor, School of Medicine, National Yang-Ming University
Attending Physician, Department of Chest Medicine, Taipei Veterans General Hospital

90% of EGFR mutations comprise a deletion within exon 19 (ex19del) or a leucine to arginine substitution mutation in exon 21 (Leu858Arg). The presence of these activating EGFR mutations in advanced NSCLC is associated with sensitivity to small-molecule EGFR tyrosine kinase inhibitors (TKIs), which are the first-line standard-of-care. However, the degree of benefit might differ by type of mutation, with greater benefit from EGFR TKIs in patients who have NSCLC with the ex19del mutation. Despite durable responses, median progression-free survival with initial therapy for advanced disease is about 1 year with first-generation TKIs (gefitinib and erlotinib). Second-generation and third-generation drugs have shown median progression-free survival of 11 months (afatinib), 14.7 months (dacomitinib), and 18.9 months (osimertinib). About 30–60% of patients whose disease progresses on a first-generation or second-generation TKI acquire the EGFR Thr790Met substitution mutation, which is sensitive to osimertinib. Thus, there is a crucial need for novel EGFR TKI-based strategies to prolong remission and promote tumour control. One such strategy supported by preclinical and clinical evidence is the dual blockade of the EGFR and VEGF pathways. Ramucirumab plus erlotinib demonstrated superior progression-free survival compared with placebo plus erlotinib in patients with untreated EGFR-mutated metastatic NSCLC. Safety was consistent with the safety profiles of the individual compounds in advanced lung cancer. Moreover, the efficacy and safety outcomes for Ramucirumab+ Erlotinib in the RELAY East Asian subset were consistent with those for the overall RELAY study population. In summary, the RELAY regimen is a viable new treatment option for the initial treatment of EGFR-mutated metastatic NSCLC.

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The Novel, Extra-Fine Triple Combination for COPD

Dave Singh, M.D.
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Respiratory Research Group, University of Manchester
Medical Director, Medicines Evaluation Unit
Honorary Consultant Respiratory Physician, Manchester University Foundation Trust

介紹小呼吸道疾病在COPD的盛行率及疾病成因，並說明超細微粒藥物降低類固醇劑量進而可得到哪些優勢。對於COPD患者而言，若症狀明顯、惡化頻繁，其藥物治療將慢慢升階至三合一療法。過去患者使用兩種以上吸入器進行三合一療法，現在市面上已經有複方三合一吸入劑，將可提高患者順從性，此次演講內容也將討論三合一藥物的臨床研究證據，包含效果、安全性等資料。

The Beneficial Effects of Triple Therapy in COPD in Taiwan

彭忠衍 / Chung-Kan Peng, M.D., Ph.D.
Director of TingJhou Campus, Tri-Service General Hospital
Director of Division of Pulmonary Medicine and Critical Care Medicine, Department of Internal Medicine, Tri- Service General Hospital
Director of Sleep Medicine Center, Tri-Service General Hospital
Associate professor, The school of Medicine, National Defense Medical Center

此次演講將討論台灣COPD患者治療現況，疾病改善情形及衍生的醫療費用。隨著新的三合一吸入劑上市，除了第三期隨機對照試驗外，國外還有那些Real World Study可以參考，對於台灣的患者有哪些適合這類藥物的治療並可以獲得更好的改善，將會在這個章節一併介紹。

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Time	Topic	Speaker	Moderator
12:00 - 12:05	Opening	王鶴健 醫師	
12:05 - 12:30	Disease Burden Associated with Patterns of SABA in Asthma in Taiwan	傅彬貴 醫師 台中榮總	王鶴健 醫師 臺大醫院
12:30 - 12:55	Anti-inflammatory reliever strategy in the whole asthma spectrum to overcome SABA burden in Taiwan	鄭世隆 醫師 亞東醫院	林慶雄 醫師 彰化基督教醫院
12:55 - 13:15	Panel discussion: How we can change Status quo?	王鶴健 醫師、林慶雄 醫師 鄭世隆 醫師、傅彬貴 醫師	
13:15 - 13:20	Closing	林慶雄 醫師 彰化基督教醫院	

This symposium will discuss about the current burden on asthma patient caused by short acting beta2 agonist (SABA) reliever in Taiwan. After GINA suggesting ICS/formoterol as the preferred reliever, how we use anti-inflammatory reliever strategy to help asthma patient to overcome the over reliance on SABA.

傅彬貴 / Pin-Kuei Fu, M.D., Ph.D.
Chief, Smoking Cessation Treatment Management Center and Respiratory Intensive Care Unit, Taichung Veterans General Hospital, Taichung, Taiwan
Attending Physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

鄭世隆 / Shih-Lung Cheng, M.D., Ph.D.
Chief, The Center of Evidence-Based Medicine, Far Eastern Memorial Hospital
Chief, The Center of Clinical Trial, Far Eastern Memorial Hospital
Professor, Yuen Ze University and Chest Division Far Eastern Memorial Hospital

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Resistance Profiles of EGFR Tyrosine Kinase Inhibitors by Targeted Next-generation Sequencing in Advanced Non-small Cell Lung Cancer

林彥廷 / Yen-Ting Lin, M.D.

Visiting Physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan
Adjunct instructor, National Taiwan University College of Medicine, Taipei, Taiwan
Adjunct Visiting Physician, Department of Medicine, National Taiwan University Cancer Center, Taipei, Taiwan

In Taiwan, around half of the lung adenocarcinomas have activating epidermal growth factor receptor (EGFR) mutations. Targeting activating EGFR mutations with tyrosine kinase inhibitors (TKIs) shows promising responses and prolongs patients' lives. After first-line gefitinib, erlotinib or afatinib treatment, the median overall survival of advanced non-small cell lung cancer (NSCLC) patients with activating EGFR mutations [EGFR(+)] has been more than 3 years. However, most of the patients experienced disease progression eventually. Secondary EGFR T790M mutation can be found in around half of the patients treated with first or second-generation EGFR TKIs. Alternative pathway activation, such as MET amplification, HER2 amplification, PIK3CA mutation and BRAF mutation are reported as well. On the other hand, loss-of-function mutations of tumor suppressor genes are also frequently seen in lung cancer, although their clinical significance is not well-known.

Rebiopsy of the tumors after disease progression is crucial, because several resistance mechanisms can be targeted. For instance, osimertinib is the drug of choice for secondary EGFR T790M mutation, and capmatinib (INC280) may overcome MET amplification secondary to EGFR TKI(s). However, not every patient is feasible for a tissue rebiopsy. Liquid biopsy to detect cell-free DNA for tumor genetic alterations study is a surrogate for tissue rebiospy. It is non-invasive and there are increasing evidences supporting its role for cancer management. In this study, we aimed to explore EGFR TKI resistance mechanisms by targeted next-generation sequencing for both tissue and liquid biopsy, from patients with advanced EGFR(+) NSCLC treated with first-line EGFR TKIs.

Uncommon driver mutations in non-small cell lung cancer

李日翔 / Jih-Hsiang Lee, M.D.

Chief, Center of Oncology Medicine, National Taiwan University Hospital (NTUH), Hsin-Chu Branch
Attending physician, Department of Oncology, National Taiwan University Hospital (NTUH), Taiwan

There had been a great progress in the treatment of advanced oncogenic driven lung adenocarcinoma patients, in addition to the well-known EGFR mutation and ALK fusion. It is a challenge to identify advanced lung adenocarcinoma patients whose tumors carry uncommon driver mutations. Physicians apply direct oncogene sequencing, Immunohistochemistry (IHC) study, fluorescence in situ hybridization (FISH), and the next generation sequencing (NGS) techniques to identify cancers with driven mutation. However, no single platform is good enough to identify all potential driver mutations simultaneously, and physicians have to be familiar of the advantage and disadvantage of each sequencing platform.

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Clinical evidences of TS-1 for advanced and metastatic NSCLC

魏裕峰 / Yu-Feng Wei, M.D.
Director, Division of Pulmonary & Respiratory Medicine, E-Da Hospital Chair, Committee of Lung Cancer, E-Da Hospital

Lung cancer is the leading cause of cancer death worldwide. Chemotherapy remains the standard of first-line treatment for patients with advanced lung cancer without driver mutation and low PD-L1 expression. For advanced non-small cell lung cancer (NSCLC) patients who have failed after first-line chemotherapy and not eligible for immunotherapy, docetaxel with or without angiogenesis inhibition or pemetrexed (in nonsquamous NSCLC) are standard therapies.

TS-1 is an oral cytotoxic drug that comprises tegafur, gimeracil, and oteracil potassium. An East Asian phase III trial comparing TS-1 with docetaxel in patients with PS 0–2 as their second- or third-line treatment was conducted. Non-inferiority of OS was demonstrated [12.8 months versus 12.5 months, HR 0.95 (95%CI 0.83–1.07), p = 0.38]. ORR and PFS were similar (ORR: 8.3% versus 9.9%, mPFS: 2.9 months in both arms). Regarding toxicity, neutropenia ≥ grade 3 and febrile neutropenia were higher in docetaxel arm. TS-1 is equally as efficacious as docetaxel but differs in toxicity and QoL profile.

TS-1 offers a treatment option for previously treated advanced NSCLC patients and strongly recommended in those with a performance status (PS) of 0–2 as their second- or further-line treatment by The Japanese Lung Cancer Society.

In this talk, I will review the development of fluoropyrimidine, clinical trials, and case sharing of S-1, explaining why S-1's fascinating combination is effective in treatment of NSCLC and S-1 may be one of the new oral alternative treatment option in advanced NSCLC patients after platinum treatment failure.

Tips to provide lung cancer patients optimal breakthrough pain control

吳志成 / Chih-Cheng Wu, M.D.
Head of Pain Management , Taichung Veterans General Hospital, Taichung, Taiwan
Attending physician, Department of Anesthesiology, Taichung Veterans General Hospital, Taichung, Taiwan

Breakthrough pain (BTP) has been defined as 'a transitory exacerbation of pain experienced by the patient who has relatively stable and adequately controlled baseline pain' [1]. Breakthrough pain can be divided into spontaneous pain at rest and incident pain (either volitional or non-volitional) [2,3]. Breakthrough pain was present in 75% of cases of cancer-induced bone pain [4]. Patients with breakthrough pain had greater interference on aspects of life (mood, relationships, sleep, activity, walking ability, work, enjoyment of life) than those with no breakthrough pain ($p<0.01$) [5,6]. Almost half of breakthrough pain episodes were rapid in onset (<5 min) and short in duration (<15 min) [5,6]. Forty-four per cent of patients with breakthrough pain had pain that was unpredictable [5,6]. The short spiking characteristics of BTP episodes make the successful treatment of cancer-induced bone pain particularly challenging, which is supported by studies revealing that up to 45% of patients with cancer-induced bone pain report poor pain control [6-8].

Currently, immediate-release oral opioids are the treatment of choice for BTcP. This approach might not always offer optimal speed for onset of action and duration to match the rapid nature of an episode of BTcP. Novel transmucosal fentanyl formulations might be more appropriate for some types of BTcP, but limited access to such drugs hinders their use. In addition, the recognition of BTcP and its proper assessment, which are crucial steps toward appropriate treatment selection, remain challenging for many health care professionals. Careful opioid application is especially important in lung cancer patients. That is because the risk of respiratory depression may incredibly increase when healthcare professionals directly increase the dose of baseline opioid medication for chronic pain in order to avoid breakthrough pain. Therefore, how to find the most appropriate maintenance dose and PRN medication for every patient is crucial in pain control.

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Year-end review of IO in locally advanced NSCLC and SCLC treatment and real-world experiences

陳鴻仁 / Hung-Jen Chen, M.D.
Attending physician and Associate professor, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, China Medical University Hospital

Treatment of locally advanced NSCLC is sticky since most of them cannot be treated by resection and CCRT is the golden standard treatment. However, the PFS of these patients is not satisfied and around 90% patients may recurred or progress after CCRT treatment. In 2017, the phase 3 trial PACIFIC indicated Durvalumab consolidation therapy can prolong patients PFS. After long-term follow-up, the latest results published in ESMO 2020 indicated the long-term benefits of Durvalumab with around half OS and over 35% PFS rate in 4-year.

The development of SCLC treatment is stagnant for many years and the prognosis is worst in all lung cancer types. Anti-PD-L1 and chemotherapy combination treatment is the only regimen indicated the survival benefits in recent decades. IMPower133 is the first study to demonstrate the IO effects on SCLC 1L treatment and CASPIAN study also shows the benefits of Druvalumab in combined with no matter cisplatin or carboplatin regimen. The long-term analysis of these 2 studies are updated in 2020 and will also presented in this presentation.

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Evolution of ALK TKI treatment: Past, present, and future

何肇基 / Chao-Chi Ho, M.B., Ph.D.
Clinical professor, Department of Internal Medicine, College of Medicine, National Taiwan University
Attending physician (Pulmonologist), Department of Internal Medicine, National Taiwan University Hospital

Targeting genomic alterations, such as epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) gene rearrangements, have radically changed the treatment of patients with non-small cell lung cancer (NSCLC). In the case of ALK-rearranged gene, subsequent rapid development of effective genotype-directed therapies with ALK tyrosine kinase inhibitors (TKIs) triggered major advances in the personalized molecularly based approach of NSCLC.

Crizotinib was the first-in-class ALK TKI with proven superiority over standard platinum-based chemotherapy for the 1st-line therapy of ALK-rearranged NSCLC patients. However, unique side effect profile with crizotinib and its diminished efficacy to the central nervous system (CNS) relapse led to the development of several novel ALK inhibitors, more potent and with different selectivity compared to crizotinib. To date, four ALK TKIs, crizotinib, ceritinib, alectinib and brigatinib have received approval from the Food and Drug Administration (FDA) and/or the European Medicines Agency (EMA) and even more agents are currently under investigation for the treatment of ALK-rearranged NSCLC. Despite the advances in new targeted therapies in ALK positive population, most patients progress under ALK inhibitors within first 2 years; being the brain the most frequent site of relapse.

However, the optimal frontline approach and the exact sequence of ALK inhibitors are still under consideration.

The updated ALEX study results revealed a 5-year survival rate of 62.5% in the Alecensa treatment group, versus 45.5% with crizotinib. Additionally, the study found that the OS benefit of Alecensa was seen in patients with CNS metastases at baseline (42% reduction in the risk of death versus crizotinib) as well as in those without CNS metastases at baseline (24% reduction in the risk of death versus crizotinib). The safety profile of Alecensa was consistent with previous data, with no new safety signals identified despite longer treatment duration.

The updated data from the ALEX trial continue to demonstrate the efficacy of Alectinib, and this is the first global randomized study of a next-generation ALK-inhibitor to demonstrate a clinically meaningful improvement in overall survival versus crizotinib in treatment-naïve ALK-positive NSCLC. The overall survival benefit was confirmed across all sub-groups, including those with central nervous system metastases at baseline.

Optimal ALK+ NSCLC therapeutic strategies from a new perspective

蔡俊明 / Chun-Ming Tsai, M.D.
Consultant Professor,
Department of Oncology, Taipei Veterans General Hospital
Deaprtment of Chest medicine, Cathay General Hospital
Deaprtment of Chest medicine, Good Liver Health Management Center, Good Liver Clinic

NSCLC represents approximately 85% of all lung cancer cases and, of these, about 5% of patients are ALK-positive, representing a significant patient population. Although overall cancer death rates are declining, 5-year survival rates for NSCLC are still shockingly low — estimated to be just 6.1% for those diagnosed between 2009 and 2015. With previous standards of care, the majority of patients with ALK-positive NSCLC would see their disease progress within a year. The disease also often affects those who least expect it;

The updated ALEX study results revealed a 5-year survival rate of 62.5% in the Alecensa treatment group, versus 45.5% with crizotinib. Additionally, the study found that the OS benefit of Alecensa was seen in patients with CNS metastases at baseline (42% reduction in the risk of death versus crizotinib) as well as in those without CNS metastases at baseline (24% reduction in the risk of death versus crizotinib). The safety profile of Alecensa was consistent with previous data, with no new safety signals identified. The OS data have not yet reached maturity.

The updated data from the ALEX trial continue to demonstrate the efficacy of Alectinib, and this is the first global randomized study of a next-generation ALK-inhibitor to demonstrate a clinically meaningful improvement in overall survival versus crizotinib in treatment-naïve ALK-positive NSCLC. The overall survival benefit was confirmed across all sub-groups, including those with central nervous system metastases at baseline.

Multiple different resistance mechanisms to ALK inhibitors were identified in post-progression tumor specimens including either “on-target” genetic alterations or “off-target” mechanisms, which may involve activation of parallel/downstream pathways or lineage trans-differentiation. Lorlatinib demonstrated clinical activity in resistant patients previously treated with two or more ALK inhibitors including second-generation inhibitors.

The Prof. Yoda study showed that compared to first or second generation drugs, the third generation drug Lorlatinib has a lower IC50 for most of resistant mutations in cell lines, and also found that increase the risk of compound mutations by 35% after treatment with Lorlatinib, and the required IC50 is also higher or even ineffective.

Therefore, when thinking about the treatment sequence, it is necessary to consider that the first line ALK-TKI should not make the gene mutations too complicated, such as compound mutations.

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Efficacy and safety of Capmatinib in MET Exon 14–Mutated or MET-Amplified Non–Small-Cell Lung Cancer

廖唯昱 / Wei-Yu Liao, M.D., Ph.D.
Attending Physician, Department of Internal Medicine, National Taiwan University Hospital
Clinical Associate Professor, Department of Internal Medicine, National Taiwan University College of Medicine

MET exon 14 skipping mutations occur in 3 to 4% of NSCLC population. Capmatinib is a selective inhibitor of the MET receptor, and its antitumor activity in patients with advanced NSCLC has been shown to be effective in a phase 2 Geometry mono-1 study (NCT02414139) in patients with a MET exon 14 skipping mutation, particularly in the treat naive population. Recent updated data showed that the objective response was observed in 41% (95% CI, 29 to 53) of 69 patients who had received one or two lines previous therapy, and in 68% (95% CI, 48 to 84) of 28 treatment naive patients; the median duration of response was 9.7 months (95% CI, 5.6 to 13.0) and 12.6 months (95% CI, 5.6 to could not be estimated), respectively. The efficacy in MET-amplified advanced NSCLC was higher in tumors with a high gene copy number than in those with a low gene copy number. Low-grade peripheral edema and nausea were the main adverse effects.

Other recent updates include an analysis assessing the clinical outcomes of patients with MET exon 14 altered NSCLC treated with first-line capmatinib in GEOMETRY mono-1 vs those of a cohort of real-world pts. Furthermore, a post hoc analysis evaluated the efficacy and safety of capmatinib in pts with METex14-mutated NSCLC from cohort 4 and cohort 6 of the GEOMETRY mono-1 study who received IO prior to study enrollment.

Optimizing Ceritinib treatment in Asian ALK-rearranged NSCLC populations

黃俊耀 / Chun-Yao Huang, M.D., Ph.D.
Chief Clinical Try Center of Reserch Department, Buddhist Tzu Chi General Hospital, Taipei Branch
Attending Physician of Chest Department, Buddhist Tzu Chi General Hospital, Taipei Branch

ALK rearrangement is one of the well-known driver mutations of NSCLC, with a prevalence rate around 10% in EGFR-wt lung adenocarcinoma in Taiwan. Ceritinib is a potent and selective second-generation ALK inhibitor, and has been evaluated broadly in ASCEND trials. In ASCEND-4, ceritinib demonstrated an 8.5-month improvement in median PFS comparing with chemotherapy in treatment naïve ALK+ NSCLC patients. A significantly higher overall response rate and durable clinical benefit were observed, either in systemic disease or intracranial lesions. The adverse events of ceritinib presented mainly in the digestive system, as all grades diarrhea was noted in 84.7% of patients. Most common grade 3/4 AEs were abnormal liver functions, e.g. ALT, AST, and GGT increase. ASCEND-8 is a randomized phase I trial, which was designed to evaluate the food effect to pharmacokinetics and adverse events. Patients in the 450 mg fed arm demonstrated comparable PK data to those in the 750 fasted arm, while the PFS and GI AEs were significantly improved. The subgroup analysis of Asian population in ASCEND-8 trial is updated in ESMO this year, which revealed remarkable improvements in PFS (median PFS: NE; 36-month PFS: 58.9%) and AE profile in 450 mg fed group when compared with 750 mg fasted group. In summary, ceritinib 450 mg with low-fat diet provides consistent efficacy results in ASCEND-8 study, while the frequency of dose reduction/ interruptions and GI AEs are diminished.

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Clinical Evidence and Case Sharing for Peramivir, the Single-Dose Intravenous Neuraminidase Inhibitor

柯信國 / Bruce Hsin-Kuo Ko, M.D., Ph.D.
Assistant Professor, Medical School, National Yang-Ming University, Taipei, Taiwan
Chief of respiratory intensive care unit, Taipei Veterans General Hospital
Attending physician, Taipei Veterans General Hospital

Neuraminidase inhibitors (NAIs), which can suppress the spread and proliferation of the influenza virus, have been the gold standard therapy of influenza for years. The appropriate usage of NAIs is critical to avoid the deterioration of influenza to serious and even lethal events. Although NAIs such as oseltamivir, zanamivir and peramivir are clinically available, the optimal method of delivery should be determined after considering an individual patient's age, weight, physical status and compliance.

Peramivir is a novel neuraminidase inhibitor with a single-dose regimen for uncomplicated influenza. A three-armed, multicenter, randomized, double-blind, multinational Asian Phase 3 study was conducted to compare the efficacy and safety between a single-dose treatment of intravenous peramivir (either 300 mg or 600 mg) and oral oseltamivir phosphate twice a day for 5 days during the 2008-2009 influenza season. A total of 1,099 uncomplicated patients infected with seasonal influenza virus were enrolled at 146 centers (Japan: 100; Korea: 25; Taiwan: 21). Both the 300 mg and 600 mg of single-dose peramivir demonstrated non-inferiority for the primary endpoint, time to alleviation of symptoms (TTAS), compared to oseltamivir. The medians of the TTAS for the peramivir 300 mg, peramivir 600 mg and oseltamivir were 78.0 hrs, 81.0 hrs and 81.8 hrs, respectively. Occurrence of adverse drug reaction was significantly lower for 300 mg of peramivir compared to oseltamivir.

In an open-label study, 191 patients with influenza were assigned to four groups of each treated with oseltamivir, zanamivir, laninamivir and peramivir, and the time to alleviate fever and other symptoms and time to eliminate the virus were compared. Alleviation of fever occurred significantly sooner with peramivir than with either zanamivir ($p = 0.0002$) or oseltamivir ($p = 0.0059$). The average (± SD) time to alleviate fever in the zanamivir, oseltamivir, laninamivir and peramivir groups after NAI administration was 2.10 (± 1.12), 1.86 (± 1.02), 1.72 (± 1.03) and 1.32 (± 0.79) days, respectively. Other symptoms were also alleviated significantly sooner with peramivir than with the other three NAIs. Peramivir tended to eliminate the virus sooner, but the difference did not reach statistical significance. The mean (± SD) time required for peramivir, laninamivir, zanamivir and oseltamivir to eliminate the influenza virus was 3.71 (± 1.38), 4.09 (± 1.23), 4.33 (± 1.38) and 4.75 (± 1.47) days, respectively.

The clinical experience of peramivir in influenza patients of Taiwan will also be presented.

Baloxavir, the Novel Cap-Dependent Endonuclease Inhibitor with Single-Dose Oral Regimen

唐士恩 / Shih-En Tang, M.D., Ph.D.
Assistant professor, National Defense Medical Center School of Medicine
Attending physician, Division of Pulmonary and Critical Care, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Baloxavir marboxil, the novel cap-dependent endonuclease inhibitor which suppresses the replication of influenza viruses by a mechanism different from neuraminidase inhibitors (NAIs), has been launched in Japan and the USA in 2018 and in Taiwan in Nov., 2019. The randomized, double-blind, multicenter, parallel-group, placebo- and active-controlled study on otherwise healthy patients diagnosed with influenza (CAPSTONE-1) showed that the median time to alleviation of symptoms was shorter in the baloxavir group than in the placebo group (53.7 hours vs. 80.2 hours, P<0.001). The median duration of infectious virus detection was also shorter in the baloxavir group (24.0 hours) than the oseltamivir group (72.0 hours, P<0.001) and the placebo group (96.0 hours, P<0.001). Baloxavir also demonstrated a statistically significant decrease in the incidence of treatment-related adverse events compared to oseltamivir (P=0.009).

The other double-blind, double-dummy, phase 3, randomized, controlled study assessing a single oral dose of baloxavir compared with placebo and oseltamivir in patients 12 years or older with influenza and at high risk of influenza complications (CAPSTONE-2) also demonstrated positive results. In this study, Baloxavir significantly reduced the median time to improvement of influenza symptoms (TTIIS, the primary endpoint) compared with placebo (73.2 hours vs. 102.3 hours; P<0.001). Baloxavir also significantly reduced the median time to sustained cessation of infectious virus detection versus placebo (48.0 vs. 96.0 hours, P<0.001) and oseltamivir (48.0 vs. 96.0 hours, P<0.001). Besides, baloxavir significantly reduced the incidence of influenza-related complications versus placebo (2.8% vs. 10.4%; P <0.05). In terms of safety, baloxavir was well-tolerated and no new safety signals were identified. Baloxavir is the first and only antiviral medicine indicated specifically for patients at high risk of developing influenza-related complications.

BLOCKSTONE study, a phase III, multicenter, double-blind, placebo-controlled study in household contacts (participants) of index patients with confirmed influenza, was conducted in Japan during the 2018/19 season and the results have been published on July 8, 2020. This study showed that the proportion of participants who developed clinical influenza was 1.9% (7/374) in participants treated with baloxavir versus 13.6% (51/375) in the placebo group (P<0.0001), demonstrating an 86% reduction in risk. The prophylactic effects of baloxavir were also observed in people at high risk of influenza related complications, as well as in children under 12 years old, irrespective of vaccination status. The incidence of adverse events was similar between the baloxavir group (22.2%) and the placebo group (20.5%), and no serious adverse events were reported for baloxavir.

The regimen for baloxavir marboxil is a single oral dose with the usual dosage of 40 mg (two 20 mg tablets) for adults and children over 12 years old. However, patients with a body weight of 80 kg or more should receive 80 mg (four 20 mg tablets) once.

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Time	Topic	Speaker	Moderator
12:00-12:05	Opening	**林孟志** 醫師 高雄長庚	
12:05- 12:30	Severe Asthma and the Guiding Role of Eosinophil	**郭炳宏** 醫師 臺大醫院	**林孟志** 醫師 高雄長庚
12:30- 12:55	Beyond the Clinical Trial: Managing Severe Eosinophilic Asthma in Practice	**張博瑞** 醫師 林口長庚	**李岡遠** 醫師 雙和醫院
12:55- 13:15	Panel Discussion: Where Are We Now For PRECISION Approach?	**林孟志** 醫師、**郭炳宏** 醫師 **李岡遠** 醫師、**張博瑞** 醫師	
13:15- 13:20	Closing	**李岡遠** 醫師 雙和醫院	

Nowadays, there are more biologic treatment options for severe asthma patients.
Benralizumab is an anti-IL-5 receptor monoclonal antibody that significantly lowers exacerbation and improves quality of life.
This symposium will discuss the key role of eosinophils in severe asthma as biomarker, and explore how recent evidence can help guide the decision-making process in clinical practice.

郭炳宏 / Ping-Hung Kuo, M.D.
Attending physician, Department of Chest Medicine, National Taiwan University Hospital Bei-Hu Branch

張博瑞 / Po-Jui Chang, M.D., Ph.D.
Attending Physician, Department of Thoracic Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan
Assistant professor, Chang Gung Memorial Hospital, Linkou

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Current treatment landscape and future trends in ALK+ NSCLC

黃俊耀 / Chun-Yao Huang, M.D., Ph.D.
Attending Physician, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan

Over the last decade, care options for ALK-rearranged NSCLC patients have improved considerably. Several new generations of ALK inhibitors have proved their superiority as first-line therapies since the approval of the first ALK inhibitor, crizotinib. Factors such as the ability to resolve mutations associated with resistance and improved penetration of the CNS have played a crucial role in enhancing efficacy1.
For patients with advanced ALK+ NSCLC, relapses are unavoidable, exploring the optimal sequencing strategies of ALK inhibitors is very crucial. Around 70 % of patients will develop metastases in the brain during treatment with crizotinib2,3. Second-generation ALK inhibitors (Ceritinib, Alectinib and Brigatinib) and third-generation ALK inhibitors (Lorlatinib) have demonstrated considerable post-crizotinib efficacy, as well as first-line therapy in treatment-naïve patients based on favorable efficacy1.
Brigatinib is a new treatment option after crizotinib progression in ALK+NSCLC. In the 2-year follow-up of ALTA trial, brigatinib demonstrated significant clinical efficacy post crizotinib, with an unprecedented median IRC-assessed PFS of 16.7 months and IRC-assessed iPFS of 18.4 months4. For the treatment-naïve patients, brigatinib represents consistent superiority efficacy in IRC-assessed PFS versus crizotinib (HR=0.49, 24.0 v 11.0 months)5, making it a promising first-line treatment of ALK-positive NSCLC.
Eventually, the best sequence of ALK inhibitors still needs to be determined, with a variety of ALK inhibitors in sequencing strategies, allowing extended survival or increased quality of life for ALK+ NSCLC patients.

Reference:
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2. Cancer Metastasis Rev.2015;34(4):797-805.
3. J Med Econ.2015;18(4):312-322.
4. J Thorac Oncol. 2020 Mar;15(3):404-415.
5. J Clin Oncol. 2020 Aug 11;JCO2000505.

Satellite Symposium

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(SARS-CoV-2) 感染症

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4.適應症：
重度新型冠狀病毒 (SARS-CoV-2) 感染症。**說明: 重度之定義為在未使用吸氧治療下之血氧飽和度 ≤ 94%、須使用吸氧治療、須使用機械呼吸器、或已裝上葉克膜 (ECMO) 之病人。**

5.適應症相關注意事項：
5.1由於目前使用 VEKLURY® 治療 SARS-CoV-2 感染之療效與安全性方面的資訊極為有限，因此，應審慎評估使用的適當性，並將最新的資訊納入考慮。5.2鑒於本藥大部份都是在臨床試驗中使用，VEKLURY® 原則上應使用於未使用吸氧治療下(room air) 血氧飽和度 ≤94%、須吸氧治療、已裝上葉克膜 (ECMO)、或已裝上侵入性機械呼吸器的 SARS-CoV-2 感染重度病人。

1.警語：
1.1由於可能會發生急性腎功能損害，因此，在投予 remdesivir 之前與之後都應每天進行腎功能檢查，嚴密監視病人的狀況。1.2由於可能會發生肝功能損害，因此，在投予 remdesivir 之前與之後都應每天進行肝功能檢查，嚴密監視病人的狀況。1.3對體重介於 3.5 公斤至 < 40公斤之間的兒童，僅能使用韋如意凍晶乾燥注射劑 100 毫克/瓶。

2.禁忌：
2.1曾對 VEKLURY®之任何組成產生過敏反應的病人。

3.1/21組成，包裝與儲存方式：

商品名	韋如意®注射用溶液劑100毫克/20毫升	韋如意®凍晶乾燥注射劑100毫克/瓶
活性成分	Remdesivir	
含量規格(每小瓶)	100毫克/20毫升	100毫克
儲存	儲存於2–8℃	儲存於30℃以下

6.用法用量：
(1)對成人與體重 ≥ 40 公斤的兒童，建議劑量為第1天 IV 注射一劑 remdesivir 200 毫克，然後從第 2 天起，每天一次 IV 注射 remdesivir 100 毫克。(2)對體重介於 3.5 公斤至< 40 公斤之間的兒童，建議依體重調整劑量，第 1 天 IV 注射一劑 remdesivir 5 毫克/公斤，然後從第 2 天起，每天一次 IV 注射 remdesivir 2.5 毫克/公斤。(3)治療開始時已裝上葉克膜或機械呼吸器之病人，總治療時間最長為 10天。(4)治療開始時未裝上葉克膜或機械呼吸器之病人為 5 天，病情未獲改善時可延長，總治療時間最長為 10 天。

7.用法用量相關注意事項
7.1將本品加入生理食鹽水中，然後以 30 至 120 分鐘的時間靜脈輸注進入體內。

8.重要注意事項(不良反應)：
8.1由於 VEKLURY® 的臨床經驗極為有限，且可能會發生尚未通報過的不良反應(包括嚴重不良事件)，因此，在使用 VEKLURY® 治療期間，應透過適當的臨床與實驗室檢驗嚴密監視病人的狀況。應每天追蹤實驗室檢驗數值。如果發現不良反應，則只有在預期治療效益超越可能之治療相關風險的情況下才可繼續治療。8.2由於可能會發生急性腎功能損害，因此，在投予 remdesivir 之前與之後都應進行腎功能方面的檢查，嚴密監視病人的狀況。8.3由於可能會發生肝功能損害，因此，在投予 remdesivir 之前與之後都應進行肝功能等方面的檢查，嚴密監視病人的狀況。8.4由於可能會發生輸注反應(低血壓、噁心、嘔吐、冒汗、顫抖等)，因此應嚴密監視病人的狀況，如果發現任何異常現象，應立即停止投予本藥，並採取適當的措施。

9.特殊族群的相關注意事項：
9.2腎功能不全的病人：由於賦形劑 sulfobutylether-β-cyclodextrin sodium 會蓄積於腎小管，因此，腎功能不全的問題可能會更加惡化。9.2.1重度腎功能不全的病人不建議使用：只有在潛在效益超越潛在風險的情況下才可考慮投予 remdesivir 。9.3 肝功能不全的病人。9.3.1 ALT ≥ 5 倍正常範圍上限的病人：最好不要使用。9.3.2 ALT < 5 倍正常範圍上限的病人：只有在潛在效益超越潛在風險的情況下才可投予 remdesivir。9.5孕婦：只有在潛在效益超越潛在風險的情況下，才可對孕婦或可能懷孕的婦女投予 remdesivir。9.6餵哺母乳的婦女：應權衡治療的效益與餵哺母乳的效益，然後決定繼續或停止哺乳。9.7兒童之使用：只有在預期治療效益超越可能之風險的情況下才可使用 remdesivir 。目前尚未進行過任何針對兒童的臨床研究。9.8老年人之使用：應謹慎投予 remdesivir，並監視病人的狀況。

16.7.藥物-藥物交互作用：
16.7.1體外研究：體外試驗顯示，remdesivir 是 CYP2C8 、 CYP2D6 及 CYP3A4 的作用受質，也是 OATP1B1 和 P-gp 的作用受質。
體外試驗顯示，remdesivir 是 CYP3A4 、 OATP1B1 、 OATP1B3 、 BSEP 、 MRP4 及 NTCP 的抑制劑。16.7.2臨床藥物-藥物交互作用：目前尚未於人體進行過 remdesivir 的藥物-藥物交互作用研究。

本簡易仿單版本依據完整版仿單之章節順序編排，詳請參閱完整版仿單資訊

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[適應症] 用於原發性肺動脈高血壓(WHO functional class II-III)之成人患者。本品應與內皮素受體拮抗劑(endothelin receptor antagonists, ERA) 及/或第五型磷酸二酯酶 (phosphodiesterase type 5, PDE 5)抑制劑合併使用；或單獨使用於病患無法適用內皮素受體拮抗劑且無法適用第五型磷酸二酯酶抑制劑時。
[用法用量] 每位病患都應進行劑量調升至個人的最高耐受劑量，其劑量範圍從200 mcg、每日兩次，到1600 mcg、每日兩次(個人化維持劑量)。建議起始劑量為200 mcg、每日兩次，兩次間隔約12小時。之後以200 mcg、每日兩次的幅度調升劑量，通常每週調升一次。在治療開始時和每次進行劑量調升步驟時，建議在晚上服用第一劑。應於早上與晚上服用本膜衣錠。為提高耐受性，建議隨餐服用Uptravi，並在每次劑量調升階段開始時，在晚上服用第一次調升的劑量。藥錠不得剝半、壓碎或咀嚼，應以白開水吞服。
[禁忌症]．對主成份或仿單第4.1節中所列的任何賦形劑過敏。．嚴重冠狀動脈心臟疾病或不穩定型心絞痛。．最近6個月內曾發生心肌梗塞。．未嚴密監控的失償性心臟衰竭。．嚴重心律不整。．過去3個月內曾發生腦血管事件(如短暫性腦缺血發作、中風)。．合併與肺高壓無關且具臨床意義的心肌功能異常之先天性或後天性瓣膜缺損。．併用CYP2C8強效抑制劑(如gemfibrozil)。
[警語和注意事項]．Uptravi具有血管擴張性質可能造成血壓降低。．使用Uptravi時觀察到甲狀腺機能亢進症。．當血管擴張劑(主要為前列腺環素)用於患有肺靜脈阻塞性疾病的病患時，曾有肺水腫的通報案例。．目前有關超過75歲病患使用Uptravi的臨床經驗有限，故此族群應慎用。．目前並無重度肝功能不全(Child-Pugh C 級)病患使用selexipag的臨床經驗，因此，Uptravi不得用於此類病患。．對於重度腎功能不全(eGFR<30 mL/min/1.73 m²)的病患，應謹慎調整劑量。．具有生育能力的女性在服用selexipag時應採取有效的避孕措施。
[不良反應]最常被通報的不良反應為頭痛、腹瀉、噁心嘔吐、顎骨疼痛、肌肉痛、四肢疼痛、關節痛和熱潮紅。這些反應在劑量調升期間較常發生。這些反應大部分屬於輕度至中度程度。

使用前請詳閱仿單警語及注意事項

Reference: UPT-TWo-v1901

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Xolair® omalizumab

喜瑞樂

減少嚴重過敏型氣喘患者急性惡化的生物製劑[1]

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- 減少 **嚴重氣喘惡化**[1]
- 改善 **氣喘症狀**[3]
- 降低 **氣喘相關急診**[1]
- 減少 **口服類固醇使用**[4]
- 降低 **因氣喘住院**[5]
- 增加 **增加氣喘相關之生活品質指數**[1]

REF: 1. Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. Allergy 2005;60:309-316. Severe asthma exacerbations in this study were defined as when a patient's lung function was reduced to <60% of personal best, and systemic corticosteroids were required 1. Primary endpoint in this study was the reduction in exacerbations. 2. Global Initiative for Asthma (GINA) 2019 3. Korn S, Thielen A, Seyfried S, et al. Omalizumab in patients with severe persistent allergic asthma in a real-life setting in Germany. Respiratory Medicine 2009;103:1725-31.4.Barnes N et al. Effectiveness of omalizumab in severe allergic asthma: A retrospective UK real-world study. Journal of Asthma 2012;50:529-36.5. Bousquet J, Siergiejko Z, Swiebocka E, et al. Persistency of response to omalizumab therapy in severe allergic (IgE-mediated) asthma. Allergy 2011;66:671-8.

商品名：喜瑞樂 凍晶注射劑 150 毫克 (Xolair 150 mg powder and solvent for solution for injection)。 衛署菌疫輸字第 000835 號 北市衛藥廣字第 108110314 號
成分：Omalizumab 為由哺乳動物細胞所製造的類人化單株抗體。賦形劑：凍晶乾粉小瓶：sucrose，L-histidine，L-histidine hyrochloride monohydrate，polysorbate 20。**適應症：**過敏性氣喘 喜瑞樂為附加療法用於改善已接受高劑量吸入性類固醇製劑及長效乙二型作用劑 (ß2-agonist) 治療下仍有頻繁的日間症狀或夜間覺醒且具有多次重度氣喘惡化記錄的重度持續過敏性氣喘成人、青少年及兒童 (6 歲及以上) 的氣喘控制。這些氣喘患者必須有經由皮膚測試或體外試驗顯示長期對空氣中過敏原呈陽性且肺功能降低 (FEV1 < 80%)。喜瑞樂僅適用於證實為IgE 媒介型的氣喘病人。慢性自發性蕁麻疹 (Chronic Spontaneous Urticaria, CSU) 喜瑞樂適用於治療對 H1 抗組織胺製劑治療反應不佳的之慢性自發性蕁麻疹成人及青少年 (12 歲及以上) 患者作為附加治療。**禁忌症：**對主成份及賦形劑的任何成份過敏者。**警語及注意事項：**當使用omalizumab 時，可能會發生局部或全身性過敏反應，包括無防禦性過敏。IgE 可能會參與某些感染的免疫反應，在蠕蟲感染的長期高風險病患中，一項針對過敏性病患安慰劑對照組試驗顯示，以omalizumab 治療時，感染率輕微上升，雖然病程、嚴重性以及對感染治療的反應，均無變化。喜瑞樂不適用於治療急性氣喘惡化，急性支氣管痙攣或氣喘重積症 (status asthmaticus)。**用法用量：**只供皮下注射使用。不得以靜脈注射或肌肉注射的方式投予。過敏性氣喘劑量 喜瑞樂適當的劑量與給藥頻率是根據開始治療前免疫球蛋白E (immunoglobulin E，IgE)(國際單位/ 毫升)的測量基底值及體重 (公斤) 而定。在投與初始劑量前，應使用市面上任何一種總血清 IgE 的分析方法檢測病患的 IgE 值藉以計算劑量。根據這些檢驗結果，每次投藥可能需要注射 1 至 4 次來投與 75-600 毫克的喜瑞樂。請參閱仿單表一：劑量與注射劑瓶數的換算表及表二及表三：兒童 (6 歲至 12 歲以下) 和成人及青少年 (12 歲以上) 使用劑量。使用喜瑞樂 150 毫克調配 225，375 和 525 毫克的劑量時，其中一瓶只需抽取 75 毫克 (0.6 毫升) 的藥量。IgE 基底值或體重 (公斤) 在劑量對應表之外的病患，不可投予喜瑞樂。慢性自發性蕁麻疹 (CSU) 每四週以皮下注射投與喜瑞樂 150 或 300 毫克。在 CSU 患者中喜瑞樂的劑量與血清 IgE (游離濃度或總濃度) 或體重無關。**不良反應：**過敏性氣喘 以成人及 12 歲或大於 12 歲的青少年所執行的臨床試驗期間最常見的副作用報告為頭痛及注射部位的反應，包括注射部位疼痛、腫脹、紅斑與搔癢。於 6 歲至 12 歲以下兒童所進行的臨床試驗中，最常見的不良反應報告為頭痛、發燒及上腹部疼痛。大部份的不良反應為輕度或中度。慢性自發性蕁麻疹 (CSU) 發生於 ≥ 2% 接受喜瑞樂治療的患者中且發生率高於安慰劑治療患者的不良事件包括：噁心、鼻咽炎、竇炎、上呼吸道感染、病毒性上呼吸道感染、關節痛、頭痛、咳嗽。

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Young Investigator Award

【Young Investigator Award】演講 8 分鐘，討論 2 分鐘

Ching-Yao Yang MD 楊景堯醫師 國立臺灣大學附設醫院

Association between programmed death-ligand 1 expression, immune microenvironments, and clinical outcomes in epidermal growth factor receptor mutant lung adenocarcinoma patients treated with tyrosine kinase inhibitors

Ching-Yao Yang [a], Wei-Yu Liao [a], Chao-Chi Ho [a], Kuan-Yu Chen [a], Tzu-Hsiu Tsai [a], Chia-Lin Hsu [a], Kang-Yi Su [b], Yih-Leong Chang [c,*], Chen-Tu Wu [c,**], Chia-Chi Hsu [d,e], Bin-Chi Liao [d], Wei-Hsun Hsu [d], Jih-Hsiang Lee [d], Chia-Chi Lin [d], Jin-Yuan Shih [a,***], James C.-H. Yang [d], Chong-Jen Yu [a]

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Abstract ***Introduction:*** Besides being a predictive biomarker of response to immunotherapy in lung cancer in general, programmed death-ligand 1 (PD-L1) is not so well correlated with treatment outcomes of lung adenocarcinoma (ADC) harbouring epidermal growth factor receptor (EGFR) mutations, as reported studies are inconclusive and seldom addressed the issues of response to treatment and resistance. The primary objective is to evaluate the association of PD-L1 and EGFR tyrosine kinase inhibitor (TKI) efficacy, resistance, and relevant clinical outcomes. The secondary objective is to further explore the tumour microenvironments of EGFR mutant tumours with different PD-L1 expression.

Methods and materials: Using immunohistochemical (IHC) staining, we retrospectively tested PD-L1 expression (Dako 22C3) in the pre-treatment tumours from advanced EGFR mutant lung ADC patients, of whom all were treated with TKIs. Multiplex IHC assay was applied for exploring immune cells in tumour microenvironments.

Results: A total of 153 Taiwanese patients were enrolled in our study, of whom a majority of cases were female (58.9%) and non-smokers (75.8%). The objective response rate (ORR) to EGFR TKI and progression-free survival (PFS) were better in patients with PD-L1 expression <50% (ORR/PFS in PD-L1 0% versus 1e49% versus _50%: 65.6%/12.5 months versus 56.4%/12.8 months versus 38.9%/5.9 months, P < 0.05). The multivariate analysis showed that PDL1 <50% was an independent prognostic factor for longer PFS (hazard ratio (HR) 0.433, 95% confidence interval (CI) 0.250e0.751, P Z 0.003). Furthermore, tumours with higher PD-L1 expression were less likely to develop a secondary T790M mutation (T790Mt in PD-L1 0% versus 1e49% versus _50%: 53.7% versus 35.7% versus 10%, P Z 0.024). Multiplex IHC tests were applied in 15 cases and revealed a potential correlation between PD-L1, immune cells, and EGFR TKI responses.

Conclusions: Lower pre-treatment PD-L1 is associated with better ORR, PFS, and higher frequency of T790M resistance in EGFR TKI-treated lung ADC patients.

【Young Investigator Award】演講 8 分鐘，討論 2 分鐘

Vincent Yi-Fong Su MD 蘇一峰醫師 臺北市立聯合醫院

Induced Pluripotent Stem Cells Attenuate Endothelial Leakage in Acute Lung Injury via Tissue Inhibitor of Metalloproteinases-1 to Reduce Focal Adhesion Kinase Activity

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ABSTRACT

Induced pluripotent stem cells (iPSCs) can reduce the severity of endotoxin-induced acute lung injury (ALI). However, the interaction between iPSCs and vascular endothelium remains unclear. In this study, we investigated the effects of iPSCs in moderating pulmonary endothelial leakage in endotoxin-induced ALI. Murine iPSCs were delivered intravenously to male C57BL/6 mice (8–12 weeks old) 4 hours after intratracheal lipopolysaccharide (LPS) delivery. Histology, blood and bronchoalveolar lavage fluid (BALF) cytokine and junctional protein assays, and regulatory signaling pathway assays were performed 24 hours later. Human umbilical vein endothelial cells (HUVECs) were used as a model of junctional protein-expressing cells and stimulated with LPS. Our results showed that iPSC treatment alleviated histological signs of ALI, protein leakage, and proinflammatory cytokines. iPSC therapy restored vascular endothelial cadherin (VE-cadherin) expression in ALI mouse lungs. In HUVECs, human iPSCs (hiPSCs) restored disrupted VE-cadherin expression and reduced the activity of Snail and focal adhesion kinase (FAK) phosphorylation in Tyr397 in response to LPS. iPSC-conditioned medium contained extra antiangiogenic factor of tissue inhibitor of metalloproteinases-1 (TIMP-1) compared with control medium. TIMP-1 inhibition diminished the beneficial effects of iPSC-conditioned medium in ALI mice. Our study suggested
that iPSCs attenuate endothelial cell leakage in endotoxin-induced ALI via a mechanism involving TIMP-1 and the FAK/Snail pathway. STEM CELLS *2019;37:1516–1527*

【Young Investigator Award】演講 8 分鐘，討論 2 分鐘

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An International Real-World Analysis of the Efficacy and Safety of Lorlatinib Through Early or Expanded Access Programs in Patients With Tyrosine Kinase Inhibitor–Refractory *ALK*-Positive or *ROS1*-Positive NSCLC

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ABSTRACT

Introduction: Lorlatinib, a next-generation central nervous system–penetrant ALK/ROS1 tyrosine kinase inhibitor (TKI), is approved to treat TKI-refractory *ALK*-positive (*ALK*+) NSCLC based on results from a phase 2 study.

Methods: A real-world analysis was performed on *ALK*+ or *ROS1*-positive (*ROS1*+) patients with NSCLC enrolled in lorlatinib early or expanded access programs in Hong Kong, Singapore, South Korea, Taiwan, Thailand, and the United States.

Results: A total of 95 patients with NSCLC (76 *ALK*+ and 19 *ROS1*+) were analyzed. Among *ALK*+ patients treated with less than two previous TKIs, two or more previous TKIs, and three or more previous TKIs, the objective response rates (ORR) and median progression-free survival (mPFS) were 42% (95% confidence interval [CI]: 26–59; n = 38) and not reached (NR) (95% CI: 4.5–NR; n = 45), 35% (95% CI: 22–49; n = 55) and 11.2 months (95% CI: 4.5–NR; n ¼ 66), and 18% (95% CI: 4–43; n = 17) and 6.5 months (95% CI: 3.5–11.6; n = 21), respectively. The ORRs and mPFSs were 13% (95% CI: 0–53; n = 8) and 9.2 months (95% CI: 3.3–NR; n = 9) for patients treated with one second generation ALK TKI as the only ALK TKI received. For *ROS1*+ patients, ORRs and mPFSs were 41% (95% CI: 18–67; n = 17) and 11.9 months (95% CI: 6.4–NR; n = 19). The intracranial ORRs were 35% (95% CI: 22–49) and 55% (95% CI: 23–83) for 52 *ALK*+ and 11 *ROS1*+ patients. Mpfs was 9.3 months (95% CI: 1.0–NR; n = 13) for patients with leptomeningeal carcinomatosis. No new safety signals were noted.

Conclusion: Lorlatinib exhibited meaningful activity in TKI-refractory *ALK*+ or *ROS1*+ patients with NSCLC enrolled in early or expanded access programs.

Keywords: Lorlatinib; Expanded access; TKI-refractory; ALK; ROS1; NSCLC

「胸腔醫學雜誌」優秀論文獎

【胸腔醫學雜誌】優秀論文獎第一名

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Effect of Surgery Waiting Times on Disease-Free Survival of Patients with Screen-Detected cT1N0 Lung Adenocarcinoma

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ABSTRACT

Introduction: The relationship between waiting time for surgery and clinical outcomes of patients with early-stage screen-detected lung cancer remains unclear. This study aimed to evaluate if delayed surgery affects disease-free survival (DFS) of patients with screen- detected cT1N0 lung adenocarcinoma.

Methods: This retrospective study reviewed the data of 700 patients with a preoperatively undiagnosed single cT1N0 lung adenocarcinoma who underwent surgical resection in our institute from March 2011 to January 2016. The patients were classified as the early group if the waiting time for surgery was 30 days or less, and the delayed group if the wait was 31 days or longer. Propensity-matched analysis was used to compare the clinical outcomes of these groups.

Results: The median waiting time for surgery was 16 days. In total, 513 (73.3%) and 187 (26.7%) patients were in the early and delayed group, respectively. The early group was correlated with a larger consolidation-to-tumor ratio, solid component diameter, and total tumor diameter. Patients in the delayed group received more staging workup before surgery than those in the early group. Multivariable analysis showed that smaller consolidation- to-tumor ratio, solid component diameter and serum carcinoembryonic antigen level were significantly correlated with better DFS. Delay in surgery did not affect DFS. After propensity- matching of clinical and demographic characteristics, there was no difference in DFS among the early and delayed groups.

Conclusion: Among patients with a preoperatively undiagnosed single cT1N0 lung adenocarcinoma, the results showed that a delay of up to 30 days from the time of diagnosis to the time of surgery may not affect DFS, and may be considered safe for such patients. ***(Thorac Med 2020; 35: 10-20)***

Key words: disease-free survival, lung adenocarcinoma, surgery waiting time

【胸腔醫學雜誌】優秀論文獎第二名

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Prevalence of Chronic Obstructive Pulmonary Disease in Cardiac Outpatient Clinics Using Questionnaire and Spirometry Screening

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ABSTRACT

Background: Patients who have COPD may visit cardiac outpatient clinics due to having similar symptoms. We aimed to investigate whether a COPD diagnostic questionnaire (CDQ) and spirometry can facilitate the early detection of undiagnosed COPD in individuals who visit cardiac clinics.

Methods: A voluntary screening for COPD was conducted for patients who visited the cardiac clinics of E-Da hospital. Subjects aged ≧35 years and who had at least 1 cardiovascular comorbidity were eligible for COPD screening with the CDQ and spirometry. COPD was defined as a ratio of forced expiratory volume in the first second/forced vital capacity less than 0.7 by spirometry. Clinical data, including the presence of COPD symptoms and questionnaire scores, were collected for analysis.

Results: A total of 808 patients were enrolled in this study. Of these patients, 21 had a confirmed diagnosis of COPD. The prevalence of COPD was only 2.6% in the subjects who visited our cardiac clinics. Compared to the non-COPD group, more of the COPD group were aged ≧70 years and were ex-smokers, and had ≧2 COPD symptoms, higher COPD Assessment Test and CDQ scores, and a smoking history of more than 20 pack/years. The prevalence, sensitivity, and specificity among patients with a CDQ score ≧21.5 were 6.6%, 62%, and 76%, with a low positive predictive value of 7% and a high negative predictive value of 99%.

Conclusion: The prevalence of COPD in patients visiting cardiac clinics was low in this study. A CDQ score ≧21.5 before spirometry screening was more effective for screening COPD in this population. ***(Thorac Med 2020; 35: 96-105)***

Key words: chronic obstructive pulmonary disease, prevalence, questionnaire, screening, spirometry

【胸腔醫學雜誌】優秀論文獎第三名

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Early Detection of Chronic Obstructive Pulmonary Disease in Patients with Coronary Artery Disease

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ABSTRACT

Objectives: Chronic obstructive pulmonary disease (COPD) and coronary artery disease (CAD) usually coexist and share the same risk factors. Early diagnosis of COPD in patients with CAD allows for early intervention, which improves the prognosis. The purpose of this study was to determine a method for early detection of COPD in this target population.

Methods: In this single-center, observational, prospective study, outpatients with CAD (aged >40 years with a history of smoking) were evaluated. Each patient underwent a COPD assessment after coronary angiography. Data on age, smoking status, pack-year history of smoking, body mass index (BMI), and dyspnea score (Medical Research Council), and the results of a COPD assessment test (CAT) and pre- and post-bronchodilator spirometry were obtained.

Results: A total of 166 patients were included in the study, most of whom were men (92.7%). A definitive diagnosis of COPD was made by spirometry in 32 patients (19.3%). Sixteen (50%) and 16 (50%) patients were assigned to group A and B respectively. Statistically significant differences in age, pack-year history of smoking, body weight, BMI, C-reactive protein (CRP) levels, serum sodium levels, and symptoms such as cough and sputum (CAT scores) were observed between CAD patients with COPD and those without COPD. Multivariate analysis revealed that aged >60 years (P<0.001), a smoking history >30 pack-year (P=0.006), body weight <60 kg (P=0.04), sputum production (CAT score, Sputum ≧1) (P=0.01) and a lower serum sodium level (Na <135 mg/dl) (P=0.028) were independent clinical characteristics of COPD development in CAD patients.

Conclusion: Approximately 19.3% of our outpatients with CAD had COPD. It is important to evaluate for COPD in CAD patients with aged >60 years, a history of smoking >30 pack- years, body weight <60 kg, more sputum production, and a low serum sodium level. ***(Thorac Med 2020; 35: 52-63)***

Key words: chronic obstructive pulmonary disease, cardiovascular disease, COPD assessment test

優秀學術論文摘要

Intervention Bronchoscopy

Diagnosis

Thoracic Oncology

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) □海報競賽 (Post)

OA01

中央氣道阻塞的年長病人接受介入性支氣管鏡治療的經驗

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Interventional pulmonology for elderly patients with central airway obstruction

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Purpose: Patients with central airway obstruction (CAO) may need endobronchial intervention to relieve their symptoms. But there are no studies evaluating the efficacy and safety of the interventional pulmonology in advanced ages. The aim of this study is to assess the safety and survival of interventional pulmonology in elderly patients with central airway obstruction.
Materials and Methods: This retrospective study was conducted in a university hospital and involved 260 elderly patients (age > 70 years old, 149 men, 111 women; mean age, 77.3 years) with benign (n=58) and malignant (n=202) tracheobronchial disease who received endobronchial intervention procedure during the period 2005-2019. Survival was analyzed using the Kaplan-Meier method while the log-rank test was used for comparisons.
Results: The most three malignant etiology of elderly CAO were lung Squamous cell carcinoma (103, 39.6%), lung adenocarcinoma (37, 14.2%) and esophagus cancer (17. 6.6%). Interventional bronchoscopy procedure included electrocautery (182, 70%), Stent implantation (40, 5.4%) electrocautery combine stent implantation (34, 13.1%) and balloon dilatation (4, 1.5%). A total of 247 patients (95%) achieved endoscopic success after interventional bronchoscopy. No patient died within 24 hours of the procedure, while the major morbidities were iatrogenic pneumonia (n=12, 4.6%). The median survival after the procedure in patients with lung cancer, other metastatic cancer, and esophageal cancer was 331, 1140, and 187 days, respectively. ($p<0.001$).
Conclusions: Interventional bronchoscopy is a safe and effective procedure that may be recommended for central airway obstruction, even in elderly patients. Elderly CAO Patients with lung metastases have longer lengths of survival than patients with primary lung cancer and esophagus cancer.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) □海報競賽 (Post)

OA02

粒腺體分裂蛋白 Dynamin-related protein 1 經由多激酶模式活化以促進肺腺癌細胞增殖及侵襲性

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Multi-kinase framework regulates activation of dynamin-related protein 1 to promote proliferation and invasion of lung adenocarcinoma

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Purpose: Recent studies revealed the role of dynamin-related protein 1 (DRP1), encoded by the DNM1L gene, in regulating the growth of cancer cells of various origins. However, the regulation and functional and clinical significance of DRP1 remain undetermined in lung adenocarcinoma.

Materials and Methods: The clinical significance of DRP1 expression and activation was explored using surgical samples from patients who received definitive surgical treatment for stage I to IIIA lung adenocarcinoma. We further investigated the role of DRP1 in mitochondrial biology and malignant features of lung adenocarcinoma, through applications of CRISPR/Cas9 techniques to establish DNM1L-knockout lung adenocarcinoma cells.

Results: Our results demonstrated that the expression and activation of DRP1 were significantly correlated with proliferation and disease extent, as well as an increased risk of post-operative recurrence. We revealed that loss of DRP1 in lung adenocarcinoma led to an altered mitochondrial morphology, fewer copies of mitochondrial DNA, decreased respiratory complexes, and impaired oxidative phosphorylation. Depleting DRP1 suppressed the proliferation and invasion of lung adenocarcinoma, while glycolytic serine synthesis was activated to support the proliferation of DRP1-depleted lung adenocarcinoma. In addition, we uncovered the role of the multi-kinase framework, including ERK/AKT and CDK2, in regulating DRP1 activation through phosphorylation at serine 616.

Conclusions: Collectively, this study revealed that the multi-kinase regulation in lung adenocarcinoma promotes the malignant properties of lung adenocarcinoma through activating DRP1. Our data suggested that biomarkers related to mitochondrial reprogramming, such as DRP1, can be used to evaluate the risk of post-operative recurrence in early-stage lung adenocarcinoma.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) □海報競賽 (Post)

OA03

ALK 酪胺酸激酶抑制劑之抗藥性機轉: 一個多中心次世代定序之研究

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Resistance Profiles of ALK Tyrosine Kinase Inhibitors in Advanced Non-small Cell Lung Cancer: A Multicenter Study by Targeted Next-generation Sequencing

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Introduction: ALK tyrosine kinase inhibitors (TKIs) crizotinib, ceritinib, alectinib, brigatinib and lorlatinib are approved for advanced non-small cell lung cancer (NSCLC) with ALK rearrangement. However, the resistance mechanisms for each TKIs are still largely unclear.

Methods: In this prospective multicenter study, we analyzed NSCLC patients' cancer tissues and/or cell free DNA (cfDNA) after ALK TKI(s) progression by targeted next-generation sequencing. Patients' clinicopathologic characteristics and ALK TKI treatment outcomes were analyzed.

Results: Totally, 88 patients were enrolled, with 30 cancer tissues and 90 cfDNA samples analyzed. Five (16%) ALK kinase domain mutations (L1196M for two, I1171T, D1203N and G1269A + F1174L) and 3 possible bypass mutations (NRAS G12V, EGFR R108K and PIK3CA E545K) were found in 32 crizotinib-resistant cancers. Four (22%) ALK kinase domain mutations (G1128A, G1202R, G1269A and I1171T + E1210K) and 3 possible bypass mutations (KIT D820E, MET E1012* and EGFR P265_C291del) were found in 18 ceritinib-resistant cancers. Four (17%) ALK kinase domain mutations (G1202R for two, W1295C, G1202R+L1196M) and 1 possible bypass mutation (EGFR P753S) were found in 24 alectinib-resistant cancers. Two (11%) ALK kinase domain mutations (G1202R + G1269A for two) and 2 possible bypass mutations (BRAF V600E and MET D1246N) were found in 18 lorlatinib-resistant cancers. Mutations were detected more frequently from cancer tissues than cfDNAs.

Conclusions: The resistant mechanisms of ALK TKIs were heterogeneous. ALK kinase domain mutations were found in less than one-third of patients. Compound ALK kinase domain mutations which may confer lorlatinib resistance can occur in crizotinib, ceritinib and alectinib-resistant lung cancers.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OA04

支氣管內視鏡超音波指引無 X 光透視法經氣管冷凍活檢在肺部疾病診斷的安全性及可行性

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The Safety and Feasibility of Radial Endobronchial Ultrasound-guided Transbronchial Cryobiopsy without fluoroscopy in the diagnosis of lung diseases

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Purpose: Transbronchial lung cryobiopsy (TBLC) has emerged as a new bronchoscopic procedure which can improve specimen size and obtain crush artifact-free tissue to increase diagnostic yield in various diffuse parenchymal lung diseases (DPLDs). However, TBLC has been associated with a higher incidence of complications, and variability in diagnostic yield. We evaluated the safety and feasibility of TBLC in combination with R-EBUS to diagnose DPLDs without fluoroscopy.

Materials and Methods: We conducted this retrospective study at a single medical center from January 2015 to March 2019. Patients with DPLDs who underwent R-EBUS without fluoroscopy to locate target lesions and confirm the absence of adjacent vessels, followed by sampling with conventional transbronchial lung forceps biopsy (TBLB) and cryobiopsy (TBLC) were enrolled. TBLC and TBLB samples were sent to the pathology department for diagnostic analysis. The sample size, diagnostic yield and complications after the procedure were recorded.

Results: A total 34 patients with DPLDs were analyzed, of whom 21 had diffuse lung infiltrates and 13 had bilateral pulmonary nodules/masses. The overall diagnostic rate was 76.4% (26/34) and the diagnostic yield increased from 44.1% with the forceps biopsy to 70.6% after adding cryobiopsy ($p=0.023$). Compared to conventional transbronchial biopsy with forceps, cryobiopsy provided a larger specimen and sample volume (38 mm^3 vs 6 mm^3; $p<0.001$). Eleven patients who initially had non-diagnostic results by TBLB received a definite diagnosis after adding TBLC. Among these patients, eight (9/11) patients got a definitely diagnosis of interstitial lung disease (ILD) ($p<0.001$). There were no severe complications after the procedure.

Conclusions: Compared to TBLB with R-EBUS guidance, the samples obtained by TBLC were significantly larger and TBLC with R-EBUS guidance without fluoroscopy increased the diagnostic yield in patients with DPLDs, particularly in those with a definitely diagnosis of ILD.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OA05

miR-204 透過靶向 CD44 並降低上皮間質轉化和幹細胞特性而逆轉 osimertinib 抗藥性

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MiR-204 reverses osimertinib resistance through targeting CD44 and decreasing EMT and stemness

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Purpose: Osimertinib, the third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), provides favorable treatment effectiveness to advanced non-small-cell lung cancer (NSCLC) patients with *EGFR* mutations. However, acquired resistance to osimertinib still developed eventually. This study was to investigate that miRNAs regulate osimertinib resistance.

Materials and Methods: TaqMan low-density arrays (TLDA) was used to identify the potential miRNAs related to osimertinib-resistance by comparing the miRNA expression between osiemrtinib-sensitive and osimertinib-resistant cells. Molecular manipulations, animal model and clinical samples were used to investigate the impact of miRNAs on osimertinib resistance in NSCLC cells. Furthermore, public database and luciferase reporter assay were used to explore the downstream target of the miRNA.

Results: MiR-204 expression was higher in osimertinib-sensitive than osimertinib-resistant cells. *In vitro*, overexpression of miR-204 reversed osimertinib resistance by increasing apoptosis, whereas functional assays showed that decreased miR-204 expression enhanced epithelial-mesenchymal transition (EMT), sphere formation and increasing stemness-related genes. *In vivo*, osimertinib treatment exhibited a better therapeutic effect in mice bearing miR-204-overexpressing tumors. In clinical, patients with higher miR-204 in serum or in tumors had a longer progression-free survival of EGFR TKIs treatment than those with lower miR-204. In addition, CD44 was the direct downstream target of miR-204. A negative correlation was observed in TCGA database of lung adenocarcinoma. Knockdown CD44 reduced cell migration, stemness, and increased osimertinib-induced apoptosis.

Conclusions: MiR-204 reversed osimertinib resistance through targeting CD44. Therefore, miR-204/CD44 plays an important role to overcome osimertinib resistance.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OA06

使用引導套管與否和支氣管內視鏡超音波導引下對於周邊肺惡性腫瘤經支氣管切片的診斷率與併發症研究－傾向評分配對的分析結果

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Endobronchial ultrasound-guided transbronchial biopsy with or without a guide-sheath for peripheral pulmonary malignancy: A propensity-score matched analysis

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Purpose: Endobronchial ultrasound (EBUS)-guided transbronchial biopsy (TBB) is a common procedure used to diagnose peripheral pulmonary lesions (PPLs), with a favorable safety profile and an acceptable diagnostic yield. In this study, we sought to investigate whether the introduction of a guide-sheath (GS) further improved the diagnostic yield of EBUS-guided TBB for peripheral pulmonary malignancy.

Materials and Methods: This study was conducted at the National Taiwan University Hospital and its branches. From January 2017 to March 2019, all patients who underwent EBUS-guided TBB for PPLs were screened for eligibility. Patients were included in this study if the final diagnosis of the PPLs was proved to be malignancy. The diagnostic yield and complication rates were compared between EBUS-guided TBB with or without the application of a GS (EBUS-GS-TBB vs. EBUS-TBB groups). A propensity-score matching method was used to balance the differences of pertinent clinical features between two groups.

Results: The original cohort consisted 975 patients (556 in EBUS-TBB; 419 in EBUS-GS-TBB) with a diagnostic yield of 80% and 78% for the EBUS-TBB and EBUS-GS-TBB groups, respectively (P =0.281). A GS was more likely to be applied in smaller (40mm vs. 44mm) and upper lobe (60% vs. 35%) lesions. After 1:1 propensity-score matching, a total of 720 (360 in each group) patients were included, and the diagnostic yield of the lesions were 79% and 78% for the EBUS-TBB and EBUS-GS-TBB groups, respectively (P =0.649). The complication rates were also similar between the two groups (7.2% vs. 5.8%, P =0.451, for bleeding; 1.9% vs. 0.6%, P =0.177, for pneumothorax).

Conclusions: The introduction of a GS did not improve the diagnostic yield of EBUS-guided TBB for peripheral pulmonary malignancy.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OA07

惡性氣管內腫瘤導致之阻塞性肺炎的微生物學與治療

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The microbiology of postobstructive pneumonia in patients with malignancy endo-bronchial lesions

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Introduction: Postobstructive pneumonia was resulted from complete or partial airway obstruction. Intraluminal mass was the most common cause of the obstruction. The postobstructive pneumonia was contributed to the mortality in the patient with the malignancy endo-bronchial lesion. However, little was known the microbiology. This aim of this study was to described the microbiology of postobstructive pneumonia in patients with malignancy endo-bronchial lesions who undergone bronchial wash.
Materials and Methods: We retrospectively analyzed the 87 patients with postobstructive pneumonia due to malignancy endo-bronchial lesions from 2011-01 to 2018-12 at China Medical University Hospital. All the patients received bronchoscopic tumor excision and bronchial wash. Both pathology of tumor and microbiological culture were done and reviewed.
Results: The mean age were 62.4 years old and 73 patients was male. The most common etiology caused endobronchial obstruction were lung squamous cell carcinoma (n=46, 48.9%), esophagus cancer (n=12, 14%) and small cell lung cancer (n=9, 10%). The most common symptoms were dyspnea (n=78, 89.7%), fever (n=52, 59.8%) and cough (n=41, 47.1%). About half of the tumors located at main bronchi (n=43, 49.4%). 56 of these patient (61.3%) had received electrocautery, whereas 14 patients (9.7%) had received both electrocautery and stent implant. Microbes were isolated from 51 of 87 patients (58.6%). Among the bacteriology of positive-culture effusions with obstructive pneumonia, *Pseudomonas aeruginosa*(n=18) , *Klebsiella pneumonia*(n=12), and *Staphylococcus aureus (OSSA)* (n=8) were the most common pathogen.
Conclusions: The patients with postobstructive pneumonia had high risk to requiring ICU care. Is was important to eliminate the endobronchial tumor and treat with accurate antibiotics. Otherwise, our study provided the common microbiology to choosing accurate treatment for the patients with postobstructive pneumonia.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OA08

循環腫瘤細胞, 可以預測肺癌的復發微觀殘留疾病的檢驗工具：一縱向前瞻性試驗

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Circulating Tumor Cells as a Tool of Minimal Residual Disease Can Predict Lung Cancer Recurrence: A longitudinal, Prospective Trial

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Purpose: The role of circulating tumor cells (CTCs) for predicting the recurrence of cancer in lung cancer patients after surgery remains unclear.
Materials and Methods: A negatively selected protocol of CTC identification was applied. For all the enrolled patients, CTC testing was performed before and after surgery on the operation day (day 0), postoperative day 1, and day 3. The daily decline and trend of CTCs were analyzed to correlate with cancer relapse. The mixed model repeated measures (MMRM) adjusted by cancer characteristics was applied for statistical significance.
Results: Fifty patients with lung mass undergoing surgery were enrolled. Among 41 primary lung cancers, 26 (63.4%) were pathological stage Tis and I. A total of 200 CTC tests were performed. MMRM analysis indicated that surgery could contribute to a CTC decline after surgery in all patients with statistical significance ($p = 0.0005$). The daily decrease of CTCs was statistically different between patients with and without recurrence ($p = 0.0068$). An early rebound of CTC counts on postoperative days 1 and 3 was associated with recurrence months later.
Conclusions: CTC testing can potentially serve as a tool for minimal residual disease detection in early-staged lung cancer after curative surgery.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA01

病例報告 - 加熱菸相關之慢性嗜伊紅性白血球肺炎

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Chronic Eosinophilic Pneumonia Associated with Heat-Not-Burn Tobacco Cigarette Use

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Introduction: Heat-not-burn (HNB) tobacco cigarettes are devices that heat tobacco below the temperature at which traditional tobacco burns, producing fewer toxic chemical compounds. However, the potential health risk of HNB tobacco cigarette use remains unclear.
Case report: We reported the case of a 25-year-old healthy male who suffered from afebrile cough with whitish sputum for 4 months after switching from conventional cigarettes to smuggled HNB tobacco cigarettes for 1 year. Chest computed tomography showed bilateral consolidation patches and ground-glass patches. Peripheral and bronchoalveolar lavage fluid eosinophilia were noted. After steroid treatment for chronic eosinophilic pneumonia (CEP), his symptoms improved rapidly.
Discussion: CEP is a rare disease. Diagnosis of CEP is made by exclusion of other possible causes of eosinophilic pneumonia. E-cigarettes, or vaping product use-associated lung injury has been widely reported recently, so smokers may choose HNB instead. Thus, we elucidate the risk to health of HNB cigarette use.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA02

反向暈輪信號之影像型態分析有助於肺結核的診斷

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Tomographic Morphology Analysis of the Reversed Halos Sign Assists in the Diagnosis of Pulmonary Tuberculosis

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We present a 22 year-old male presented to Pulmonary Medicine Clinic with 2 months of productive cough, whose chest computed tomography characteristically depicted a reversed halo appearance(Figure1). His sputum cultured mycobacteria tuberculosis.

The reversed halo sign on computed tomography is increasingly recognized as a valuable imaging finding in lung diseases. Careful evaluation of the sign's features and descriptions enable narrowing of differential diagnosis including tuberculosis, pulmonary infarction, invasive fungal infection, and implicate clinical need for additional examination in certain circumstances.

This case emphases the importance of tomography morphology analysis and broaden clinical perspectives.

(Figure 1)

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA03

多發性肺結節證實為肺部免疫球蛋白 G4 疾病-案例報告

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Multiple pulmonary nodules are finally identified as pulmonary immunoglobulin G4 related disease: a case report

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Case summary: A 43 year-old male smoker, who was found multiple pulmonary nodules/masses via chest x-ray, was firstly suspected malignancy of lung. The physical examination was negative finding. We have performed laboratory tests for further survey but no any clues regarding to malignancy was noted. Operation with lung wedge resection was done for tissue proof. The pathologic results showedabundant IgG4-positive plasma cells. We have reviewed the 2019 ACR/EULAR criteria for IgG4-RD and confirmed that the patient is a case of pulmonary IgG4 related disease. The disease is no any involvement of other organs in the patient. He is treated with oral steroid and the disease is controlled well.

Conclusion: Pulmonary IgG4 related disease can mimic lung malignancy and the disease should be taken into consideration in the differential diagnosis of pulmonary nodules/masses.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA04

電腦斷層導引肺肋膜病變切片(超音波抽吸乾抽):案例系列分析

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CT-Guided Pleural Biopsy results as U.S. guided aspiration failure: case series review

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Introduction: This small number of cases review about evaluate the accuracy, complications of CT-guided biopsy of pleural lesion while U.S guided aspiration failed and related complication and outcomes.

Materials and Methods:

Separate patients (2 men mean age, 30 ± 4.4 Y/O) were performed CT-guided pleural biopsy performed all were diagnosed as TB pleurisy confirmed by tissue proof. The diagnostic rate, complication were evaluated.

Results:

Pathologic results depicted caseous necrosis, multinuclear giant cells inside individually. Diagnostic accuracy were 100%, complication 0%. Complications included occurrence of pneumothorax, hemothorax were all 0%,

Discussion:

CT-guided of pleural biopsy is a safe procedure with distinguished result carried very low risk of complications. Either benign or malignant pleural disease can display similar features. US in the chest is limited when compared with CT. US has been for standard procedure in evaluating pleural effusion. VATS required resources and expertise, including general anesthesia .CT become the guidance choice for performing biopsy of pleural lesion whenever US guided aspiration fail.

Conclusion :

CT-guided biopsy offered minimally invasive, quick approach in comparison with VATS to obtain tissues sample.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA05

Dasatinib 導致的雙側乳糜胸

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Dasatinib related bilateral chylothorax

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Introduction: Chylothorax refers to presence of chyle in the pleural space and associated with high morbidity and mortality. The etiology of chylothorax would be divided into traumatic and non-traumatic cause, accounting around 50% respectively in a large single center study. We propose an unusual case of dasatinib related chylothorax and make a brief summary of current available literature.

Case report: This 57-year-old male has underlying disease of chronic myeloid leukemia. He had received tyrosin kinase inhibitor(TKI) with Dasatinib since November 2018. Progressive dyspnea was complained and chest plain film disclosed bilateral pleural effusion at June 15, 2020. Bilateral thoracentesis was then performed as evaluation after discussion with the patient. Surprisingly, milky content of pleural effusion was drained bilaterally. Pleural effusion analysis was performed and revealed lymphocyte predominant(86%) in cell count and high triglyceride level(429mg/dL). After review of possible etiology of non-traumatic and non-malignant etiology, Dasatinib related chylothorax is the most favored cause. After switch of TKI to Imatinib, gradually improving bilateral pleural effusion had been noted on series chest plain film.

Discussion: Any disruption of chyle flow in the thoracic duct from cisterna chyli to systemic circulation may cause chylothorax. Malignancy is the first priority to be excluded, including direct invasion of thoracic duct or obstruction of lymphatic drainage. In our case, there is no existing solid tumor history nor mass lesion with mediastinal involvement defined on image. Finally, after excluding other common etiology, Dasatinib related chylothorax is presumed in our case.

According to available literature, there is less than 10 cases of Dasatinib related chylothorax reported. Exudative pleural effusion is a common adverse effect of Dasatinib and affects 25% patients but chylothorax being rare. The mechanism is not fully elucidated but inhibition of platelet-derived growth factor receptor beta (PDGFR-β) and Src kinase may contribute to pericyte dysfunction, endothelium permeability and pleural epithelial instability which cause lymph leakage diffusely. Treatment of Dasatinib related pleural effusion includes short term steroid and diuretics. Repeated thoracentesis also help in symptom relief. However, Dasatinib related chylothorax often needs dose reduction and even switch to another TKI as further management. Furtunately, most of cases present with marked resolution of chylothorax after discontinuing Dasatinib. In our case, ceasing Dasatinib therapy and shift to Imatinib leads to regression of bilateral chylothorax.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA06

第四型免疫球蛋白 G 相關疾病

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IgG4-Related Disease - A Case Report

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Introduction: IgG4-related disease is an immune mediated condition involving multiple organs, charaterized by lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells. It could be misidentified as many malignant or infectious diseases, and histopathology proof is required for the diagnosis. We will introduce a 68-year-old man with IgG4 related disease involving bilateral lung.
Case report: A 68-year-old male, with chroic obstructive pulmonary disease under regular inhaled corticosteroid and bronchodilator, presented with progressive exertional dyspnea for two weeks. Initial chest x-ray showed bilateral multiple consolidation. There was no bronchospasm during hospitalization, and he remained dyspnea after control of acid reflux. High resolution chest computed tomography showed bilateral multiple lung consolidation of variable size. Similar lung infiltrate of different size and location was noted since one year ago in another medical center. Thoracoscopic wedge resection of left lower lung lesion reported inflammatory change with mainly lymphocytes and plasma cells infiltrate. Significant cells were positive for IgG and IgG4. He was diagnosed as IgG4-related disease. After oral prednisolone, dyspnea improved rapidly, and complete resolution of bilateral lung consolidation was noted one months later. There was no recurrence of lung consolidation with continuation of oral corticosteroid.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA07

肺病灶融化的案例

李忠恕
林口長庚 胸腔內科

A Case of Melting Ice Cube Sign

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A 43-year-old woman had sputum tinged with blood for 1 week. Neither chest pain nor shortness of breath was noted. Chest X-ray (Fig.1) showed right round-shaped shadow. There was high D-dimer level up to 711 FEU ng/mL. Chest-tomography angiography showed pulmonary embolism. Follow-up chest X-ray (Fig.2) revealed melting ice cube sign.

Fig.1 2020.09.29

Fig.2 2020.10.12

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA08

以支氣管鏡成功移除聲帶氣管處活體水蛭 – 病例報告

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A live Leech across the vocal cord with removal successfully by bronchoscopy - A case report

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Introduction：

Leeches are segmented worms found in rivers, ponds, lakes, swamps and water-logged ditches. Human infestations may be due to drink non-boiled river water, swimming in lakes, or skin attach the environment with Leeches. The worm has suckers at both ends and preys on the host's blood which in airway may cause hemoptysis or airway obstruction.

Case Report：

A 55-year-old female patient has history of oral cancer post operation with nasogastric tube dependent. She visited Otolaryngology clinics for feeling lump throat with hemoptysis for three weeks. A live leech over the glottic space was found under nasopharyngolaryngoscopy and she was referred to pulmonary department for removal of the leech by bronchoscopy. According to the patient, she lives in mountains and has the habit of gargling with the water from river. Under bronchoscopy, there was a live leech moving across the vocal cord (Figure A and B). Forceps through bronchoscopy was used to scratch it (Figure C). A 10 cm × 1 cm live leech was removed successfully (Figure D).

Conclusion：

Leeches may invaded human body via different methods of attachment. An infestation of Leech in airway may cause airway obstruction and hemoptysis. Physician visit if there was symptoms with a history of suspicious environment encounter for adequate medical management.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA09

虛擬支氣管鏡導引之經支氣管切片可幫助周邊型肺部病灶之診斷

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Virtual bronchoscopy-guided transbronchial biopsy for aiding the diagnosis of peripheral lung lesions

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Background: This study aimed to evaluate the clinical value of virtual bronchoscopy (VB) in aiding the diagnosis of peripheral lung lesions by transbronchial biopsy (TBB).

Methods: A total of 24 consecutive patients with peripheral pulmonary shadows or lesions who received VB-guided TBB were evaluated retrospectively. VB was reconstructed from 1 mm-thick slice images of multi-detector computed tomography (MDCT) and established by OsiriX, an open source software. Experienced pulmonologists inserted the conventional ultrathin bronchoscopes into the target bronchus under direct vision following the VB images.

Results: A total of 24 patients were finally enrolled (17 men and 7 women; age range, 33–93 years; median, 65.5 years). Diagnosis was established in 20 patients (17 malignant and 3 benign lesions) with diagnostic yield of 83.3% (sensitivity: 89.5%, specificity: 40.0%, positive predictive value: 85.0%, negative predictive value: 50.0%, and accuracy: 79.17%). The diagnostic rate was 92.3% with CT bronchus sign and 72.7% without CT bronchus sign ($p = 0.209$). The diagnostic rate was 80% with the lesions measuring less than 30 mm and 85.7% with lesions more than 30 mm ($p = 0.717$). One patient whose lesion was 24 mm over RUL exhibited a complication of pneumothorax and recovered spontaneously without drainage.

Conclusion: The use of an ultrathin bronchoscope and simulation with VB reconstructed using high-quality MDCT image with OsiriX is considered to improve the pathological diagnosis of peripheral lung lesions. The proposed method is also easy, low cost and an available measure for correct diagnosis by interventional pulmonologist when no endobronchial ultrasound bronchoscopy is available.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA10

利用支氣管鏡縱膈腔超音波細針抽吸(EBUS-TBNA)及支氣管鏡超音波經食道細針抽吸(EUS-B-FNA)在縱隔腔及肺部病灶來尋寶：制定一個完美路徑的地圖

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Treasure hunt in the mediastinum lesions or lung lesions by EBUS-TBNA and EUS-B-FNA: A road map for the best route

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Purpose: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound with an echobronchoscope guided fine needle aspiration (EUS-B-FNA) are useful modalities in the evaluation of mediastinal lymphadenopathy (LAP) and pulmonary lesions in adults; however, a guided on how to choose a best one from these two methods is limited.
Materials and Methods: 43 Consecutive patients with mediastinum LAP underwent EUS-B-FNA with or without EBUS-TBNA (EUS-B group) from January 2017 to December 2019. We matched another 44 patients with mediastinum LAP underwent EBUS-TBNA alone randomly (TBNA group). We tried to identify the independent clinical characteristics of these patients who needed to undergo EUS-B-FNA for the target lesion assessment.
Results: The LAP size in the EUS-B group is larger than those in the EBUS-TBNA group (3.47 cm vs 2.93 cm; $p < 0.001$.) The location of lymph nodes or lung lesions were significant difference between these two groups. (53.5% vs 9.1%; $p < 0.001$) The EUS-B group had much higher proportion of airway narrowing compared to the EBUS-TBNA group. (44.2% vs 13.6%; $p < 0.001$) The availability of rapid-on-site evaluation (ROSE) was higher in EUS-B group than EBUS-TBNA group. (83.7% vs 63.6%; $p = 0.034$) After univariate and multivariate analysis, the location, airway narrowing and the availability of ROSE were independent factors influencing diagnostic methods decision.
Conclusions: EBUS-TBNA and EUS-B-FNA are safe techniques in the assessment of patients with mediastinum LAP or lung lesions. We choice the best one from these two methods based on the location of target lesions, airway narrowing or not, and the availability of ROSE.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA11

經支氣管鏡切片後併發感染的治療並不會延遲肺癌病人的治療

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Adequate treatment of post-bronchoscopy biopsy-related infectious complication did not delay treatment for lung cancer patients.

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Purpose: We aimed to determine the risk factors of post bronchoscopy biopsy-related infectious complications and whether it would delay the treatment in patients with lung cancer.
Materials and Methods: We retrospectively reviewed medical records of 206 patients receiving bronchoscopic biopsy with assistance of fluoroscopy Basic profiles, image features, and pathological diagnoses were compared between patients with and without infectious complication. For the patient who were diagnosed to have lung cancer, the time from biopsy to cancer-specific treatment was analyzed
Results: Among the 206 patients receiving bronchoscopic biopsies with assistance of fluoroscopy, twelve patients developed post-biopsy related infectious complication requiring hospitalization, including five lung abscesses, five lobar pneumonia, and two empyema. The median duration of hospitalization was 21 days (range, 8-49 days) and the median time in need of antibiotics treatment was 28.5 days (range, 12-58 days). Risk factors to develop post-biopsy related infectious complication included large lesion size (diameter more than 5.65 cm) ($p < 0.001$), sedation during procedure ($p = 0.011$), and squamous cell carcinoma cell type ($p = 0.03$). In our study, 110 (53.4%) patients were diagnosed with lung cancer, received complete staging and started cancer-specific treatment, including eleven patients with post-biopsy infectious complication. All eleven patients received adequate treatment including antibiotic with or without surgical intervention, followed by chemotherapy as a part of first-line treatment. Of note, there was no difference in time from biopsy to cancer-specific treatment between lung cancer patients with or without post-biopsy related infectious complication (21 days versus 22 days, $p = 0.864$)
Conclusions: Adequate treatment for post-bronchoscopic related infectious complication did not delay lung cancer patients to receive cancer-specific treatment.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA12

支氣管鏡超音與細針抽吸探頭壓迫右側肺靜脈誘發之急性肺水腫

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Acute pulmonary edema due to critical right pulmonary vein stenosis aggravated by endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA)

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Introduction: We report a rare and intriguing complication of endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) in a patient with advanced non-small cell lung cancer.
Case report: A 43 year-old female with advanced non-small cell lung cancer was under her first treatment course consisting of systemic chemotherapy plus immune checkpoint blockade and palliative radiotherapy to mediastinal lymphadenopathy. The mediastinal structures were infiltrated by tumor lymphadenopathies and the right pulmonary vein was compressed by the confluent group 7 lymph nodes. She underwent an uneventful sampling of group 4R and 7 lymph nodes by EBUS-TBNA 3 months ago for diagnostic purpose. Due to disease progression, rebiopsy using EBUS-TBNA was planned. The patient reported orthopnea since weeks before the procedure, and was under minimal oxygen support through the nasal cannula. She was sedated by intravenous anesthesia but became agitated particularly when the tip of the scope engaged the left main bronchus to sample the group 7 lesion. Oxygen desaturation occurred just after the 2nd puncture to group 7 lesion, thus, the procedure terminated prematurely. Chest X-ray exam after the procedure showed acute pulmonary edema and increased right pleural effusion. Her oxygen demand improved several days later after receiving non-invasive positive pressure ventilation.
Discussion and Conclusions: The acute pulmonary edema was possibly due to critical flow obstruction of the already compromised right pulmonary vein by the EBUS-TBNA scope. This is a rare yet potentially lethal condition, and should be considered in patients with major vessel compression by tumors.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA13

病例報告: 一個罕見復發性支氣管內之肝細胞癌肺轉移

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A Rare Case of Recurrent, Endobronchial Pulmonary Metastasis of Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma (HCC) distributes the fourth leading cause of cancer-related death worldwide, and the second in Taiwan. According to reported reviews, lung (55%) contributes to the most frequent involved organ of extrahepatic metastases. The typical presentation of pulmonary metastasis of HCC is noncalcified soft-tissue nodules with lower lobe predominance. The other frequently reported radiologic finding of lung metastasis of HCC is pulmonary tumor emboli. Here, we presented a rare case with recurrent, easily-detached endobronchial pulmonary metastasis of HCC.

Case Presentation: A 62-year-old male with lung metastasis of HCC suffered from progressive shortness of breath and intermittent hemoptysis. Recurrent left lower lung metastasis leaded to left main bronchus obstruction, left upper and lower lung collapse, and hematemesis for 2 times, which was improved after bronchoscopic intervention and emergent endotracheal intubation.

Discussion: Extrahepatic HCC can occur in three ways: direct extension, hematogenous spread, or lymphatic invasion. Pulmonary HCC metastases occurs via hematogenous dissemination to the pulmonary capillary network, leading to the common presentation of parenchymal soft-tissue nodules and pulmonary vascular emboli. The common sources of endobronchial metastases are kidney, breast, and colorectal cancers, but not hepatoma. Even though symptoms caused by HCC metastases were observed more frequently in the patients with bone and brain metastases, lung metastases can lead to death of respiratory failure caused by the growth of the metastatic tumors. Owing to the evolution of bronchoscopy, we got easier to approach to the intra-bronchial tumor causing respiratory stress and airway obstruction. We presented a rare case with recurrent, easily-detached intra-bronchial pulmonary metastasis of HCC, and the patient can survive better after bronchoscopic intervention. It maybe the first time we discover the unique character of HCC lung metastasis for unknown mechanism. Further study may be needed for whether the bronchial microenvironment or special bronchial tissue cell related to easily peripheral necrosis of HCC and difficulty of trans-bronchial invasion.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA14

胸膜鏡檢查在結核性胸膜炎診斷中的應用：彰基經驗分享

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Role of pleuroscopy in the diagnosis of tuberculous pleuritis : The experience in CCH

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Purpose: Pleuroscopy or medical thoracoscopy is a procedure for the diagnosis of tuberculous pleuritis. Though ADA, can help to distinguish between TB and malignancy, we can have tuberculous culture sample and susceptibility testing report via pleuroscopic biopsy. This retrospective study aimed to assess the efficacy of pleuroscopy in patients with suspected tuberculous pleural effusion and the positive rate of tuberculous culture .

Materials and Methods: A total of 59 patients with exudative pleural effusion who underwent pleuroscopy and 14 patient was diagnosed with TB pleuritis. ADA, cultures of pleural fluid, sputum, and pleural biopsy for the detection of Mycobacterium tuberculosis and pathological findings were evaluated. The diagnosis of TB infections was established by identification culture of Mycobacterium tuberculosis in the pleural effusion, sputum and/or bronchial specimens, or by evidence of caseous granulomatous inflammation on pleuroscopic biopsies.

Results: Sputum, pleural fluid, and pleural biopsy cultures were positive for M. tuberculosis in 28%, 35%, and 64% of patients with TB diagnosis, respectively. The percentage of high adenosine deaminase (ADA) levels in pleural fluid (>40 U/L) was 92% in these patient. There was one patient's tissue grew TB with low ADA levels. Under pleuroscopy, we observed pleural nodules, pleural adhesion, hyperemia, plaque-like lesions in patients with TB pleuritis. No severe adverse events were noted, and the most common minor complication was chest pain from the chest tube. Pathology report revealed granulomatous inflammation in 86% of patients with TB pleuritis. All positive TB cultures had reports of susceptibility testing.

Conclusions: Pleuroscopic biopsy had a higher accuracy than sputum and pleural effusion study in diagnosis of TB pleuritis. Though ADA levels had high sensitivity and specificity in TB diagnosis, it should not be considered an alternative to biopsy and culture. Cultures of pleural fluid and biopsy specimens have a greater diagnostic yield, and offer the susceptibility testing report . In summary, pleuroscopy is effective for diagnosis for tuberculous pleuritis compare with traditional methods.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA15

經皮擴張氣管切開術期間意外發現支氣管內或氣管內腫塊

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Unexpected Found Endobronchial or Endotracheal Masses during Percutaneous Dilation Tracheostomy

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Keywords: Endobronchial mass, Endotracheal mass, Tracheostomy

Introduction: The percutaneous dilation tracheostomy (PDT) is a common procedure in the intensive care unit (ICU). The bronchoscopy is suggested in the previous studies to guide the PDT that it may decrease the complication rate, but no study mentioned the findings of bronchoscopy during PDT. In this study, we study the bronchoscopy findings during the PDT and survey the outcome predictors in these patients.

Material and Method: In this retrospective study, we collected all the patients who received PDT from May. 2018 to May. 2020 by our group. All of the PDT operations are guided by bronchoscopy, and we all checks the airway deep to the third order of bronchi by the bronchoscopy.

Results: Thirty-two patients were done the PDT during the period. Seventeen patients could liberate from a ventilator in this admission course, 11 patients were ventilator-dependent, and 4 patients were in-hospital mortality. Nine patients (28.1%) had abnormal bronchoscopy findings that included 4 patients (12.5%), 1 patient (3.1%) had peripheral airway oozing, 1 patient (3.1%) had mucosal patches, and 3 patients had endobronchial or endotracheal masses (9.4%). Two of the 3 patients with endobronchial or endotracheal masses were ventilator dependent after then. In the multivariate binary Logistic regression analysis, the duration from respiratory failure to tracheostomy is the independent factor to predictor weaning success (Odd ratio: 1.123, p value = 0.048).

Conclusion: In this study, we found a nonnegligible high incident of unexpected found endotracheal or endobronchial mass in chronic respiratory failure patients during PDT, and a high rate of weaning failure was noted in these patients. The duration from respiratory failure to tracheostomy is one of the most important factors to predict weaning success in these patients.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA16

以細支氣管鏡及支氣管內超音波施行切片生檢時，術中使用錐狀束電腦斷層對於周邊型肺部病灶之成效

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Intra-procedural cone-beam CT combined with thin bronchoscopy and endobronchial ultrasound for biopsy of peripheral pulmonary lesions

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Purpose: The diagnostic yield of transbronchial biopsy for peripheral lung lesions (PPLs) remained challenging without navigation systems. The newly developed electromagnetic navigation bronchoscopy and augmented fluoroscopy provided the navigation ability. However, they could not confirm the final position of biopsy instruments. This study aims to evaluate the efficacy of intra-procedural cone-beam CT (CBCT) in patients who underwent peripheral bronchoscopy.

Materials and Methods: Between August 2019 and June 2020, we enrolled 54 patients underwent transbronchial biopsy using thin bronchoscopy (4.2mm of outer diameter)), radial endobronchial ultrasound (EBUS), and intra-procedure CBCT. During the patient underwent thin bronchoscopy with the guidance of radial EBUS and fluoroscopy, the bronchoscopy with biopsy forceps was kept in place and CBCT was performed. The feasibility and safety of the procedure were assessed.

Results: The median size of nodules was 22 mm [interquartile range (IQR) 21.0 mm]. A total of 22 lesions (40.7%) were invisible by fluoroscopy. The median bronchoscopy duration was 3.3 min (IQR 3.4 min), and the median fluoroscopy duration was 3.3 min (IQR 2.6 min). The median radiation exposure (expressed with dose area product) was 3225.3 μGym2 (IQR 1088.4 μGym2). The diagnostic yield was 75.9% (41/54) (95% confidence interval, 64.5% - 87.3%). By the intra-procedural CBCT image, the diagnostic yields of forceps within the lesion, adjacent to the lesion, and away from lesions, were 91.7% (33/36), 51.7% (8/14), and 0% (0/4), respectively. There were no major complications in the study.

Conclusions: For patients with PPLs, tissue sampling by radial EBUS and thin bronchoscopy combined with intra-procedural CBCT for final confirmation was feasible. The radiation dose CBCT was in an acceptable range. Further randomized clinical trial is necessary to verify the applicability.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA17

使用 Bevacizumab 的病患在執行支氣管鏡超音波合併氣管細針抽吸時非預期性出血全

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Unexceptional Bleeding of EBUS-TBNA in patient with Bevacizumab therapy

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Introduction: Vascular endothelial growth factor (VEGF) inhibitors, Bevacizumab, combined with cytotoxic chemotherapy provides additional survival benefit in lung cancer patients. Even when combined with tyrosine kinase inhibitor, Bevacizumab also demonstrated better progression-free survival rate. Although bevacizumab is beneficiary to cancer treatment, risk of bleeding must be carefully evaluated if the one needs to do invasive procedure. Previous meta-analysis study stated that bevacizumab is associated with significant increase risk of all-grade bleeding and percentage of high-grade bleeding. Despite safety of Bevacizumab related adverse effects including bleeding risk were assessed for gastrointestinal endoscopic procedure, still there is limited data about EBUS-TBNA. Here, we are going to present a patient who encounter active massive bleeding after one time of transbronchial needle aspiration without significant blood vessel on doppler examination at the time of aspiration.

Presentation of case: Under conscious sedation, the patient received real-time EBUS examination. Mediastinum lymphadenopathy at group 11R, 10R and 4 were detected. Enlarge lesion (depth 3cm and length 3cm) at 10R was focused for biopsy and doppler ultrasound was done at the same site to evaluate vascularity. EBUS-TBNA was carefully performed at 10R with needle depth of 1.5cm. Negative pressure was created with a 10-mL syringe and the procedure was done smoothly. 1.0 X 0.3 X 0.2cm length specimen was obtained. Bronchoscopic finding at that time showed blood in the lumen. Estimated amount reached nearly 300 cc with still active bleeding from puncture site. Urgent compression to bleeding site was done with endobronchial blocker. Hemostasis was obtained after compression for 30 seconds for 3 times at the puncture site. Blood clot was removed after hemostasis. Throughout the procedure, the patient was provided with nasal cannula 3 liters per minute to avoid desaturation. After the procedure, the patient was transferred to intensive care unit for observation. Next day the patient was transferred back to ordinary ward next day under stable condition without further bleeding and hemoptysis. He received further definitive treatment for his lung cancer and was discharged 5 days after the procedure.

Discussion: To our knowledge, there was limited retrospective study or case report on the EBUS-TBNA bleeding risk and safety in bevacizumab treatment patient. Here, we would like to share our experience of rare incidence of massive bleeding with EBUS-TBNA in patient taking Bevacizumab. Those patients who need to take invasive procedure should be given great precaution and detail evaluation.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA18

支氣管鏡導航系統合併內視鏡超音波對周邊肺病灶切片的角色:年輕與資深操作者的差異

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The role of virtual bronchoscopic navigation combined with endobronchial ultrasound guided transbronchial lung biopsy for Peripheral Pulmonary Lesions: The difference between the senior and junior operator.

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Purpose: This study aimed to evaluate the diagnostic value and operation time of endobronchial ultrasound (EBUS) combined with or without virtual bronchoscopic navigation (VBN) guided transbronchial lung biopsy for peripheral pulmonary lesions (PPLs) between senior and junior operators.

Materials and Methods: The 34 patients with PPLs underwent EBUS guided transbronchial lung biopsy with or without VBN. Of these patients, 15 patients were underwent by senior operator (EBUS experience 11 years) and 19 patients were underwent by junior operator (EBUS experience 2 years). The diagnostic yield, the operation time and complications were evaluated in this two groups.

Results: The mean age were 61.9 years and 24 patients were male. The mean size of PPLs were 4.1±1.8 cm. In senior operator group, 5 patients underwent EBUS with VBN and 10 patients underwent EBUS without VBN. There was no significant difference in the diagnostic yield between the VBN+EBUS group and the EBUS group (80% vs. 90%, P=0.571). The operation time in VBN+EBUS group was similar in EBUS group (16.6±6.1 min vs. 12.5±2.8 min, P=0.093). In junior operator group, 5 patients underwent EBUS with VBN and 14 patients underwent EBUS without VBN. There was no significant difference in the diagnostic yield between the VBN+EBUS group and the EBUS group (80% vs. 79%, P=0.624). The operation time in VBN+EBUS group was less than that in EBUS group (14.2±4.5 min vs. 17.6±2.5 min, P=0.046). No severe procedure related complications were observed.

Conclusions: VBN combined with EBUS is a safe and effective technique for PPLs. No matter the operator were high or less EBUS experience, VBN cannot improve the diagnostic yield. Nevertheless it can shorten the operation time if the operator were less EBUS experience.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA19

以支氣管鏡介入術處置氣管隆凸下的巨大腫瘤而成功治療惡性中央氣道阻塞之實例

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Successful treatment of central airway obstruction caused by huge subcarinal tumor: a case report

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Introduction

Malignant central airway obstruction (CAO) is most commonly a result of primary lung cancer, although it can result from any primary or metastatic intrathoracic malignancy. Clinical heterogeneity in the presentation of malignant CAO provides opportunities to adapt and utilize endoscopic technology and tools in many ways. Bronchoscopic interventions with great trained hands provide a rapid symptomatic improvement even in the critically ill patients.

Case presentation

This is a 64-year-old male patient who admitted in regular ward from MER due to progressive dyspnea, with impending respiratory failure, assisted by NIPPV. Hours later, he was transferred to MICU and received endotracheal intubation and mechanical ventilation.

Bronchoscopy exam was performed and showed a huge tumor at lower trachea and carinal area, extraluminal tumor with mass effects and endoluminal involvement, causing near complete obstruction of right main bronchus (RMB) and left main bronchus (LMB). Biopsy was done and showed squamous cell carcinoma. Self-expandable metallic stent (SEMS) was placed at LMB to keep the airway patent, but at the same time it caused complete obstruction of RMB. Occlusion of the proximal orifice of SEMS by tumor was relieved by removal of residual tumor, also assisted by electrocautery. And concurrent chemo-radiotherapy (CCRT) were initiated.

After 45 days of treatment, both main bronchus are patent and the patient discharged in good performance status.

Conclusion

We present a case of CAO with near complete obstruction of main bronchus, after successful treatment with stent placement, tumor removal, electrocautery and CCRT. Under critical dyspnea condition, it could be challenging to perform available bronchoscopic interventions. However, bronchoscopic interventions are indeed highly efficacious in management of malignant CAO.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA20

支氣管肺泡灌洗之診斷收獲率對加護病房感染社區性及院內感染肺炎病人之影響

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林口長庚呼吸胸腔內科

The Impact of Diagnostic Yield of Bronchoalveolar lavage on Outcomes between Patients with **Community-Acquired and Nosocomial Pneumonia in the Intensive Care Units.**

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RATIONALE: Bronchoscopic lavage is a useful tool to retrieve specimens for pathogen survey in clinical practice. This diagnostic tool may benefit differently in patients with community-acquired vs. nosocomial pneumonia. The results of bronchoalveolar lavage (BAL) may have important impacts on patients' outcomes.

METHODS: The study retrospectively recruited patients received bronchoscopic BAL in an intensive care unit of a tertiary care hospital. The impact of positive diagnostic yield on different types of pneumonia for the clinical outcomes was determined.

RESULTS: There were 39 patients enrolled in the study with 14 (35.9%) of them died during their ICU stay. Positive diagnostic yield with pathogens were found in 21 (53.8%) patients. The ICU mortality rate (28.6% vs. 44.4%, O.R.: 0.50; 95%C.I.: 0.13-1.89; p=0.303), ICU length of stay (35.2±4.78 days vs. 22.8±3.78 days; p =0.079), and hospital length of stay (51.5±5.11 days vs. 39.3±6.25 days; p =0.846) were similar in patients with and without positive pathogen result. However, the duration of ventilator use in patients with positive results was longer than those in patients with negative results (23.2±3.22 days vs. 15.2±1.99 days; p =0.02). The diagnostic yield was noted to be higher in patients with community acquired pneumonia (13/22,59.1%) than nosocomial pneumonia (4/17, 23.5%;O.R.: 4.69; 95%C.I.: 1.15-19.17 ; p=0.026).

CONCLUSIONS: The diagnostic yields of BAL study in community-acquired pneumonia were increased compared with those in nosocomial pneumonia. Patients with positive results in BAL study had longer duration of ventilator use than those with negative results.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA21

支氣管內雞骨頭異物梗塞-個案報告

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Chicken bone in main bronchus- Case report

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Introduction: We present here a case suffered from chronic cough over 6 months due to chicken bone aspirated in the airway.

Case presentation: This is a 73 years old female who came due to cough for more than 6 months. She was in her usual health status until 1 year ago. Intermittent dry cough developed. She then suffered from progressive productive cough in recent 6 months. There was no fever, no sore throat, no post nasal dripping, no hemoptysis, no orthopnea, no heart burning sensation. Travel history, contact history and cluster history were negative. She ever received some antitussive medication at the local clinic but in vain. She then visited our chest outpatient department. Chest CT showed bone density foriegn body located at left main bronchus with segmental consolidation. Bronchoscopy arranged and found a bony structure located at left bronchus 8 to 10 with granulation tissues surrounding and purulent secretions suctioned from obstructed orifice. Removal by forceps and basket had tried but failed due to the size and fragile bone density. A peanut accidentally found over right lower lung bronchus and was removed. Chest surgeon was consulted for foreign body removal via single port video-assisted thoracic surgery, VATS. Pathology of the foriegn reported a 2.5cm chicken bone. After the surgery, patient's cough symptoms improved after recovery.

Discussion: Foreign body aspiration into the airway is less common in adults than children. The most common aspirated foreign body by adults are organics, especially fragments of bones and seeds. Symptoms including cough, choking and dyspnea may be seen. Right localization, especially bronchus intermedius and right lower lobe, is more common. Chest X ray can be normal in upto 20 % of the case and foreign body can be detected in 26% of the patients. Foreign bodies can be removed in the majority of patients under flexible bronchoscopy. Surgical intervention may be necessary for cases that the bronchoscope fails.

Conclusions: Foreign body aspiration, although less common in adults, still should be awarded in patients who had symptoms of choking or cough. Bronchoscopy for foreign body removal should be firstly considered. In certain difficult removal cases, surgical intervention should be performed.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA22

運用內視鏡超音波、螢光透視與錐狀斷層掃描導引同次進行經氣管與經皮肺穿刺肺腫瘤切片：病例報告

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Combined Endobronchial Ultrasound, Augmented Fluoroscopy, and Cone Beam CT Guided Concomitant Transbronchial and Percutaneous Lung Tumor Biopsy: A Case Report

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With the huge advance in lung cancer treatment in this two decades, the importance of sufficient biopsy tissue for diagnosis and genetic studies could not be overemphasized. Multiple modalities are available for tissue sampling, including endobronchial ultrasound guided transbronchial biopsy (EBUS-TBB), percutaneous ultrasound-guided and computed tomography (CT)-guided biopsy. However, each method has its own limitations which lead to variable yield rates. Recently, augmented fluoroscopy (AFB) and cone beam CT (CBCT) were used for the assistance of bronchoscope guidance and lung lesion localization. Here, we reported a case whose non-samll cell lung cancer (NSCLC) was diagnosed using concomitant transbronchial and percutaneous lung tumor biopsy under combined EBUS, AFB and CBCT guidance.

A 64-year-old male patient with underlying disease of coronary artery disease and hypertension presented to our pulmonology outpatient clinic with the chief complaint of intermittent blood-tinged sputum for about 5 months. The chest radiograph showed right lower lung lesion and the carcinoembryonic antigen (CEA) level was 34.95. The chest CT revealed a lobulated lung mass measuring about 4.8cm in largest dimension with pleural traction at right lower lung. The whole body bone scan disclosed right 4^{th} rib metastasis. The endobronchial ultrasound guided transbronchial biopsy (EBUS-TBB) was performed to the RB6 peribronchial lesion. The pathology reported adenocarcinoma, but the number of the tumor cells was less than 100 which was insufficient for further immunohistochemical and molecular studies. Repeated bronchoscopy with EBUS-TBB still only showed fibrotic bronchial tissue without evidence of malignancy. Due to the sharp angle of RB6 bronchus, we performed the third trial of tumor biopsy under augmented fluoroscopy and cone beam CT guidance in the hybrid operating room. With the patient under general anesthesia, concomitant transbronchial biopsy (TBB) and percutaneous transthoracic needle biopsy (TNB) were performed to the RLL tumor. Successful tissue sampling was achieved this time with the specimen from the TBB and the TNB both reported adenocarcinoma. The EGFR study showed L858R mutation and the afatinib treatment was started 9 days later.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA23

支氣管鏡超音波併用冷凍切片在肺週邊性病灶之診斷

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Endobronchial Ultrasound with Cryobiopsy in Peripheral Lung Lesions

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Purpose: Diagnosis of peripheral pulmonary lesions by endobronchial ultrasound (EBUS) with cryobiopsy has great potential to development. We hereby report our practice experience for this new skill.

Materials and methods: This is a retrospective observational study. The aim of this study is to evaluate the benefit and complication of the transbronchial lung biopsy (TBLB) with cryo-probe compared to forceps. Consecutive patients were enrolled from July 1st, 2020, to October 15th, 2020 in a medical center MacKay Memorial Hospital, Taipei, Taiwan. Total 52 patients with peripheral lung lesion were detected by endobronchial ultrasound. 17 patients accepted TBLB with cryo-probe, and the other 35 patients accepted conventional forceps biopsy.

Results: The sample size is larger in cryobiopsy compared to forceps biopsy (mean: 0.76cm vs 0.28cm, $P<0.001$). The diagnostic yield in cancer patients is without significant difference. (93.3% vs 71.4%, $P=0.2853$). And pneumothorax after TBLB was noted in only one patient from forceps biopsy (1/35, 2.86%). There is no pneumothorax or life-threatening bleeding observed in endobronchial cryobiopsy.

Conclusions: TBLB with cryo-probe can offer larger sample size. There is no significant difference in diagnostic yield and complication rate in our study. Further large scale studies are needed to verify our results.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA24

早期肺腺癌以單純毛玻璃陰影表現使用胸腔鏡肺楔形切除的經驗：四例切除個案報告分析

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Early Lung Cacner Manifested as Ground-Glass Opacity: Report of Four Cases Undergoing Sublobular Resection Through Video-Assisted Thoracoscopic Surgery.

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Purpose: GGO-dominant clinical stage IA lung adenocarcinomas are a uniform group of tumors that exhibit low-grade malignancy and have an extremely favorable prognosis. These patients can be successfully treated with wedge resection through video-assisted thoracoscopic surgery (VATS).

Materials & Methods: Herein three patients were found with four sub-centimeter pure GGOs by low dose, high resolution thoracic CT scan. There were no other metastatic sites were noted after staging procedures.

Results: These patients underwent wedge resections through VATS. The mean operation time was 35 ±12 minutes. Carcinoma in situ (non- invasive bronchoalveolar type) were pathologically proved. They were followed from 3 months to 8 years without recurrence or metastasis.

Conclusion: For patients with stage IA pure GGO lung adenocarcinoma, Limited resection through VATS will be minimally invasive as well as achieve satisfactory outcomes.

Keywords: Ground glass opacity, Sublobular resection, Adenocarcinoma, Video-assisted thoracoscopic surgery.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA25

血漿環狀核糖核酸 hsa_circ_0000190 與晚期肺癌之腫瘤進展和治療反應的關聯性

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Plasma Level of Circular RNA hsa_circ_0000190 Correlates with Tumor Progression and Poor Treatment Response in Advanced Lung Cancers

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Purpose: Lung cancer (LC) causes the majority of cancer-related deaths. Circular RNAs (circRNAs) were reported to play roles in cancers by targeting pro- and anti-oncogenic miRNAs. However, the mechanisms of circRNAs in LC progression and their prognostic value of treatment response remain unclear.
Materials and Methods: Combining next-generation sequencing (NGS) with bioinformatics analysis in lung adenocarcinoma and human lung cell lines, we identified hsa_circ_0000190 as a potential marker in lung cancer and further detected its secreted levels from lung cancer cell lines in the conditioned media. To validate if hsa_circ_0000190 reflects disease status, we monitor lung cancer patients' hsa_circ_0000190 levels in peripheral blood samples using liquid biopsy (LB)-based ddPCR, and correlate the plasma levels of hsa_circ_0000190 with clinical disease status of advanced-LC patients.
Results: By using next-generation sequencing (NGS) of LC cell lines' transcriptomes, we identified highly overexpressed hsa_circ_0000190 and hsa_circ_000164 as potential biomarkers. By using the highly sensitive RT-ddPCR method, these circRNAs were shown to be secreted by cell lines and were detected in human blood. Clinical validation by RT-ddPCR was carried out on 272 (231 LC patients and 41 controls) blood samples. Higher hsa_circ_0000190 levels were associated with larger tumor size ($p < 0.0001$), worse histological type of adenocarcinoma ($p = 0.0028$), later stage ($p < 0.0001$), more distant metastatic organs ($p = 0.0039$), extrathoracic metastasis ($p = 0.0004$), and poor survival ($p = 0.047$) and prognosis. Using liquid biopsy-based RT-ddPCR, we discovered the correlation between increased hsa_circ_0000190 plasma level ($p < 0.0001$) and higher programmed death-ligand 1 (PD-L1) level in tumor ($p = 0.0283$). Notably, long-term follow-up of the immunotherapy treated cases showed that upregulated plasma hsa_circ_0000190 level correlated with poor response to systemic therapy and immunotherapy ($p = 0.0002$, 0.0058, respectively).
Conclusions: Secretory circRNAs are detectable in blood by LB-based RT-ddPCR and may serve as blood-based biomarkers to monitor disease progression and treatment efficacy.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA26

少見的良性骨腫瘤-纖維性發育不良的臨床表現：病例報告及文獻回顧。

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Unusual Benign Bone Tumor- A Presentation of Fibrous Dysplasia: A Case Report and Literature Review.

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Introduction

It is difficult to evaluate rib tumors through chest X-ray. Chest CT and biopsy are often needed to determine the nature of the tumor. The commonest rib tumor is metastasis from other sites, such as lung, breast, and prostate. Otherwise, fibrous dysplasia is the commonest benign rib tumor. Here we present a case of a large rib tumor. After surgical excision, fibrous dysplasia is diagnosed by pathology.

Case Report

The 38 year-old gentleman denied systemic disease before. He had a chest wall mass for 10+ years. He denied chest pain, cough or body weight loss. The chest wall mass progressed gradually for 7 years. Therefore, he visited our Chest surgeon for help. CXR showed a left extrapulmonary lesion. Chest CT showed left third rib expansile osteolytic bone tumor. Chest wall excision and thoracoplasty were performed smoothly. The pathology showed fibrous dysplasia, 14*11*10cm. He was discharged under stable condition.

Discussion

Fibrous dysplasia often happens in patients during 10 y/o to 40 y/o. It may occur in proximal femur, tibia, ribs, skull or any other bone area. Patients with fibrous dysplasia are often asymptomatic. If pain happens, it suggests fracture or compression of the neighboring tissues. Radiography would show osteolytic medullary lesion, and thick, sclerotic reactive bone (rind sign). CT would show ground glass areas. About the treatment, it is largely dependant on patient's symptoms. About our patient, due to progressive enlargement, surgical intervention and pathology proof are suggested to him to rule out other etiology. Regular image follow-up is needed to avoid recurrence.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA27

探討晚期具有上皮生長因子(EGFR)基因突變之肺腺癌病人在第一線標靶藥物與後續化療藥物的選擇與治療成效：台灣癌症登記資料庫世代研究

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Treatment options using first-line tyrosine kinase inhibitors and subsequent systemic chemotherapy agents for advanced EGFR mutant lung adenocarcinoma patients: Taiwan cancer registry cohort study

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Objectives: Large-scale, population-based real-world studies on the treatment outcomes of first-line tyrosine kinase inhibitors (TKIs) and subsequent systemic chemotherapy agents for lung adenocarcinoma (with activating epidermal growth factor receptor [EGFR] mutations) remain limited.
Materials and Methods: From March 2014 to December 2016, patients with advanced lung adenocarcinoma, identified from the Taiwan Cancer Registry were included in this study if they received any of the three TKIs as first-line treatment. The primary outcome was overall survival (OS). The secondary outcome was time-to-treatment discontinuation (TTD).
Results: A total of 4,889 patients (median age: 67 years and two-thirds with distant metastasis) were recruited (1,778 gefitinib, 1,599 erlotinib, and 1,512 afatinib users). A 1:1 propensity score (PS)-matched cohorts of 1,228 afatinib/erlotinib and 1054 afatinib/gefitinib was created. After PS matching, it was found that afatinib was not associated with better OS (afatinib vs. erlotinib, HR: 0.96, 95% CI: 0.86–1.07; afatinib vs. gefitinib, HR: 0.91, 95% CI: 0.81–1.02). In the subgroup analysis, afatinib demonstrated a survival benefit in patients with active smoking (afatinib vs. erlotinib, HR: 0.69, 95% CI: 0.51–0.93; afatinib vs. gefitinib, HR: 0.67, 95% CI: 0.48–0.94) and ECOG > 1 (afatinib vs. erlotinib, HR: 0.79, 95% CI: 0.63–0.99; afatinib vs. gefitinib, HR: 0.78, 95% CI: 0.62–0.98). A total of 41.1% (n = 1992) of first-line TKI users received subsequent chemotherapy. Among the three TKI groups, pemetrexed usage was associated with better OS compared with other chemotherapy agents, with the exception of gemcitabine in the afatinib and gefitinib groups. Pemetrexed and gemcitabine had the longest TTD of 3–4 months.
Conclusions: Among patients with EGFR mutant lung adenocarcinoma, afatinib use may not provide longer OS compared with first-generation TKIs. Afatinib may be preferably considered among patients with active smoking and should not be withheld among those with worse performance status. With 40% of patients receiving subsequent chemotherapy, pemetrexed may be the preferred agent, while gemcitabine can be a reasonable alternative.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA28

臺灣之非小細胞肺癌合併 KRAS 基因突變的病人特徵

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Characteristics of *KRAS* Mutation in Taiwan with Never-smoking Predominant Non-small Cell Lung Cancer

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Introduction: Kirsten rat sarcoma (*KRAS*) mutation (*KRASm*) is associated with smoking and poor prognosis in non-small cell lung cancer (NSCLC) patients. We aimed to survey NSCLC harboring *KRASm* in Taiwan, where never-smoking lung adenocarcinoma predominates.

Methods: NSCLC patients with *KRASm* were enrolled and tested on 4 driver genes and programmed death-ligand 1 (PD-L1) expression. We analyzed their clinical features, pathological reports, co-driver genes, PD-L1 status, responses to immune check point inhibitor (ICI), and survivals.

Results: We studied 131 patients, aged 66.0 year-old as median, 22.9% female, and 22.1% never-smokers. In ever-smokers, 62.7% of primary tumors were located in upper lobes, compared with 58.6% in lower lobes (p=0.009) of never-smokers. G12C (38.2%) were the most common *KRASm*, with similar incidence between never and ever-smokers (27.6% vs 41.2%, p=0.266). There were two *EGFR* co-mutation, one *ALK* translocation, and one *BRAF-V600E* co-mutation, but not co-mutation with *HER2* exon 20 insertion. The median overall survival was 57.0 months in early stage, and 9.0 months in late stage patients. In early stage patients, G12D appeared to associate with less recurrences (p=0.031) and better survival (p=0.049). PD-L1 expression were positive in 57.9% patients, and the expression level were higher in ever-smokers (p=0.011). Half of those with high PD-L1 expression responded to ICI.

Conclusion: Never-smokers composed more than one-fifth *KRASm* in NSCLC in Taiwan, majorly female, with primary tumors located mostly in lower lobes, with similar G12C mutation rates compared with smokers. Smoking was associated with PD-L1 expression. Patients with high PD-L1 expressions responded well to ICIs.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA29

晚期非小細胞肺癌病人接受第一線表皮生長因子接收器-酪胺酸酶抑制劑治療後產生 T790M 抗藥性，其使用的不同種類第一線酪胺酸酶抑制劑對接續 osimertinib 治療臨床預後的影響

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The Impact of Different First-Line EGFR-TKIs on the Clinical Outcome of Sequential Osimertinib Treatment in Advanced Non-Small-Cell Lung Cancer Patients with Secondary T790M Mutation

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Objectives: The main objective was to investigate the impact of different first-line Epidermal Growth Factor Receptor (EGFR)-Tyrosine Kinase Inhibitor (TKI)s to the clinical efficacy of osimertinib in *EGFR*-mutant Non-small-cell Lung Cancer (NSCLC) patients who were T790M-positive after progressive disease to first-line EGFR-TKIs.

Materials and Methods: From 2011 to 2018, we enrolled advanced NSCLC patients who harbored exon 19 deletion or L858R with gefitinib, erlotinib and afatinib as first-line EGFR-TKIs treatment.

Results: A total of 733 patients were enrolled for analysis. 347 patients received gefitinib, 295 patients received erlotinib and 91 patients received afatinib as first-line treatment. The Objective Response Rate (ORR) was 72.1%, 73.2%, 67.8% in patients with gefitinib, erlotinib and afatinib, respectively. The median progression-free survival of first-line EGFR-TKI (PFS1) was 10.9 months, 11.5 months and 16.9 months in the gefitinib, erlotinib, and afatinib group, respectively. Patients given gefitinib (adjusted HR 1.35; 95% CI, 1.19 to 1.53, p <0.001) and erlotinib (adjusted HR 1.10; 95% CI, 0.98 to 1.25, p = 0.090) as first-line treatment had a higher risk of progressive disease than patients given afatinib. 151 patients who harbored T790M after progressive disease to first-line EGFR-TKIs received osimertinib as subsequent treatment. The ORR was 56.3%, and the Disease Control Rate (DCR) was 88.0%. The median PFS of osimertinib (PFS2) was 10.1 months, and the median PFS1 + PFS2 was 27.5 months. The median OS of osimertinib was 30.2 months, and the median OS from first-line EGFR-TKI was 61.3 months. Concerning different first-line EGFR-TKI use, there was no significant difference in median PFS2 and PFS1+PFS2.

Conclusion: Our research demonstrated that advanced *EGFR*-mutant NSCLC patients given afatinib as first-line EGFR-TKI treatment experienced better PFS than patients given gefitinib and erlotinib. Not only afatinib but also gefitinib and erlotinib sequential osimertinib treatment provided good clinical efficacy in patients harbored acquired T790M.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA30

以瀰漫性細小結節表現之原發性肺癌

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Primary Lung Cancer Presenting as Diffuse Pulmonary Tiny Nodules: A Case Report

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BACKGROUND

Diffuse pulmonary tiny nodules with chronic clinical course can usually arise from atypical infection such as miliary tuberculosis, pneumoconiosis, malignancy and other miscellaneous disease. Primary lung cancer rarely presents with this unique radiologic pattern, which creates a diagnostic challenge.

CASE PRESENTATION

We report a case of 57-year-old female patient without smoking history, who had chronic cough and dyspnea on exertion. Radiologic image study presented with diffuse pulmonary tiny nodules and final pathologic study revealed primary lung adenocarcinoma. Disseminated distal metastasis was noted after staging. Epidermal growth factor receptor(EGFR) showed exon 21 L858R mutation. Tyrosine kinase inhibitors was prescribed and spectacular regression on following image was noted.

CONCLUSIONS

Our case's image pattern is similar to that of miliary intrapulmonary carcinomatosis, which may mimic miliary tuberculosis or other origin hematogenous metastases. Further histologic evidence is important for the definitive diagnosis. This radiologic pattern of primary lung cancer may have high rates of adenocarcinoma and EGFR mutation rate.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA31

研析傳統中藥茵梔黃之主成分透過抑制 PD1/PDL1 訊遞勝任新穎輻射增劑之機制

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The evaluation for Yin Zhi Huang components as a novel radio-sensitizer in lung cancer cells

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Purpose: For many years, lung cancer is a life-threatening disease to people in Taiwan and all over the world. In literature, Yin Zhi Huang has been reported to effectively inhibit T-cell activities. However, whether it is cytotoxic to the normal cells and feasible to serve as a radiosensitizer are never studied.

Method: We have selected ten major components from Yin Zi Huang and examined their effects on normal and lung cancer cells with the cell viability assay, cell cycle distribution analysis, radio-sensitization assay. Then, for the useful individual prescriptions, we performed the Western blotting to clarify its molecular mechanism.

Results: 1. Among the ten components examined, Scoparone, Chlorogenic acid, Ursolic acid, Luteolin, Baicalein and Baicalin can inhibit the cell viability, and Ursolic acid is most effective. 2. These six compounds can also induce cell cycle arrest, and enhanced radio-induced cell cycle arrest. Similarly, Ursolic acid is most effective. 3. Ursolic acid and Luteolin can obviously enhanced radio-induced cytotoxicity and cell death. 4. In Western blotting, several molecules are altered by these compounds. Interestingly, Ursolic acid and Luteolin are firstly found to inhibit the expression of PD-L1, which is one of the potential targets in cancer immunotherapy.

Conclusion: Our results show that alone or combined with radiation, several of the major components of Yin Zhi Huang are effective in killing the lung cancer cells but do no harm to the normal cells. We will further figure out and understand the mechanism of how Ursolic acid and Luteolin to induce apoptosis and radio-sensitization in lung cancer cells via the suppression of PD-L1, and whether these breakthrough findings in vitro can also work in BALB/c nude mice lung cancer xenograft model.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA32

慢性炎症會促進煙草致癌物誘發的肺癌並決定免疫療法的功效

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Chronic inflammation promotes tobacco carcinogen-induced lung cancer and determines the efficacy of immunotherapy

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Background
Chronic obstructive pulmonary disease (COPD) is an inflammatory disease that is associated with an increased risk of lung cancer. *Pseudomonas aeruginosa* (PA) infections are frequent in COPD patients, which increases lung inflammation and acute exacerbations. However, the role of PA-induced inflammation in lung tumorigenesis and the efficacy of immune checkpoint blockade remain poorly understood.
Materials and Methods
A murine model of lung cancer was initiated by treating FVB/NJ female mice with tobacco carcinogen nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) alone, or in combination with PA-lipopolysaccharide (LPS). The cell, cytokine, and transcript profile from the bronchoalveolar lavage (BAL), lung protein, and tumor tissues were evaluated. The anti-tumor efficacy of immunotherapy using anti-programmed cell death-1 (PD-1) and anti-lymphocyte antigen 6G (Ly6G) antibodies was determined in NNK and NNK/LPS-induced tumor-bearing mice. Immune gene signatures were analyzed for the correlation of PD-1 blockade responsiveness in human non-small cell lung cancer (NSCLC) cohort and the murine lung cancer model.
Results
LPS-mediated chronic inflammation enhanced NNK-induced lung tumor growth and increased inflammatory cell infiltrates, including macrophages, neutrophils, and lymphocytes. Cytokine/chemokine and recruitment of $CD4^+$ T cells, Th1, Th17, and Tregs cells, and myeloid-derived suppressor cells (MDSC) increased in NNK/LPS-treated mice. Induced gene expression of inhibitory checkpoint molecules was accompanied by the expansion of exhausted tumor-infiltrating T cells and co-localized PD-1 expression in NNK/LPS-induced lung tumors. Anti-PD-1 antibody reduced tumors in NNK/LPS-treated mice with a 10-week LPS treatment, but failed to inhibit tumor growth when LPS exposure was prolonged to 16 weeks. Anti-Ly6G antibody with depletion of MDSCs alone reduced tumor growth and combined with anti-PD-1 antibody further enhanced the anti-tumor activity in 16-week NNK/LPS-treated mice. Finally, we identified immune gene signatures from human lung cancer dataset of PD-1 blockade, which predicted treatment responses and survival outcome, and overlapped with those from the mouse model.
Conclusions
This study demonstrated that LPS-mediated chronic inflammation creates a favorable immunosuppressive microenvironment for tumor progression and correlates with the efficacy of anti-PD-1 treatment in mice. Immune gene signatures overlapped with human and mouse lung tumors provide potentially predictive markers for NSCLC patients under immunotherapy and connected this murine lung tumor model with clinical relevance.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA33

慢性腎臟病在肺腺癌病患使用愛寧達存活之影響

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The impact of chronic kidney disease in adenocarcinoma patients receiving pemetrexed

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Purpose: Lung cancer is the leading cause of cancer-related deaths worldwide. In patients without druggable driver mutations, platinum based doublet chemotherapy is the standard therapy. In previous studies, pemetrexed plus platinum doublet provided same survival benefit compared with other platinum based doublet with fewer side effects. However, in phase II and phase III pemetrexed studies, patients with estimate 24 hours Creatinine Clearance Rate (Ccr) <45 (ml/min) were excluded. Thus, pemetrexed is not suitable for patients with impaired renal function. In clinical practice, not all clinical physician prescribed pemetrexed after checking creatinine clearance rate and some patients with borderline renal function still received pemetrexed without significant complications. Thus, we conduct a retrospective study to evaluate pemetrexed in lung adenocarcinoma patients with impaired renal function.

Materials and Methods: This is a retrospective cohort study of lung adenocarcinoma patients without sensitive driver mutations, receiving 1st line pemetrexed in National Taiwan University Hospital Hsinchu branch from January 1, 2010 to Dec 31, 2015. Cancer registration data from our cancer center were collected. After case selection, chart review for demographic data, comorbidities, pathology, and EGFR, ALK mutation status were completed. Progression free survival and overall survival after receiving first line pemetrexed were compared between Ccr <45 (ml/min) and Ccr≧45 (ml/min) using logistic and Cox regression analyses, respectively.

Results: In our study, 901 patients were enrolled, and a total 70 patients fit our criteria. Among them, 65(92.9%) patient with Ccr≧45 (ml/min) and 5 (7.1%) patient with Ccr<45 (ml/min).
In survival analysis, progression free survival (PFS) are lower in patient with impaired renal function (Ccr<45 ml/min) (3.46 v 8.2 months; HR, 3.13; 95% CI, 1.09 to 8.91). However, the overall survival (OS) (6.6 v 12.8 months; HR, 1.26; 95% CI, 0.30 to 5.29) shows no difference between the 2 groups. The other significant poorer prognostic factor in PFS is patient with COPD. In overall survival (OS), patients with male gender, age ≥ 65, and lung cancer with distant metastasis were poorer prognostic factors.

Conclusions: In conclusion, using pemetrexed in fist line treatment in wild-type lung adenocarcinoma in patients with estimate Ccr <45 ml/min may result in lower PFS but not OS.
However, there was a trend toward decrease OS possible statistically insignificant because of small sample size. Further large scale studies are required for clarifying this issue.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA34

原發性肺部淋巴上皮瘤樣癌:病例報告

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Primary lymphoepithelioma-like carcinoma of the lung : A Case Report

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Abstract

Small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC) comprise approximately 95 percent of all lung cancers. Other cell types comprise approximately 5 percent of malignancies arising from the lung. We present a case of a 63-yr-old Taiwanese male, smoker, with history of Chronic hepatitis B and Diabetes mellitus on regular medication. He was referred to the chest OPD for abnormal chest x- ray noted during company check-up. Diagnostic evaluation revealed two masses in the left lower lung. Bronchoscopy and CT guided biopsy did not reveal a definite diagnosis. Thus thoracoscopic lung wedge resection was done and revealed carcinoma with a dense inflammatory background under intraoperative frozen sections. Thoracoscopic lobectomy of the left lower lobe, radical lymph node dissection and pneumolysis were done. Pathologic diagnosis was found to be lymphoepithelioma-like carcinoma and was positive for lymph node metastasis (TNM stage cT2bN2M0, pT2bN2M0), Stage IIIA. Serum EBV viral load was less than 200 copies/ml. ENT consultation and neck CT scan were done to rule out nasopharyngeal carcinoma.
Lymphoepithelioma like carcinoma are tumors mainly found in Asians, and are associated with the Epstein Barr virus and not with smoking. They are thought to have a better prognosis and to be more chemosensitive. The need for surgical treatment and recognition of lymphoepithelioma-like carcinoma as a distinct clinicopathological entity is emphasized. A review of literatures will be presented.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA35

ALK 陽性非小細胞肺癌病患使用 lorlatinib 治療之療效與安全性研究

Real-world efficacy and safety of lorlatinib in advanced ALK-positive NSCLC patients

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Background: In Taiwan, about 4.3% patients with lung adenocarcinoma were found to have *Anaplastic Lymphoma Kinase (ALK*) translocation. Although clinical trial has disclosed the efficacy and adverse events of lorlatinib and it has been approved for second- or third-line treatment of *ALK*-positive metastatic non-small cell lung cancer (NSCLC), the real-world data in Taiwan is still limited.
Methods: This retrospective study was conducted on ALK-positive NSCLC patients at Taichung Veteran General Hospital. We enrolled patients treated with lorlatinib during the period from December 2017 to August 2020. Those treated with first line lorlatinib were not included. We evaluated the efficacy of lorlatinib and its association with prior ALK inhibitor(s) treatment and accessed the adverse events, which focused on the dyslipidemia.
Result: A total of 22 *ALK*-positive patients were analyzed. The median age was 49 years. Of them, 12 patients were female, 17 patients were non-smokers, 15 patients had ECOG performance status 0-1, and 18 patients had brain metastasis. All patients had received at least one second-generation ALK inhibitor(s), while 12 patients had history of crizotinib treatment. After exclusion of 8 patients without measurable lesion, the objective response rate and disease control rate were 35.7% and 64.3%, respectively. The median progression-free survival was 6.2 months. The overall survival was not reached. With regards to the impact of prior therapies, patients with only second-generation ALK inhibitor(s) treatment (n =10) experienced a numerically longer progression-free survival than those with both crizotinib and second-generation ALK inhibitor(s) treatment (n =12) (15.2 vs. 6.2 months). Moreover, patients who benefited more from prior ALK inhibitor(s) (n =15) also had a numerically longer progression-free survival than those who did not (n =7) (6.5 vs. 3.5). In the case of adverse events, 94.7% patients had dyslipidemia and 21.1% patients were in Grade 3 or 4. None of patients discontinued the treatment owing to dyslipidemia.
Conclusion: The real-world efficacy of lorlatinib and adverse events were similar with that of clinical trial. History and efficacy of prior ALK inhibitor(s) treatment may influence the efficacy of subsequent lorlatinib treatment.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA36

晚期肺腺癌病患細胞程式死亡-配體 1 高表現 :接受緊急愛寧達注射併放療及轉移切除術接續免疫療法案例分享

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A 52y/o male patient with Advanced NSCLC(adenocarcinoma T4N3M1C PD-L1> 50%,EGFR-,ALK-,ROS-),received concurrent pemetrexed plus local R/T plus metastasectomy plus pembrolizmab :experience sharing

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Introduction:
Lung cancer ranked most common cancer in nationwide. Majority of these patients have advanced stage while diagnosis. These patients were managed exclusively with C/T improved QOL. Update therapies have increased survival in patients with metastatic disease. Patients with oligo-metastatic disease have a better long-term prognosis than those with more advanced NSCLC and may benefit from systemic therapy combined with local treatment (mainly radiotherapy and/or surgery. The most common metastatic site in NSCLC is the brain, metastases to the contralateral lung, liver, and bone.
Materials and Methods: case brief description
The 51 years old male had past illness of T2DM, Bipolar disorder, hyperlipidemia and old CVA with right hemiparesis. He was diagnosed LUL adenocarcinoma with bone metastases of T8/T9 since June 2020.This time, he admitted on Aug 2020 for dyspnea and productive bloody sputum. After admission, On 8th day. rescue radiotherapy and neurosurgeon consultation for surgical decompression and stabilization all were urgently disposed. Then he received chemotherapy with pemetrexed on Sep 2020 Suddenly left leg weakness was told, MRI revealed osseous metastasis in T8 vertebra with epidural extension and cord compression. He was received T8 laminectomy and T6/7, T9/10 spinal fusion-posterior spinal fusion with spinal instrumentation, the very next day then transferred to ward. Immunotherapy with pembrolizemab was performed on mid-Sep stable after surgery and after stitch removaland no side effect was found.
Results The ECOG, hemoptysis , oxygenation and his following CXR all improved.
Discussion:
The strategies for the different oligo-metastatic disease remain to be defined. Evidence on the management of patients with oligo-metastasis (NSCLC), focusing on the role of R/T or surgery is area of controversy and needed future guide.
Conclusion:
Survival in patients who present with oligo-metastatic NSCLC at diagnosis and who will respond to the initial systemic therapy still unclear. Multimodal strategy about managing oligo-metastatic patients needed to be searched.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA37

不同驅動突變對非小細胞肺癌 PD-L1 表現的影響

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Various impacts of driver mutations on the expression of PD-L1 of non-small cell lung cancer

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Background: We've recognized the association of driver mutations with the programmed cell death-ligand 1 (PD-L1) expression in non-small cell lung cancer (NSCLC), where patients without actionable driver mutations were more likely to present strong positive PD-L1. However, the impact of individual driver mutation on the PD-L1 expression is still not yet well-documented.
Methods: This is a retrospective study that included patients with NSCLC at TCVGH from December 2009 to August 2020. Six oncogenic drivers were tested; *EGFR*, *KARS*, *HER2*, and *BRAF*^{V600E} were assessed by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS), *ALK* fusion was tested with Ventana IHC, and *ROS1* fusion was detected by fluorescent in situ hybridization. The PD-L1 status was accessed by the SP263 assay.
Result: A total of 1,001 NSCLC patients were included. The median age was 64 years (range 22-97). Patients with younger age, male gender, smoking history, and non-adenocarcinoma histology were more likely to have positive PD-L1 expression. Patients with smoking history and non-adenocarcinoma histology were more likely to have strong PD-L1 expression. As compared with *EGFR*/*ALK*-wild type population, *EGFR*-mutant (aOR 0.74 [0.53-1.03], P = 0.078 and 0.67 [95% CI 0.42-1.07], P = 0.094) and *HER2*-mutant (aOR 0.92 [95% CI 0.31-2.76], P = 0.886 and 0.42 [95% CI 0.05-3.35], P = 0.413) patients had a similar low PD-L1 and strong PD-L1 positive rate. *BRAF*^{V600E}-mutant patients had a numerically higher PD-L1 and strong PD-L1 positive rate (aOR 2.64 [95% CI 0.49-14.23], P = 0.258 and 1.89 [95% CI 0.35-10.19], P = 0.461). Patients with fusion mutation (*ALK* and *ROS1*) (aOR 2.32 [95% CI 1.10-4.88], P = 0.027 and 2.33 [95% CI 1.11-4.89], P = 0.026), *KRAS* mutation (aOR 2.58 [95% CI 1.16-5.75], P = 0.020 and 2.44 [95% CI 1.11-5.35], P = 0.026), and non-adenocarcinoma histology (aOR 2.73 [95% CI 1.72-4.34], P < 0.001 and 1.93 [95% CI 1.13-3.30], P = 0.016) all had a significantly higher PD-L1 and strong PD-L1 positive rate.
Conclusion: Individual driver mutations had various impacts on the PD-L1 expression of NSCLC. Our prior study has identified strong PD-L1 expression as a poor prognostic factor in *EGFR*-mutant patients treated with EGFR-TKI. Its role among the others are still under investigated.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA38

轉移性尿路上皮癌引起的肺空化類似肺癌表現：病例報告

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Pulmonary Cavitation lesions from metastasized urothelial carcinoma mimic lung cancer, a case report

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Abstract

Urothelial carcinoma (UC, also called transitional cell cancer, TCC) of the upper urinary tract is uncommon, accounting for only 5-10% of UCs and 5−10% of all renal tumors. Some recurrent cases associated with the bladder UC have been reported after long-term latency [1,2]. However, there have been few cases of late pulmonary metastasis of upper urinary tract UC. Here, we present a case of urothelial carcinoma complicated with lung metastasis and pulmonary cavity lesions after 5 years follow-up. This case illustrates several distinctive aspects for lung cavitary lesions formation in patient with UC. First, primary lung cancer must be considered when lung cavitary lesion are detected. Second, diagnosis of infection related to lung cavity lesions, like pulmonary Tuberculosis (TB), pulmonary aspergillosis, or even lung abscess, should be carefully excluded in the immunocompromised host. Third, UC has a similar histology to adenocarcinoma. Therefore, we could distinguish UC from lung adenocarcinoma with immunohistochemistric stains by GATA3 and TTF-1. In conclusion, if lung cavity formation in the host with malignancy is detected, further survey of infection, primary lung cancer, and metastasized cancer should be considered.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA39

RELAY, ERLOTINIB 併用 RAMUCIRUMAB 或安慰劑於未經治療的 EGFR 突變轉移性非小細胞肺癌：依據 EGFR 突變類型結果

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RELAY, erlotinib plus ramucirumab or placebo in untreated EGFR-mutated metastatic NSCLC: outcomes by EGFR mutation type

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Purpose: In *EGFR*-mutated, metastatic NSCLC, outcomes from EGFR tyrosine kinase inhibitors have differed historically by mutation type (lower benefit reported in patients with exon 21-L858R [ex21] versus exon 19 deletion [ex19]). In phase 3 RELAY, ramucirumab+erlotinib provided superior progression-free survival (PFS) versus placebo+erlotinib. Additional efficacy and safety by mutation type are reported here for the first time.

Materials and Methods: Patients with untreated metastatic NSCLC, an *EGFR* ex19 or ex21 mutation, and no CNS metastases were randomized(1:1) to erlotinib (150mg/day) with either ramucirumab (10mg/kg) or placebo, Q2W, until RECIST1.1-progression or unacceptable toxicity. Stratification factors included ex19/ex21 and East-Asian/Other. Primary endpoint: PFS. Secondary and exploratory endpoints included objective response rate (ORR), disease control rate (DCR), duration of response (DOR), safety, PFS2, biomarker analyses. Statistical analyses included Cox regression and Kaplan-Meier estimation. NCI-CTCAE 4.0 evaluated adverse events (AEs).

Results: More patients with ex21(83%) versus ex19(72%) were of Asian race. Ramucirumab+erlotinib demonstrated PFS benefit in ex19(0.651[0.469-0.903], p=0.01) and ex21(0.618[0.437-0.874], p=0.006). ORR showed consistent improvements across mutation types for ramucirumab+erlotinib (ex19:79%; ex21:74%) versus placebo+erlotinib (ex19: 83%; ex21: 66%). DCR for ex19 and ex21 was 96% and 95%, respectively, regardless of treatment arm. Safety profile (Grade≥3, serious AEs, dose adjustments) was similar between mutation types. Exploratory data are forthcoming.

Conclusions: Ramucirumab+erlotinib-treated patients with ex21 mutation had similar treatment benefit as patients with ex19 mutation, which was consistent with that of ITT. Safety profiles were as expected. Results support ramucirumab+erlotinib as first-line therapy for both ex19/ex21-positive metastatic NSCLC.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA40

Ramucirumab 和 Erlotinib 治療 EGFR 突變轉移性非小細胞肺癌全球第三期研究 RELAY 中台灣患者的有效性和安全結果

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Efficacy and Safety of Ramucirumab (RAM) plus Erlotinib (ERL) in Taiwanese Patients with Untreated, *EGFR*-Mutated Metastatic Non-Small-Cell Lung Cancer (mNSCLC) Participating in the Global Phase 3 RELAY Study

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Purpose: In the RELAY study, RAM plus ERL demonstrated superior progression-free survival (PFS) to placebo (PBO)+ERL in patients with untreated, *EGFR*-mutated mNSCLC, with no new safety signals. We present efficacy and safety data for the Taiwanese participants from RELAY.
Methods: RELAY included patients aged ≥18 years (≥20 years in Taiwan) with *EGFR*-mutated stage IV mNSCLC and ECOG PS 0/1.[1] Primary endpoint was investigator-assessed PFS, defined as time from randomization to radiographic progression (by RECIST v1.1) or death due to any cause, whichever was earlier. Secondary endpoints included overall response rates (ORR: complete plus partial responses), duration of response (DoR), and tolerability. Descriptive statistics were used for the analysis of the Taiwanese patients from RELAY.
Results: Fifty-six Taiwanese patients (RAM+ERL:26/PBO+ERL:30) were enrolled in RELAY; respective baseline characteristics included: median age 55.0/60.5 years; females 57.7%/66.7%; ever smokers 26.9%/26.7%; ECOG PS 0 26.9%/33.3%. Median follow-up was 20.7 months (interquartile range:15.8–27.2 months). For patients in the RAM+ERL/PBO+ERL arms, respectively, median PFS was 22.05/13.40 months (hazard ratio [HR]:0.445, 95% confidence interval [CI]:0.219, 0.902); ORR was 92.3% (95% CI:82.1, 100.0)/60.0% (95% CI:42.5, 77.5); median DoR was 18.17 (95% CI:9.69, 26.22)/12.68 (95% CI:9.69, 16.62) months. All patients experienced ≥1 treatment-emergent adverse event (TEAE), most commonly (RAM+ERL/PBO+ERL) diarrhoea (57.7%/70.0%), dermatitis acneiform (57.7%/43.3%), and paronychia (46.2%/63.3%). Grade ≥3 TEAEs were experienced by 61.5%/30.0% of RAM+ERL/PBO+ERL recipients, respectively; most commonly dermatitis acneiform (19.2%/6.7%), hypertension (11.5%/6.7%), and pneumonia (11.5%/0%).
Conclusion: The results of this exploratory subgroup analysis, conducted in Taiwanese patients with untreated, *EGFR*-mutated mNSCLC who participated in the Phase 3 RELAY study, are consistent with those observed in the overall study population.[1] These findings should be interpreted with caution due to the low number of included patients.

[1]Nakagawa K et al. Lancet Oncol 2019;20:1655–69

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA41

痰液細胞學診斷粘液腺癌

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Diagnosing Mucinous Adenocarcinoma Using Sputum Cytology

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Introduction: According to the World Health Organization, lung cancer is the most common cancer and most common cause of cancer-related death. There are 2 main types of lung cancer and they are treated very differently. About 80% to 85% of lung cancers are non-small cell lung cancer (NSCLC). The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Though adenocarcinomas are common among NSCLC, mucinous adenocarcinomas are rarely detected by chest computed tomography (CT) scans. However, a sample biopsy or sputum cytology can reveal mucinous adenocarcinomas. The other 10% to 15% of all lung cancers are small cell lung cancer (SCLC), also called oat cell cancer. Prior research indicates that of all patients with lung cancer and had produced adequate specimens, 74.6% had sputum that was positive for premalignant or atypical cells, though we only detected malignant cells in 48.7% of these cases. The research also indicates that the presence of premalignant or worse cells in sputum depended only moderately on disease stage (82.9% of stage IV cancers), tumor size(78.6% of tumors >2 cm), and location(83.3% of central lesions).
Case report: This 68 years old man experienced dyspnea and expressed symptoms of coughing with sticky sputum for one year and a body weight loss 6kg in one year. He visited our hospital in June 2020 and received a chest computed tomography (CT) scan, which revealed pneumonia in both lungs with a tree-in-bud pattern, total consolidation of right middle lobe (RML), bronchiectasis, and right-side pleural effusion. Under the microscope, a sputum smear revealed mucinous adenocarcinoma. The pathology report of the bronchoscopic biopsy showed grade 2 adenocarcinoma composed of hyperplastic and pleomorphic neoplastic cells, at the right middle lobe bronchus (RB4).
Discussion: Since the patient started using a tyrosine kinase inhibitor (TKI) with Ceritinib in 2020/7, he had expressed its effectiveness and a good quality of life. However, in September he had dyspnea as well as a fever. A chest chest computed tomography (CT) scan detected ground-glass opacity (GGO), so he turned to Alectinib therapy. According to research, when a patient has symptoms of interstitial lung disease (ILD), changing to Alectinib therapy improves the condition of patients with interstitial lung disease (ILD), then leads to longer survival.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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病例報告：pembrolizumab 導致腫瘤超進展

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Hyperprogression disease after treatment with pembrolizumab: a case report

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Background/Introduction: Immune checkpoint inhibitors (ICIs) are considered as a standard treatment modality for non-small cell lung cancer (NSCLC), which is associated with poor prognosis. However, there are emerging data from retrospective studies on a subset of patients experiencing very rapid progression, a phenomenon known as hyperprogression disease (HPD). As expected, HPD confers a worsen prognosis.

Case presentation: A 49-year-old man, an active smoker (20 pack-years) experienced a seizure and was referred to Division of Chest Medicine for a lung mass discovered accidentally by chest imaging examination (Figure 1A). Enhanced chest computed tomography (CT) revealed a tumor with a 6-cm diameter in the left lower lobe. A 2.6-cm nodule, considered to be lung metastasis, was detected in the right upper lobe (Figure 1B).

He underwent bronchoscopy with biopsy. Histology of his lung mass was consistent with squamous cell carcinoma. Immunohistochemical staining indicated that 90% of the patient's tumor cells expressed PD-L1. Brain CT showed 3.4 x 2.7 cm focal hyperdense lesion seen in the left high frontal lobe causing edema of the surrounding parenchyma and mass effect. Bone scintigraphy did not reveal any abnormal uptake. The tumor was classified as clinical T4N0M1b, stage IVA according to the 7th edition of AJCC TNM staging system. The Eastern Cooperative Oncology Group performance status at the time of admission was 1. Owing to the high PD-L1 expression (tumor proportion score greater than 90%) demonstrated by the patient, pembrolizumab was initiated 46 days after the first visit (200mg IV over 30 min). On chest CT on day 20 after pembrolizumab administration, the primary tumor increased in size accompanied by new lung-to-lung and scapular metastases (Figure 1C). The lung cancer progressed very rapidly. The patient died on day 35 after pembrolizumab administration.

Discussion: The incidence of HPD ranges from 2.5% to 29.4% from the studies reported [1-2]. A recent immunotherapy cohort study shows that the development of HPD is more common caused by ICI versus chemotherapy in pretreated NSCLC patients [3]. Patients with HPD experienced a poor prognosis, such as shorter progression-free survival and overall survival compared with those patients with progressive disease. HPD was associated with the presence of aged over 65 years, regional recurrence, high metastatic or tumor mutational burden prior to the administration of ICIs [4]. MDM2/MDM4 amplification, EGFR alterations were also shown to be independently associated with HPD. Pre-existing antitumor immunity may also lead to spontaneous regression of the tumor. The research by Kim et al. [5] provides clues on a phenotyping of CD8+ T lymphocytes from the peripheral blood before PD-1/PD-L1 blockade able to predict HPD. There is significant for further studies to identify better biomarker for HPD.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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具抗藥性 T790M 突變非小細胞肺癌病患的預後：來自真實世界的數據

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The Clinical Outcomes of Non-small Cell Lung Cancer Patients with Acquired *T790M* mutation: The Real-world Data

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Introduction: Most *EGFR*-mutated non-small cell lung cancer (NSCLC) respond to epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs), whereas tumors harboring *T790M* mutation are frequently resistant to EGFR-TKIs. Osimertinib is frequently used to treat *T790M*-mutated NSCLC after EGFR-TKI treatment failure. The relationship between the timing of osimertinib use and survival benefit remains unclear.

Methods: In this retrospective study, we enrolled NSCLC patients with acquired *T790M* mutations in two hospitals. Medical records were reviewed and analyzed. Patients were classified as group 1, received osimertinib treatment within 2 months after acquired *T790M* mutation reported; group 2, received osimertinib treatment after acquired *T790M* mutation reported for more than 2 months; and group 3, never received osimertinib. The survival after acquired T790M mutation reported was selected as primary endpoint for analysis.

Results: A total of 122 patients with NSCLC harboring acquired *T790M* mutation were identified, including 44 patients in group 1, 38 in group 2, and 30 in group 3. After acquired *T790M* mutation reported, the median survival in group 1, 2 and 3 were 29.7 (95% confidence interval (CI), 21.6- 37.8 months), 38.4 (95% CI, 15.3- 61.5 months), and 5.9 months (95% CI, 0-12.8 months), respectively ($p < 0.001$). Pairwise analyses showed no significant difference in survival between group 1 and 2 ($p = 0.443$). In multivariate analysis for those with osimertinib use, no significant difference in survival was found between group 1 and 2 (Hazard ratio, HR= 0.64, 95% CI = 0.30-1.34). Aged ≥ 70 at acquired *T790M* reported was associated with a longer survival (HR= 0.46, 95% CI = 0.22-0.97) compared with patients who aged < 70 years at acquired *T790M* reported. Acquired *T790M* mutation detected by plasma cell-free DNA analysis was associated with a shorter survival (HR = 4.55, 95% CI = 1.99-10.36) as compared with those detected by tissue specimen analysis.

Conclusions: After acquired *T790M* mutation was reported, the survival period is similar in patient who started osimertinib treatment within 2 months to those after 2 months. For these patients, age and the detection method for *T790M* mutation may be important prognostic factors.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA44

病例報告：轉移性絨毛膜癌與絨毛膜癌症候群

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Case report: Metastatic choriocarcinoma with choriocarcinoma syndrome

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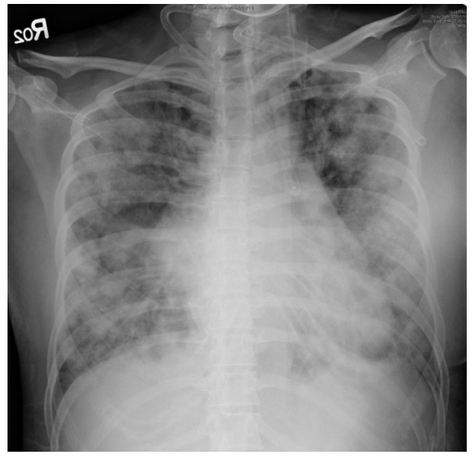
Abstract

Choriocarcinoma syndrome is a life-threatening tumor lysis syndrome caused by blood vessel rupture and subsequent tumor bleeding, which is characterized by widespread metastases and a high choriogonadotropin level. We report an extremely rare case of a 32-year-old woman who presented immediately after normal delivery, with pulmonary hemorrhage, liver and T spine metastases of choriocarcinoma. Multiple hypervascular mass at the posterior wall of uterus was found. She was treated with Cisplatin-etoposide chemotherapy. Hemothorax, hemoperitonium, and progressed pulmonary hemorrhage with rapidly increasing choriogonadotropin level were noted soon after the chemotherapy. This case report shows the diagnosis of metastatic choriocarcinoma with the initial presentation of pulmonary hemorrhage and choriocarcinoma syndrome presenting during the chemotherapy.

Key words

Alpha-fetoprotein, choriocarcinoma, choriocarcinoma syndrome



A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA45

形似轉移性腸胃道腫瘤之肺腺癌:診斷與治療

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Lung Adenocarcinoma Mimicking Metastatic Gastrointestinal Carcinoma: Differentiating Identification and Treatment

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Introduction: Pulmonary enteric adenocarcinoma (PEAC) is a rare subtype of lung adenocarcinoma. It is defined as an adenocarcinoma in which the enteric component exceeds 50% and shows the expression of at least 1 immunohistochemical marker of enteric differentiation. The major markers of intestinal differentiation include CK20, CDX2 and/or MUC2. The positive staining for CK7 and TTF-1 is also displayed in approximately half of cases, despite its histologic pattern mimics metastatic colorectal cancer (MCC). The main clinical symptoms in PEAC are dyspnea, cough, hemoptysis, and back pain. The principal treatments for PEAC are surgery and systemic chemotherapy. The most used regimen is carboplatin and paclitaxel, which is typical chemotherapy for primary lung adenocarcinoma. The survival for stage IV PEAC is widely varied, ranging from 2 to 12 months, which may be related to the patient's own physical well-being.

Case presentation: A 68-year-old women had chronic cough for more than one month. Chest X-ray showed a mass lesion over left upper lung. Initially, a bronchoscopic biopsy showed metastatic carcinoma favoring gastrointestinal origin. The tumor cells are immunoreactive for CDX2(+), TTF-1(-), Napsin A(-). However, a whole-body PET scan, EGD, and colonoscopy showed no gastrointestinal lesion, but malignant pleural effusion and bone metastases were detected. As a result, gastrointestinal origin adenocarcinoma was not likely, resulting in our diagnosis of pulmonary enteric adenocarcinoma. The genetic mutation examination for targeted therapy was checked, but the reports returned negative. The patient was enrolled in clinical trial during 2019/6/5 ~ 2020/01/29 (paclitaxel + carboplatin + bevacizumab; ONO-4538-52/Placebo + Avastin) and also received palliative radiotherapy for left chest wall. Unfortunately, the chest CT displayed progressive disease (PD). Treatment was changed to targeted therapy with Erlotinib since 2020/2/26~ and bevacizumab since 2020/4/1~. After targeted therapy, followed chest CT revealed stable disease (SD).

Discussion: PEAC is an extremely rare type of non-small cell lung cancer (NSCLC) with a histologic pattern that mimics MCC. A case of primary pulmonary tumor with enteric differentiation was reported by Tsao et al. (1991). This tumor is highly heterogeneous and shares several morphological features with pulmonary and colorectal adenocarcinomas. PEAC exhibits an ‘entero-like’ pathological morphology in more than half cases, expressing at least one of the typical immunohistochemical markers of enteric differentiation, namely CDX2, CK20 or MUC2.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA46

案例報告：一個 ROS1 基因融合的非小細胞肺癌病人在使用 crizotinib 後產生轉化小細胞肺癌且仍保有 ROS1 基因融合

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A rare ROS1-rearranged NSCLC patient with acquired resistance to crizotinib by small cell transformation but with retainment of ROS1 fusion

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Abstract:

ROS (ROS1) is an orphan receptor tyrosine kinase (RTK) that forms fusions and reported in approximately 1.4% of NSCLCs. ROS-1 tyrosine kinase inhibitors, such as crizotinib and entrectinib can provide survival benefit for advanced stage NSCLC patients. Previous studies showed that the crizotinib resistance in ROS1+ NSCLC may come from the secondary ROS1 kinase domain mutations, such as G2032R, which confers resistance to the majority of ROS1 TKIs. However, two-thirds of TKI-resistant ROS1+ lung cancers do not result from the kinase domain mutation and the associated mechanism remained unclarified.

Small cell transformation has been identified as one of the mechanisms of resistance to EGFR or ALK-mutant NSCLC and been found associated with poor prognosis because of aggressive behavior and poor response to chemotherapy. And the study showing the significance of small cell transformation in mediating ROS1 resistance remained rare. Here we present a 63-year-old male with ROS1-rearranged advanced NSCLC, who developed new mediastinum lymph nodes after 8 months on crizotinib. The immunohistochemical staining of the tumor cells from lymph nodes biopsy showed positive for thyroid transcription factor-1 and synaptophysin, consistent with the diagnosis of small cell transformation. Especially, the ROS-1 gene rearrangement by fluorescence in situ hybridization demonstrated that the ROS1 fusion is retained. Unfortunately, the patient didn't respond to chemotherapy with cisplatin and etoposide as previously reported cases with EGFR or ALK-mutant NSCLC. We emphasized the need of rebiopsy in ROS-1 rearrangement NSCLC patient with acquired resistance and small cell transformation is one of the important resistance mechanisms.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA47

病例報告：Afatinib 引起之藥物疹合併嗜伊紅血症及全身症狀

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Drug Rash with Eosinophilia and Systemic Symptoms Induced by Afatinib: A Case Report

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Abstract

The epidermal growth factor receptor (EGFR) mutation is the most common oncogenic driver gene in non-small cell lung cancer. The EGFR-tyrosine kinase inhibitors (TKIs) provides better progression free survival and objective response rate than chemotherapy. However, the use of EGFR-TKI will cause some adverse events, including pneumonitis, hepatitis, folliculitis or skin rash.

Here we presented a case of 53-year-old female with advanced stage EGFR-mutant lung adenocarcinoma, who developed eosinophilia and multiple erythematous maculopapules over face, trunk, and extremities after the use of afatinib. After skin biopsy, drug rash with eosinophilia and systemic symptoms (DRESS) was diagnosed. This side effect was less reported with the use of second-generation EGFR-TKI. After high dose of steroid use, the skin lesion recovered gradually. Then the EGFR-TKI re-challenge was given with erlotinib and no further skin toxicities developed.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA48

在台灣使用較低起始劑量的 Afatinib 在帶有 Exon 19 或 exon 21 的轉移性肺腺癌病患

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Lower Starting Dose of Afatinib for the Treatment of Metastatic Lung Adenocarcinoma Harboring Exon 21 and Exon 19 Mutations in Taiwan

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Purpose Afatinib has shown favorable response rates (RRs) and longer progression free survival (PFS) in lung cancer patients harboring EGFR mutations compared with standard platinum-based chemotherapy. However, serious adverse drug reactions (ADRs) limit the clinical application of afatinib.

Methods We designed a retrospective study, enrolled all patients with metastatic lung adenocarcinoma who were diagnosed and treated with 30 or 40 mg afatinib as their starting dose in three Kaohsiung Medical University-affiliated hospitals in Taiwan

Results A total of 179 patients were enrolled in the study, of which 102 (57%) and 77 (43%) received 30 mg and 40 mg afatinib daily as their initial treatment, respectively. The patients initially using 30 mg afatinib daily had a similar RR (74% vs. 82%, $p = 0.1661$), median PFS (14.5 months vs. 14.80 months, log-rank $p = 0.465$) and median OS (34 months vs 25.2 months, log-rank $p = 0.5982$) compared with those initially using 40 mg afatinib daily. Patients with the lower starting dose had fewer ADRs compared with patients receiving 40 mg as their starting dose. The overall incidence of moderate (49% vs 77%, $p=0.002$) or severe (7% vs 24%, $p<0.0001$) ADRs was significantly lower in patients receiving 30 mg afatinib compared with those receiving 40 mg.

Conclusion Patients receiving 30 mg afatinib as their starting dose had non-inferior RRs, PFS, OS and significantly fewer serious ADRs compared with those patients who received standard 40 mg afatinib as their starting dose.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA49

病理報告:小細胞肺癌病人治療後因咽峽炎鏈球菌肺膿瘍併發上腔靜脈侵犯

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Lung abscess caused by Streptococcus anginosus with superior vena cava invasion in a small cell lung cancer patient

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Abstract:
In previous studies, around 4-9 % small cell lung cancer patient developed lung abscess during treatment. We reported a case with limited stage small cell lung cancer, who developed lung abscess during concurrent chemoradiotherapy. Blood culture revealed Streptococcus anginosus, and superior vena cava invasion was diagnosed later. Fever recurred after antibiotics treatment, so patient received parasternotomy, debridement and SVC stenting. Patient get over the infection and completed CCRT.

Discussion:
Streptococcus anginosus is normal human flora of the oral cavity with the ability to cause abscesses and systemic infections. The presence of S. anginosus bacteremia should prompt investigation for the presence of underlying focal or multifocal abscess(es). We report a case of Streptococcus anginosus bacteremia due to lung abscess with SVC invasion. This is a rare complication in lung cancer treatment with a rare presentation.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA50

波蘭症候群(Poland's syndrome)與大細胞神經內分泌肺癌 – 病例報告

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Poland's syndrome with large cell neuroendocrine lung cancer - A case report

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Introduction：

Poland's syndrome, a rare congenital anomaly characterized by pectoralis muscle defect, has been reported in association with malignancies. Lung cancer associated with Poland's syndrome has been rarely described, especially the histology type of large cell neuroendocrine carcinoma. We present a case of Poland's syndrome associated with lung cancer and demonstrate the CT findings.

Case Report：

This 57-year-old man has known history of Poland's syndrome with left chest muscles defect. He present to chest out-patient department for progressing dyspnea accompanied with face and neck edema. Physical examination found absence of left chest wall muscles and tortuous dilatation of the subcutaneous veins of the chest wall. Chest CT reported a right upper lung tumor which invaded superior vena cava and right pulmonary artery and the absence of the left pectoralis muscles which consistent with Poland's syndrome. Echo-guided percutaneous core needle biopsy of the tumor was performed and large cell neuroendocrine carcinoma was histologically and immunohistochemical confirmed.

Conclusion：

The relationship between malignancy and Poland's syndrome is controversial. We present a rare case of Poland's syndrome with large cell neuroendocrine lung cancer.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA51

第四期鱗狀細胞癌之治療型態與預後因子：真實世界數據分析

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Real-world Treatment Pattern and Prognostic Factors for Stage IV Lung Squamous Cell Carcinoma Patients

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Introduction

Lung squamous cell carcinoma (LUSC) represents a lesser proportion among non-small cell lung cancer (NSCLC). Distinct from adenocarcinoma, fewer treatment options are feasible for LUSC and which confers the poor prognosis of LUSC. Herein, we investigated the real-world treatment pattern among LUSC patients and tried to identify the associated prognostic factors.

Methods

Retrospective medical record research was performed in Kaohsiung Medical University Hospital (KMUH) and Kaohsiung Municipal Tatung Hospital. Patients with stage IV lung LUSC diagnosed between 2010 to 2017 were recruited. Clinical demographic data, metastatic status and treatment regimens were recorded. The primary outcome is overall survival (OS), which is analyzed with each clinical variable by log rank test. The study protocol was approved by the Institutional Review Board (IRB) of KMUH (KMUHIRB-E(I)-20200180).

Result

A total of 221 metastatic LUSC patients were enrolled. After excluding those with concurrent malignancy, incomplete data or loss of follow-up, 183 patients with a median age 68 years were remained for further analysis. Male is predominant in the study population (*n*=150, 82%) and the current or ex-smokers contributed to 77% of this cohort. Pleura and lung were the most commonly metastatic sites whereas brain metastasis was only 7%. Upon diagnosis, 71% of the patients had ECOG 0 or 1. However, 66 patients (36%) did not receive any line of chemotherapy and had the poorest survival of 2.9 months, in contrast to 10.0 months among those underwent chemotherapies. Among the clinical variables, the female sex, over-weight and pleural metastasis harbored statistically significant longer survival.

Conclusion

In the real world, patients with metastatic LUSC have poor outcome and more than one third of this group of patients in southern Taiwan did not receive chemotherapy. Female sex, over-weight and pleural metastasis are associated with better prognosis. However, further investigations are warranted to elucidate the underlying mechanisms.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA52

監測晚期肺癌治療療效之游離腫瘤 DNA 甲基化生物標記

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Novel circulating methylated DNA markers for monitoring the treatment response in advanced non-small-cell lung cancer

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Introduction

Blood-based ctDNA assays represent a minimally invasive approach for molecular profiling of lung cancer. Nevertheless, longitudinal assessment of therapeutic response and disease dynamics remains challenging for tumors without common driver mutations or for tumors with evolving mutational clones.

Methods

We identified a four-gene methylation marker panel through iterative computational algorithms on genome-wide methylation data in Western and Asian lung cancer tissue cohorts. Patients with advanced non-small cell lung cancers and noncancer volunteers were prospectively enrolled. The methylation signals of the identified markers in the plasma cfDNA were measured by customized multiplex methylation-specific droplet digital PCR (MS-ddPCR) at baseline and follow-up visits. A model fitting with k-fold cross-validation was used to calculate methylation risk scores.

Results

At the initial presentation, the plasma cfDNA methylation risk scores derived from the four-gene combination could distinguish between 74 lung cancer patients and 63 noncancer controls (AUC= 0.95, sensitivity= 90.5, specificity= 84.1). Longitudinal assessment of methylation risk scores from 268 serial blood samples in 58 lung cancer patients revealed that the visit-by-visit methylation scores were highly correlated with clinical disease status regardless of mutation profiles and regimen choices. Notably, the risk scores can hint at progressive disease three months prior to definite radiographic progression.

Conclusion

Our results highlight the clinical applicability of the methylation scoring system based on the four-gene combination and provide a cost-effective and noninvasive way to help guide clinical decisions in the treatment of lung cancer with or without common driver mutations.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA53

抑制 EGFR 會誘導 PD-L1 的表達在 EGFR 突變的非小細胞肺癌內

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Inhibition of EGFR induces PD-L1 expression in EGFR mutation non-small cell lung cancer

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Abstract

Propose: Our purpose is to elucidate the involvement of Non-small-cell lung cancer (NSCLC) on Programmed death-ligand 1 (PD-L1) regulation in EGFR-mutated cancer cells and provide a novel strategy for combining target therapy and a PD-L1-inhibiting antibody in NSCLC patients with EGFR mutation.

Materials and Methods: To demonstrate the effect of PD-L1 expression upon EGFR TKI treatment, we used the EGFR mutation lung cancer cell line HCC827 to investigate our hypothesis. In addition, to further identify the apoptotic induced PD-L1 expression, induction of apoptosis by Staurosporine was treated in H3255 EGFR mutant lung cancer cell line. Furthermore, the PD-L1 expression was detected by Western Blot.

Results: We found that EGFR-mutant HCC827 lung cancer cells were treated with 0.1 μM EGFR TKI gefitinib for 8 and 24 h, the expression of PD-L1 was induced. Our results suggested that EGFR TKI inhibits EGFR activation but induces PD-L1 expression in EGFR mutation of NSCLC cell lines. In addition, to further investigate whether apoptosis signaling could induce PD-L1 expression, we used the apoptosis inducer staurosporine and the tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), which is known to induce apoptosis through caspase-dependent and -independent pathways. Compared with the untreated group, PD-L1 expression was significantly induced by staurosporine and TRAIL in NSCLC H3255 cells Therefore, this result suggested that apoptosis signaling induced PD-L1 expression in both exon 19 and L858R EGFR-mutant cells.

Conclusions: PD-L1 has been suggested to serve as an immunosuppression responsive factor in many cancers. Interestingly, several recent clinical trial and our preliminary results showed that apoptosis signaling serve as an important mediator in regulating downstream target PD-L1 in EGFR mutant NSCLC. In this study, we focused to dissect the rational of combination therapy with EGFR-TKI and anti-PD-L1 in NSCLC through intrinsically unknown pathway. Understanding the PD-L1 in the role of apoptosis in NSCLC may provide a novel therapeutic strategy through application of the specific treatment. The outcomes can provide new insights and valuable markers and therapeutic targeting of NSCLC.

Keywords: NSCLC, PD-L1, EGFR nutation, EGFR TKI, apoptotic signaling

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA54

含有梭狀細或/且巨細胞的非小細胞肺癌臨床表現與免疫檢查點抑制劑的使用效果

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Clinical outcome and benefit of immune checkpoint inhibitors in patients with advanced non-small cell lung carcinoma with spindle cell and/or giant cell elements

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Purpose: A definitive diagnosis of pulmonary sarcomatoid carcinoma (PSC) cannot be made with small biopsies. In clinical practice, a diagnosis of advanced non-small cell lung carcinoma with spindle cell and/or giant cell elements (NSCLCsg), or possible sarcomatoid carcinoma, is acceptable. Optimal treatment for advanced NSCLCsg has not yet been defined. We aimed to investigate the clinical outcome and efficacy of immune checkpoint inhibitors (ICIs) for the treatment of advanced NSCLCsg.

Materials and Methods: Between January 01, 2012 and January 01, 2019, patients with pathologically proven advanced NSCLCsg were enrolled. The choice of treatment was based on the clinicians' discretion.

Results: 67 patients with advanced NSCLCsg were enrolled. The median age was 69 years (range: 34-93 years). The majority of patients were men (68.7%) and smokers (64.2%). The median overall survival (OS) was 4.1 months (95% CI: 2.6-5.6 months). 14 patients (20.9%) were given ICI; 9 of the 14 (64.3%) received ICI monotherapy, and the remaining 5 (35.7%) received ICI in combination with chemotherapy. For those who had received ICI, the median OS was 18.2 months (95% CI: 12.8-23.7 months), and for those who had not, 3.6 months (95% CI: 2.9-4.3 months). Having received any systemic treatment (HR = 0.29, 95% CI = 0.14-0.62, p = 0.001) and ICI (HR = 0.17, 95% CI = 0.17-0.44, p < 0.001) were independent factors for better OS. Patients with PD-L1 expression ≥50% had better OS than those without PD-L1 expression (HR 0.23, 95%: 0.12-0.55, p = 0.001). However, newly diagnosed advanced NSCLCsg patients had worse OS than patients with recurrent disease (HR = 2.86, 95% CI = 1.35-6.02, p = 0.006).

Conclusions: Although advanced NSCLCsg has a poor survival outcome, our results showed that ICI may prolong OS in patients with advanced NSCLCsg. Further prospective studies are warranted to gain more understanding of the role of ICI in this specific patient population.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA55

膽道乳突瘤引起支氣管膽道廔管--病例報告

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Bronchobiliary fistula secondary to intraductal papillary neoplasm of the bile duct—Case report

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Abstract:
Bronchobiliary fistula (BBF)is a rare condition that one-third patients are related to neoplasm from liver. We represent a case with uuneventfully recovery condition who was treated with pulmonary wedge resection, fistula closure and abscess drainage.

Clinical summary:
A 80 year-old DM male patient was referred to our clinic with cough and RLL consolidation for a month. He suffered from pneumonia episode two month ago . Fever relapsed sometimes with frequently biliptysis during admission. He had no jaundice nor gastric outlet obstruction. He had been received liver resection surgery decade ago due to cholidocholitheasis and another two times cholidocholithotomy within recent three years. The Chest CT revealed pulmonary abscess formation over RLL with fistula tract across the diaphragm that connected to the cystic tumor of liver .Gastroenterologist also found an exophytic tumor over the antrum . For the medical treatment was unsuccessfully, we choose the surgery to protect the respiratory tract. The operation was began with posterolateral thoracotomy followed with RLL wedge resection, diaphragm fistula closure, and drianage of the cystic tumor. The patient was discharged in good medical condition thereafter.

Discussion:
Intraductal papillary neoplasm of the bile duct is a stepwise progression from low grade dysplasia to high grade dysplasia to invasive carcinoma that related to hepatolithasis. The carcinoma histology was confirmed in either the gene mutation (TP53, p16, KRAS, loss of SMAD4/DPC4) or invasive character (BBF formation in our case). Surgery is often the first choice of treatment after carefully recognition the disease to prevent further pulmonary complication. The BBF may involve from the iatrogenic damage, diaphragm invasion, intrahepatic or extrahepatic biliary obstruction. Next step treatment would be the biliary tumor treatment.

Conclusion:
Early diagnosis and treatment can alleviate such complicated sufferings of the patient. Good recovery of the patient can be achieved with cautious recognition and experienced operation.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA56

比較機械扶鏡手臂與人工扶鏡在單孔胸腔鏡手術短期成效

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Comparative results of robotic assisted endoscope holder and human assisted in single port thoracoscopic surgery in the era of Covid19

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Purpose: Single port video assisted thoracoscopic surgery (SPVATS) has been evolved in recent two decades. The innovation of surgical instruments has made single port surgery more widely accepted. The fewer incision wounds, the less surgical assistants will be needed. While the coronavirus (Covid-19) is ravaging the world, maintaining minimum medical manpower requirements and proper social distance are issues worthy of attention. We try to evaluate the feasibility of single surgeon in single port video assisted thoracoscopic surgery with the help of robotic camara holder.

Materials and Methods : Operative time, blood loss, set-up time, length of hospital stay, and the number of participating surgeons in single port video assisted thoracoscopic lung resections were investigated before and after the introduction of Endofixexo robotic endoscope holder system. Furthermore, we case-matched 50 patients in the robotic arm assisted group with patients in the human assisted group by a propensity score-matched analysis.

Results: For single port VATS wedge resection, all lobes of target lesions could be completely done by single surgeon. For single port VATS anatomic resection, nearly 80 percent of enrolled cases could be completely done by single surgeon. There was no significant difference between set-up time, blood loss and operative time between two groups

Conclusions: Considering our preliminary results, the combination use of Endofixexo robotic scope holder reduced the manpower requirement in most of single port VATS surgeries without increasing set-up and operative time.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA57

成功再次使用 Osimertinib.於 Osimertinib 治療失敗後的化學藥物治療期間，顱內和顱外不一致的表皮生長因子受體突變結果

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Successful rechallenge of osimertinib. Inconsistent EGFR mutation results between intra-cranial and extra-cranial lesion during chemotherapy treatment after osimertinib failure.

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Introduction: Osimertinib is the standard treatment in patient with lung cancer harboring T790M resistance mutation after 1st or 2nd generation TKI failure. However, there was no clear effective treatment strategy for intracranial progression during chemotherapy after osimertinib failure. Herein, we report a patient with leptomeningeal seeding and successful rechallenge osimertinib.

Case Report: This 38 year-old man was diagnosed with lung cancer, adenocarcinoma, stage IVb, cT4N3M1c, brain, bone and lung to lung metastasis in July 2015. He received whole brain radiotherapy and subsequently received afatinib 30mg daily due to harboring exon 19 deletion. About two and a half years later, the primary lung lesion progressed while metastatic site remain stable during scheduled follow-up. T790M mutation was detected on Liquid biopsy. Osimertinib 80 mg was administered daily since May 2018. About 9 months later, in February 2019, he complained easy abdominal fullness and decreased appetite for weeks. Abdominal CT with contrast disclosed multiple peritoneal nodules and thickening, compatible with peritoneal carcinomatosis. We performed laparascopy tumor biopsy. NGS analysis of the specimen showed exon 19 deletion, T790M and C797S in *cis*. After that, Cisplatin with pemetrexed and bevacizumab were administered every three weeks for six cycles and maintain with pemetrexed and bevacizumab. In December 2019, during the maintenance phase of the chemotherapy, he developed nausea and dizziness. Brain MRI revealed diffuse increased contrast enhancement of leptomeninges in bilateral cerebral hemisphere. There was also nest of malignant cells on cerebrospinal fluid smear. Subsequent NGS analysis of CSF cancer cells disclosed only exon 19 deletion and T790M mutation without C797S. In the consideration of the poor penetration rate of the chemotherapy regimen and previous WBRT history, we rechallenged osimertinib and keep treatment with pemetrexed and bevacizumab. The neurologic symptoms improved gradually and we did not perform lumbar puncture again for treatment purpose.

Discussion: We should consider cancer cells heterogeneity when treating lung adenocarcinoma, especially in patient under EGFR TKI treatment with intra-cranial progression. Rechallenge osimertinib is an option in selected patient.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA58

非小細胞肺癌經表皮生長因子標靶藥物治療後獲得性抗藥基因 EGFR T790M 在組織再切片及液態切片臨床表徵的不同：一家醫學中心的觀察性研究

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The Difference Clinical Features of Acquired EGFR T790M between Tissue Biopsy and Liquid Biopsy in Patients with NSCLC Progressed to EGFR-TKI Therapy: A single center observational study

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Purpose: Re-biopsy is important for exploring resistance mechanisms, especially for non-small cell lung cancer (NSCLC) patients who develop resistance to EGFR-tyrosine kinase inhibitors (TKIs). Liquid biopsy using circulating tumor DNA has come into use for this purpose. The aim of this study is to compare the clinical features difference between these two methods in our clinical practice.
Materials and Methods: We conducted this retrospective study at a single medical center from December 2014 to September 2020. Two hundred and thirty-seven NSCLC patients with resistance to EGFR-TKIs were included and divided into two groups: tissue re-biopsy (TB) and liquid biopsy(LB) in the first time after progression of NSCLC with first line EGFR-TKI treatment.
Results: One hundred and thirty-one patients underwent tissue re-biopsy; 42%(55/131) were positive for T790M. One hundred and thirty-six patients underwent liquid biopsy; The T790M detection rate was 38.2% (52/136). The clinical characteristics of detection of T790M between TB and LB in patients with NSCLC progressed to EGFR TKI were significantly difference including stage, initial metastatic sites, specific organ metastasis, progression site, receiving chemotherapy previously, and the time to re-biopsy. Patients with T790M-positive from TB seems to have better outcome than those from LB. Multivariate analysis showed that the detection of T790M from LB or TB and osimertinib treatment had impact on overall survival.
Conclusions:
Between the detection of acquired of EGFR T790M from TB and LB, there were not only significantly difference the clinical features of patient with NSCLC progressed to EGFR-TKI, but the different impact on overall survival.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA59

罕見肺腺癌突變顯示較差之預後

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Rare mutation of adenocarcinoma of lung indicated poor prognosis

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Purpose: Non-small-cell lung cancers (NSCLCs) containing EGFR mutations are exquisitely sensitive to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs). This is the case of the rare EGFR mutations affecting mutation A871G, supposed to poor prognosis.

Method: This 64-year-old male patient was a case of adenocarcinoma of left lower lobe of lung with lung to lung, lymph nodule and pleural metastasis, also malignant pleural effusion. EGFR mutation was detected with A871G. No ALK mutation was noted. The patient received TKI with Glotrif FC (40mg) during 2018/10/03~2018/12/21, shifted to Tarceva since 2018/12/21, then two course Bevacizumab on 2018/11/21 & 2018/12/13. Patient pass away on 2019/01/13.

Result: Poor response of TKI therapy was noted, including with Glotrif FC (40mg) or Tarceva. Although add-on Bevacizumab but still poor response.

Conclusion: Although EGFR mutation had response to TKIs, but A871G seems related to poor prognosis. If we can identify poor prognosis to TKIs, may consider trying another therapy including chemotherapy or immune therapy for patient with A871G mutation.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA60

胸部 X 光影像人工智慧輔助肺部單一結節良惡性偵測與辨識

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Malignancy or Benign? Single Lung Nodule analysis with artificial intelligence in adult CXR

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Purpose: Lung cancer is the deadliest with the lowest 5-year survival rate among all malignancies in Taiwan. Early detection of lung cancer has been proven to benefits in survival in NLST and NELSON study. However, to identify a nodule in CXRs is a challenge for doctors, even for specialists. In this study, we want to build a computer aided diagnosis (CAD) system to detect and diagnose lung nodules in CXRs.

Materials and Methods: Our dataset was collected from Taipei Veterans General Hospital (VGHTPE) retrospectively, including 477 CXRs of newly diagnosed early-stage lung cancer and 193 CXRs of benign pulmonary nodules, ranging in size from 6mm to 50mm, and 300 normal CXRs. Open source datasets were also collected for training. The pipeline of our CAD system consists of 4 following steps: 1. InceptionV3 trained with the dataset (12608 CXRs) and tuned with the VGHTPE dataset to classify nodule and normal CXRs, 2. U-net lung mask trained with Shenzhen (516 CXRs) and Montgomery (88 CXRs) dataset for lung segmentation, 3. YoloV3 trained based on lung nodules in our original VGHTPE dataset (670 CXRs) for nodule detection, 4. Machine learning classifier trained with traditional radiomic features and VGHTPE dataset for nodule classification.

Results: The accuracy of InceptionV3 for image classification was 92%. The sensitivity was 90% with 8.2 false-positives per-image and 83% with 5 false-positives per-image for nodule detection by YoloV3. The accuracy was 72% by the radiomic features based classifier to distinguish malignant nodules from benign nodules.

Conclusions: We have developed a computer aided diagnosis system based on deep learning and radiomics to effectively detect and differentiate benign and malignant lung nodules in CXR.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA61

一例晚期(stage IIIB)肺部淋巴上皮瘤樣癌個案，對於含 etoposide 及鉑劑之同步化學放射治療，有良好反應

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Good Response to Etoposide plus Platinum-based Concurrent Chemoradiotherapy in a Case of Locally-Advanced Pulmonary Lymphoepithelioma-like Carcinoma

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Previous case series studies have reported chemotherapeutic response with various platinum-based regimens administrated in patients with pulmonary lymphoepithelioma-like carcinoma (LELC), but few reports have demonstrated the response to etoposide plus platinum chemotherapy concurrent with radiotherapy (CCRT) in the advanced stage of this disease. We here present a 68-year-old man with stage IIIB pulmonary LELC in 2020. The patient had a smoking history of 27 pack-years and had quit smoking for 17 years. He was treated with CCRT since April 14, 2020. He received 2 cycles of etoposide plus platinum-based chemotherapy, and a dose of 6600 cGy in 33 fractions delivered to the primary tumor. The treatment was completed on June 22, 2020. The patient showed a good response to the treatment and the tumor shrinkage was ongoing until September 2020. His recent two computed tomography (CT) scans of the chest, in June and September 2020 respectively, showed stationary lymph nodes in the mediastinum and bilateral pulmonary hila, with calcifications. The depth of response was 36.7%, with the tumor size decreased from 60 mm to 38 mm, measured in June 2020. And regression of the lesion was also seen in September 2020. In a retrospective study of 23 patients from Taiwan, in the 6 patients who received docetaxel plus cisplatin CCRT, the response rate ranged from 18~100%, while the median response rate was 52.5%. In this report, we present the case of a 68-year-old man who showed an exceptionally favorable response to etoposide plus platinum-based CCRT, as demonstrated by a prominent tumor shrinkage.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA62

經低劑量肺部電腦斷層檢查篩檢確診為肺部惡性腫瘤患者之電腦斷層影像型態分析

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Low dose computed tomography (LDCT) in lung cancer screening: Experience from single medical center in Southern Taiwan

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Purpose: Lung cancer is the most prevalent cancer type and leading cause of cancer death in Taiwan.1 Low-dose computed tomography (LDCT) allows identification of lung nodules using as low as radiation dose. We set up a management program to follow up the patient with positive findings and reduce unnecessary CT examination for the benign nodules.

Materials and Methods: According to the management plan formulated by the multidisciplinary team of NCKUH, each person will receive consultation in family medicine clinic before LDCT examination. After the LDCT examination, the subject will receive formal report of LDCT, interpreted by radiologist, and chest physician clinic appointment will be arranged for recommendation of future follow up in terms of the LDCT findings and risk evaluation of lung cancer. The program had been set up since November 2017, and run for 3 years.

Results: During the span from November 2017 to November 2020, LDCT was performed in 5709 subjects. 1543 of them were recruited to our management plan since positive findings of lung nodules or ground glass opacity (GGO). 80 subjects of those with positive findings of lung lesions by LDCT were referred to chest surgeon for surgical resection, and 63 of resected lung lesions yielded positive findings of lung malignancy (atypical adenomatous hyperplasia/ adenocarcinoma in situ: 28 person; minimally invasive adenocarcinoma: 9 persons; adenocarcinoma: 26 person). Of the 63 patients, GGO was revealed by LDCT before surgical resection in 47 subjects while the remaining 16 persons bear lung nodule findings by LDCT.

Conclusions: In our cohort under the case management model recruited in 3-year period and followed to date, 63 subjects are diagnosed pulmonary malignant lesions. We believe with the integration of multidisciplinary teamwork and case management, LDCT is effective in screening early stage lung cancer.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA63

惡性肺部類肉瘤經免疫治療的反應: 病例報告及文獻回顧

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Response of immunotherapy in the pulmonary sarcoma: A Case report and literature review

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Purpose: Pulmonary sarcomatoid carcinoma (PSC)is a rare subtype of non-small cell lung cancer. It is only account for 0.3-3% of all primary lung malignance. We aim to know the response of immunotherapy for PSC that it's PD-L1 showed high expression.
Materials and Methods: We present this case of a patient who failed on the curative surgical intervention. The tumor growth rapidly(almost double size) within 2 months. Fortunately it's PD-L1 showed high expression(via method Ventana SP-263). We start pembolizumab for her since 109/8. We can see the obvious tumor regression after 2 course of pembrolizumab(200mg Q3W). Also patient's discomfort(chest pain and dyspnea) got improve after pembrolizumab. No obvious immunotherpay related side effect was noted. Till now she is under regular pembrolizumab injection.
Discussion and Conclusions: . According to the 2015 World Health Organization (WHO) classification, PSC includes several different types of malignant epithelial tumors or totally loss a common component of non-small cell lung cancer (NSCLC). PSC include pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, pulmonary blastoma, and carcinosarcoma and it's golden diagnosis usually based on the tissue pathology from surgical intervention. The common characertisic of PSC is smoking, older male and chest X-ray showed a large with well defined margin tumor. According to the review article of a single Medical center, systemic chemotherapy don't provide the better outcome, unless add on surgical intervention. Back on this case, PSC is a rapidly growth NSCLC but it had a good response of pembrolizumab. We also notice PSC had some intersting characteristic including over-expression of PD-L1 and c-MET amplification. It provide us the some new treatment plan about PSC patient who is unable to receive surgical intervention.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA64

具 EGFR 突變與骨轉移的肺腺癌病患其預後因子分析

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Prognostic Factors In Lung Adenocarcinoma With Bone Metastasis Treated With EGFR-TKIs

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Abstract: Patient who has advanced lung cancer and bone metastasis (BM) often suffered from skeletal-related events (SREs) that lead to poor quality of life and poor prognosis. Our study aimed to investigate the prognostic factors in patients with BM from epidermal growth factor receptor (EGFR) mutation-positive lung adenocarcinoma. This retrospective study included 77 lung adenocarcinoma patients with BM who underwent first-line EGFR tyrosine kinase inhibitors (EGFR-TKIs) between January 2017 and December 2019. Among them, 42 patients were treated with subcutaneous denosumab 120 mg monthly. We investigated their baseline characteristics, cancer management, SREs, progression-free survival (PFS) and overall survival (OS). As a result, those who took afatinib as first-like EGFR-TKIs had significantly longer PFS than those treated with other TKIs. Denosumab has no prognostic effects, and the performance status score at diagnosis was the only prognostic factor for OS.

Keywords: survival; denosumab; EGFR-TKIs; afatinib; bone metastasis; lung cancer

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA65

在表皮生長因子受體突變的非小細胞肺癌患者第一線使用不可逆酪氨酸激酶抑制劑有較長的整體存活期

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First-line treatment with irreversible tyrosine kinase inhibitors associated with longer OS in EGFR mutation-positive non-small cell lung cancer

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Background :
Few studies have compared the efficacy of the irreversible epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), afatinib, with that of reversible EGFR-TKIs. Therefore, this study assessed the effectiveness of afatinib, erlotinib, and gefitinib in terms of OS (overall survival) and progression-free survival (PFS) in EGFR mutation-positive advanced non-small cell lung cancer (NSCLC) patients.
Materials and Methods:
Patients with EGFR mutation-positive advanced NSCLC who sought treatment from December 2013 to June 2018, at a tertiary referral center were retrospectively analyzed. These patients were treated with afatinib or a reversible EGFR-TKI (erlotinib or gefitinib) until disease progression, intolerable adverse events, or death. The Kaplan-Meier and log-rank tests were then used to compare the OS and PFS of the patients. We further analyzed the survival differences among the subgroup of patients without brain metastases.
Results:
Of the 363 patients enrolled, 134 and 229 received first-line afatinib and first-line reversible EGFR-TKI, respectively. Those given afatinib had better OS (39.3 vs. 26.0 months; HR 0.65, $P = 0.033$) and PFS (14.1 vs.11.2 months; HR 0.58, $P < 0.001$). Of the 246 patients without brain metastases, 93 and 153 received first-line afatinib and a first-line reversible EGFR-TKI, respectively. Those given afatinib had a better OS (52.6 vs. 24.9 months; HR 0.62, $P = 0.0030$) and PFS (17.7 vs. 11.1 months; HR 0.51, $P < 0.001$). The survival benefit was more significant in the subgroup of patients with L858R substitutions.
Conclusions:
The results indicated that afatnib resulted in significantly better OS and PFS than gefitnib and erlotinib for EGFR mutation-positive advanced NSCLC patients without brain metastases.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA66

以民眾為中心的輔助決策工具對低劑量電腦斷層掃瞄肺癌醫病共享決策之影響

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Effects and factor related to implantation of multi-component PDA toolkit in shared-decision making for lung cancer screening

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Purpose: Shared-decision making is recommended by various professional association and organization before lung cancer screening by LDCT. Patient decision aid (PAD) is tools designed to support SDM by providing up-to-date evidence and balanced information about benefits and harmful of screening. Although there is a need for PDAs to support shared decision-making about lung cancer screening using LDCT, few tools have been developed and evaluated. In this study, we aim to develop and evaluate the effect of a novel multi-component PDA (patient-centered decision aid, information card, and route decision support tool) for lung cancer screening by LDCT on shared decision making process.

Materials and Methods: Based on up-to-date evidence, a user-centred design, multi-component PDA toolkit were developed. The toolkit was reviewed by experts including chest medicine, thoracic surgery, radiation oncology, and family medicine) for accuracy and comprehensiveness. Throughout the development process, the multi-component PDA toolkit refined through various cycles of feedback and redesign. Participants completed a self-report demographic form and subjective measures of decision-making preparation, decision conflict, knowledge following PDA interaction and clinician SDM.

Results: A total of 32 subjects and 6 clinicians (5 physician and 1 nurse practitioner) participated in the interviews. From interviews with subject, we found that shared decision-making interaction of multi-component PDA toolkit improve knowledge about lung cancer screening with LDCT and reduce anxiety; 53.1% (17/32) subjects had total decisional conflict scores of 25 or less (scores lower than 25 will be associated with absence of decisional conflict); and 96.8% (31/32) subject suggest multi-component PDA toolkit is useful in preparing the respondent to communicate with their practitioner at a SDM process focused on making a decision. From clinicians, we identified that multi-component PDA toolkit improve the improve clinician-patient communication and relationship. Furthermore, the factor of influence on decision conflict included time of SDM process, subject's age, education level, and division.

Conclusions: In this study, we develop a novel multi-component PDA toolkit for supporting shared decision-making about lung cancer screening using LDCT. Our findings suggest that implementation of multi-component PDA toolkit is useful for proving balanced information about benefits and harmful, facilitating clinician-patient dialog improving, and optimal decision making.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA67

大細胞神經內分泌肺癌：病例系列研究

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Large Cell Neuroendocrine Carcinoma of Lung: A case series study

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Rationale: Large cell neuroendocrine carcinoma (LCNEC) is a rare histologic type of lung cancer. The clinical features and treatments are seldom investigated and remain poorly understood.

Methods: From 2000 to 2020, patients with a diagnosis of lung cancer were screened from Cancer Registry, Cancer Administration and Coordination Center, National Taiwan University Hospital. Those with a pathologic diagnosis of LCNEC were included. The data on clinical characteristics, treatments, and survival were collected from medical records and analyzed.

Results: A total of 21 patients were included. The median age is 74 (range: 56-82) years old. Most patients were male (90.5%) and ever-smokers (71.4%). Nineteen patients had positive for synaptophysin (90.5%) and 15 patients for chromogranin (75%). Two patients had NSCLC component, including one adenocarcinoma and one squamous cell carcinoma, respectively. For patients with stage I disease (n=8, 38.1%), all underwent tumor resection, with 2 recurrence after 11.7 and 22.9 months, respectively. Two patients had stage II (9.5%) disease and both underwent tumor resection, with 1 recurrence (50%) after 5.2 months. For patients with stage III disease (n=4, 19.0%), 2 had neoadjuvant therapy + tumor resection, one had lobectomy + adjuvant chemotherapy, the other underwent tumor resection only. As for those with stage IV disease (n=7, 33.3%), only 1 (14.3%) received chemotherapy therapy with etoposide + cisplatin. Two patients (28.6%) had brain tumor resection and were lost follow-up after discharge. One (14.3%) had palliative radiotherapy, and 3 (42.9%) received only palliative care. The median overall survival (OS) for patients with early stage (stage I and II, n=7) was 60.2 (1.9-155.9) months, and 12.6 (0.5-24.3) months for advanced disease (stage III and IV, n=7). The median disease free survival was 41.7 (11.7~146.9, n=6) months for those with stage I disease.

Conclusions: The diagnosis of LCNEC may be underestimated in late stage diseases. The treatment modalities were complicated in the real world setting. Further studies on the diagnosis and treatments of LENEC are warranted.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PA68

因治療副作用改變第一線表皮生長因子受體標靶治療之肺癌病人預後

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The Prognosis After Switching of Frontline Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Due to Treatment Related Adverse Effect

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Purpose: Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI) has been the mainstay treatment in advanced-stage lung adenocarcinoma with *EGFR* mutation. However, various treatment-related adverse effect (TrAE) leads to switch to different EGFR TKIs. The impact of TrAEs related TKI switching on the prognosis of lung adenocarcinoma patients has not yet been reviewed. we aimed to investigate whether TrAE related EGFR TKI-switching has an effect on treatment effectiveness and prognosis.

Materials and Methods: From 2009 to 2020, We retrospectively reviewed advanced-stage lung adenocarcinoma patients harboring *EGFR* mutation who received EGFR TKI as first-line treatment. “TKI-switching group” was defined as patients changed first-line EGFR TKI due to TrAEs. The other patients were classified as “Non-switching group” due to no switching of first-line EGFR TKI treatment. TrAEs was recorded according to CTCAE guideline version 5. Clinical characteristics, *EGFR* status, disease status, treatment response, disease progression details were also collected.

Results: Of the 129 patients, 107 (82.9%) patients took afatinib as first-line EGFR TKI, and 22 patients took gefitinib/erlotinib. TKI-switching group included 33 patients (25.5%). The majority of TKI related TrAEs included skin problems (51.7%), diarrhea (28.6%) ,and hepatotoxicity (10.7%). The TrAE severity was mostly grade 2 (70.4%) and grade 3(18.5%) with no TrAE related mortality was recorded. There were no significant differences in PFS (median: 15.3 versus 15.8 months, p = 0.60) and OS (median: 30.2 versus 32.9 months, p = 0.17). After acquired resistance to EGFR TKIs, 59 patients underwent biopsy, and 21 patients (35.6%) had acquired T790M. There was no significant difference in T790M acquisition rate between the two groups (36.8% versus 35%, p = 0.89)

Conclusion: EGFR TKI-switching related to TrAEs showed no significant effect on disease progression and overall survival. Further extension with other database for larger study is ongoing.

Airway Disease

Sleep Medicine

Interstitial Lung Disease

Other

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB01

利用小呼吸道功能參數導引原發性肺纖維化病患的支氣管擴張劑使用

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Utilizing functional parameters of small airways to guide bronchodilator use in patients with idiopathic pulmonary fibrosis

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Purpose: Idiopathic pulmonary fibrosis (IPF) may present comorbid obstructive lung diseases with small airway dysfunction (SAD). Existing guidelines suggest that inhaled bronchodilators should be used if airflow obstruction is present as $FEV_1/FVC < 0.7$ in IPF. However, most IPF patients have $FEV_1/FVC > 0.7$ even with coexisting emphysema. This study aimed to investigate the functional parameters of the small airways measured using impulse oscillometry (IOS) and whether these parameters could guide bronchodilator therapy in IPF patients with SAD.
Materials and Methods: We retrospectively reviewed medical records of 63 IPF patients who confirmed their diagnosis based on the ATS/ERS/JRS/ALAT guideline and completed computed tomography (CT) scan, lung function tests, and symptom questionnaires evaluation from October 1st 2017 to October 31st 2019. The changes of pulmonary function and symptom scores before and after bronchodilator treatment in the 14-week follow-up period were evaluated. .
Results: Among the 63 patients, 85.71% (n=54) received antifibrotic treatment and 60.32% (n=38) received inhaled long-acting bronchodilator treatment according to the physicians' judgement. The median FEV_1/FVC was 0.86 and only 4.76% (n=3) had FEV_1/FVC <0.7. CT scan-confirmed emphysema was seen in 34.92% (n=22) of patients and 68.18% (n=15) of them received bronchodilator treatment. However, bronchodilator treatment did not have significant effect either on lung function or symptom scores in patients with emphysema. On the other hand, 79.36% (n=50) IPF patients had IOS-confirmed SAD and 64% (n=32) of them received bronchodilator treatment. A significant improvement in FEV_1, $FEF_{25\%-75\%}$, and symptom scores were observed after bronchodilator treatment. In contrast, this bronchodilator efficacy was not seen in patients without SAD.
Conclusions: FEV_1/FVC cannot reflect the airflow limitation in IPF. Emphysema in IPF is not a determinant to decide whether patients should receive bronchodilator treatment. IOS parameters may be useful to guide bronchodilator therapy in patients with IPF coexisting with SAD.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB02

運用尖端吸氣流速模擬器指引吸入型藥物治療，有助於降低肺阻塞病人的嚴重急性惡化及死亡率-一個世代研究

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Peak-inspiratory-flow-rate guided inhalation therapy to reduce severe exacerbation and mortality in COPD: a cohort study

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Purpose: Optimal peak inspiratory flow rate (PIFR) is crucial for inhalation therapy in patients with chronic obstructive pulmonary disease (COPD). However, little is known about the impact of PIFR-guided inhalation therapy on the clinical outcomes among patients with varying severities of COPD.
Materials and Methods: PIFR was measured against the simulated resistance of the prescribed inhaler and used to educate patient's inhalation techniques. The incidence of execration and mortality before and after introduction of PIFR-guided inhalation therapy were compared.
Results: A total of 223 COPD patients were enrolled in National Taiwan University Hospital. Among them, 160 patients received PIFR-guided inhalation therapy (PIFR group) and 63 patient received usual inhaler education (control group). During one-year follow-up, the PIFR group had significantly less severe exacerbation (11.9% vs. 31.7%, p=0.001) and less all-cause mortality (2.5% vs. 15.9%, p=0.001) than control group. The median time to first severe exacerbation was longer among PIFR group than control group (177 vs. 86.5 days, p=0.019), especially among patients with inappropriate PIFR. Subgroup analysis found PIFR-guided inhalation therapy was beneficial to all the patients, irrespective of their age, gender, body stature, severity of COPD, and the type of inhaler used. A multivariable Cox's proportional-hazards analysis revealed that the PIFR-guided inhalation therapy was a significant, independent factor associated with the reduced risk of severe exacerbation of COPD (adjusted hazard ratio=0.28, 95% confidence interval, 0.14-0.54, p<0.001).
Conclusions: The PIFR-guided inhalation therapy significantly reduced the risk of severe exacerbation and all-cause mortality than conventional inhalation therapy in patients with COPD.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB03

Caspase-1 抑制劑減少 focal adhesion kinase 來調控在 bleomycin 誘發肺纖維化中的血管內皮間質轉化

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Caspase-1 inhibitor reduces focal adhesion kinase activity to regulate endothelial to mesenchymal transition in bleomycin-induced pulmonary fibrosis

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Purpose: Pulmonary fibrosis is a major manifestation of end-stage interstitial lung disease and late period of acute respiratory distress syndrome. Recently, nucleotide-binding domain leucine-rich repeat-containing receptor, pyrin domain-containing-3 (NLRP3) inflammasome and endothelial to mesenchymal transition (EndoMT) were shown to be involved in the pathogenesis of pulmonary fibrosis and were possibly associated with each other. However, the detailed mechanism is unknown. Our study aimed to investigate the role of caspase-1 inhibitor in the regulation of EndoMT in bleomycin-induced pulmonary fibrosis.
Materials and Methods: Caspase-1 inhibitor, Ac-YVAD-cmk (YVAD), was intraperitoneally administered to male C57BL/6 mice (8-12 weeks old) one hour before bleomycin intratracheal injection (1.5 U/kg). Immunohistochemical staining, Masson's trichrome staining, enzyme-linked immunosorbent assay, immunofluorescence, and Western blotting were used to assess the activity of NLRP3 inflammasome and EndoMT in lung samples from mice. Human pulmonary microvascular endothelial cells (HPMECs) were used as a model of EndoMT in vitro with YVAD and bleomycin stimulation.
Results: We observed the activation of NLRP3 inflammasome signaling pathway and EndoMT (decreased vascular endothelial cadherin [VE-cadherin] with increased alpha-smooth muscle actin [α-SMA], and vimentin) in the lung samples after bleomycin. However, a caspase-1 inhibitor, Ac-YVAD-cmk (YVAD) significantly attenuated NLRP3 inflammasome and reduces focal adhesion kinase (FAK) expression to regulate EndoMT. In vitro study of human pulmonary microvascular endothelial cells also confirmed these findings.
Conclusions: Caspase-1 inhibitor could reduce EndoMT by downregulating NLRP3 inflammasome and the FAK pathways, and thus, help ameliorate bleomycin-induced pulmonary fibrosis.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB04

肺纖維化與懸浮微粒提高血管收縮素轉化酶 2 與跨膜絲氨酸蛋白酶 2 表現：在 2019 新冠肺炎可能的角色

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Idiopathic pulmonary fibrosis and particulate matter upregulate ACE2 and TMPRSS2: A potential role for COVID-19 aggravation

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Purpose: We aimed to explore the lethal effect of air pollution in idiopathic pulmonary fibrosis (IPF). Angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) are the keys to the entry of severe acute respiratory syndrome coronavirus 2.
Methods: We assessed the levels of ACE2 and TMPRSS2 using immunostaining in lung tissues sections of non-IPF and IPF patients and in murine models of bleomycin-induced pulmonary fibrosis combine with or without particulate matter (PM) exposure. In addition, we demonstrated the knock out mice and the inhibitor to recognize the potential signaling pathway.
Results: In non-IPF patients, cells expressing ACE2 and TMPRSS2 were limited to human alveolar cells. ACE2 and TMPRSS2 were largely upregulated in IPF patients, and were co-expressed by fibroblast specific protein 1 (FSP-1)+ lung fibroblasts in human pulmonary fibrotic tissue. In animal models, PM exposure increased the severity of bleomycin-induced pulmonary fibrosis. ACE2 and TMPRSS2 were also expressed in FSP-1+ lung fibroblasts in bleomycin-induced pulmonary fibrosis, and when combined with PM exposure, they were further upregulated. The severity of pulmonary fibrosis and the expression of ACE2 and TMPRSS2 caused by PM exposure were blocked by deletion of KC, a murine homologue of IL-8, or treatment with reparixin, an inhibitor of IL-8 receptors CXCR1/2.
Conclusion: These data suggest that poor prognosis after COVID-19 infection caused by air pollution and IPF is mediated through upregulation of ACE2 and TMPRSS2 in pulmonary fibroblasts, which can be prevented by blocking the IL-8/CXCR1/2 pathway.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB05

間歇性缺氧對於吞噬細胞吞噬能力、敗血症預後之影響

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Intermittent hypoxia contributes to defective phagocytosis of phagocytes and poorer sepsis outcomes

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Purpose:
To explore the impact of intermittent hypoxemia (IH)-the principal pathophysiologic change of obstructive sleep apnea (OSA) on sepsis survival and the phagocytic abilities of phagocytes in OSA patients, which was further verified in a murine model.
Materials and Methods:
Firstly, sepsis patients who had ever received polysomnography were retrospectively collected. Survival of those with and without OSA were compared. Secondly, we prospectively enrolled OSA patients and controls, whose peripheral venous blood was collected to measure the phagocytic abilities of phagocytes (neutrophils and monocytes) with commercial kits. We used a murine model of IH, which allowed O2 concentration in the chamber cycling from 21% to 5.7% every 90 seconds. C57BL/6 mice were treated with IH or room air 8 hours per day for 3 weeks and sacrificed to collect neutrophils and macrophage (bone-marrow-derived macrophage, BMDM) from the bone marrow, which were further tested with Vybrant™ Phagocytosis Assay Kit. Another set of mice treated with IH and room air were induced sepsis with cecal ligation puncture procedure and survival/severity were compared.
Results: Sepsis patients with OSA had poor survival compared with those without OSA. The phagocytic abilities of monocytes and neutrophils of OSA were lower than that of controls. As well, IH-treated mice had phagocytes with poorer phagocytic abilities and had poor survival in induced sepsis compared with mice treated with room air.
Conclusions: IH may suppress the phagocytic abilities of phagocytes and be linked to poor sepsis outcomes.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB06

睡眠呼吸中止症病人之睡眠體位及睡眠階段對於下顎前突口內裝置治療反應之探討

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The Effects of Positional Dependency and Sleep Stage Dependency on Mandibular Advancement Device Treatment Outcome in Obstructive Sleep Apnea

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Purpose: This study aimed to investigate the relationship between polysomnographic (PSG) phenotype, sleep stage dependency and positional dependency, and mandibular advancement device (MAD) treatment response in patients with obstructive sleep apnea (OSA).
Materials and Methods: This retrospective study recruited patients with OSA (apnea-hypopnea index (AHI) > 10/h), 20 to 80 years old and treatment naïve, who received MAD treatment more than 3 months from 2009 to 2017. $AHI_{supine}/AHI_{non\text{-}supine} \geq 2$ and <2 meant supine predominant OSA and non-positional OSA, respectively. $AHI_{REM}/AHI_{NREM} \geq 2$, <0.5, and 0.5 to 2 indicated REM-predominant OSA, NREM-predominant OSA, and stage-independent OSA, respectively. Three criteria defined successful MAD treatment (i.e., criterion 1: residual AHI<5/h with >50% reduction; criterion 2: residual AHI<10/h with >50% reduction; criterion 3: reduction > 50%). Multivariable logistic regression models were applied to identify the dependent association between positional and sleep stage dependency on three criteria of MAD response.
Results: A total of 218 patients with a median age of 52.5 years, body mass index (BMI) of 25.4 kg/m^2, and AHI of 28.2/h were recruited. Patients with supine predominant OSA had higher MAD treatment response than those with non-positional OSA (criterion 1: 43.2% vs 34.1%; criterion 2: 63.6% vs 34.1%; criterion 3: 77.3% vs 51.2%). Patients with NREM-predominant OSA had lower MAD treatment response for all 3 criteria (REM-predominant vs NREM-predominant vs stage-independent: criterion 1: 57.6% vs 0% vs 42.0%; criterion 2: 75.8% vs 16.7% vs 56.5%; criterion 3: 75.8% vs 33.3% vs 77.1%). The supine-predominant group had lower neck and waist circumferences than the non-positional group. The REM-predominant group had lower AHI and more female than the other groups. Positional dependency and sleep stage dependency were independently associated with MAD treatment response for criterion 2 and 3 after adjusting age, gender, comorbidities, smoking status, BMI, waist circumference, and baseline AHI.
Conclusions: Supine predominant OSA was associated with higher response of MAD treatment while NREM-predominant OSA was associated with lower response on AHI reduction. PSG phenotype may be used as a biomarker for personal-tailoring treatment for MAD treatment.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB07

次世代定序分析阻塞性睡眠呼吸中止患者之小分子核糖核酸全貌: miR-15b-5p 的低表現量會藉由其標的基因 COX1 來調節間歇性缺氧與再氧和所誘導的細胞凋亡

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Next generation sequencing for microRNA profiling in Patients with Obstructive Sleep Apnea: miR-15b-5p under-expression Modulates Intermittent Hypoxia with Re-oxygenation–Induced Cell Apoptosis by Targeting COX1

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Purpose: We hypothesized that microRNAs (miRs) may contribute to disease severity or the development of adverse consequences in patients with obstructive sleep apnea (OSA).
Materials and Methods: Illumina MiSeq next generation sequencing chip was used to identify differentially expressed miRs by comparing peripheral blood mononuclear cell samples between 8 OSA patients and 4 healthy non-snorers. Ten candidate miRs were selected for validation by quantitative RT-PCR method in an independent cohort of 20 primary snoring (PS) subjects, 45 treatment-naïve OSA patients, and 13 OSA patients on long-term CPAP treatment. Human monocytic THP-1 cells were induced to undergo apoptosis under intermittent hypoxia with re-oxygenation (IHR) exposures.
Results: Whole genome analysis identified 77 differentially expressed miRNAs (52 up-regulated and 25 down-regulated; Fold change >2 or< -2, Transcript per Million>1000, $p<0.05$). Enriched predicted target pathways of the candidate miRNA gene sets included Focal adhesion, PI3K-Akt signaling, and Hippo signaling. In the validation cohort, gene expressions of both the miR-92b-3p and miR-15b-5p were decreased in treatment-naïve OSA versus either PS or OSA on CPAP group, and negatively correlated with apnea hypopnea index (all p values<0.05). *PTGS1* (*COX1*) gene expression was increased in treatment-naïve OSA versus either PS or OSA on CPAP group (both p values<0.05). IHR treatment in vitro resulted in down-regulations of both the miR-92b-3p and miR-15b-5p, while transfection with miR-15b-5p mimic at 25 nM reversed IHR-induced early apoptosis (percentage of Annexin V(+) THP-1 cells) and IHR-induced up-regulations of its predicted target genes, including *PTGS1*, *ADRB1*, *GABRB2*, *GARG1*, *LEP*, *TNFSF13B*, *VEGFA*, and *AMOT*.
Conclusions: The findings reveal the potential of miRs detected in blood as clinical markers, and indicate that over-expression of the miR-15b-5p may be a new therapeutic strategy for OSA.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OB08

從細胞, 動物及人類研究發現 PM2.5 透過 NF-kB/ETS-1 路徑所致之呼吸道發炎及肺纖維化

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PM2.5 induced airway inflammation and pulmonary fibrosis through NF-kB/ETS-1 dependent pathway from cell line, animal to human study

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Purpose: We aim to identify novel signal pathway by which PM2.5 could induce airway inflammation and lung fibrosis in cell line, animal and human study.
Materials and Methods: We analyzed A549 cell line and C57BL/6 mice treated with PM2.5 standard reference material (SRM1649b) for cytokine and signal pathway. The blood samples from COPD patients with smoking history to mimic PM2.5 exposures were tested for cytokine study and human lung fibrosis tissue array was tested for signal pathway.
Results: **O-**PMs (organic solvent-extractable fraction of SRM1649b)-induced oxidative stress increased the expression of proinflammatory intracellular adhesion molecule-1 (ICAM-1) through the IL-6/AKT/STAT3/NF-κB pathway in A549 cells. The intratracheal instillation of PMs significantly increased the levels of the ICAM-1 and IL-6 in lung tissues and plasma in WT mice, but not in IL-6 knockout mice. COPD patients had higher plasma levels of ICAM-1 and IL-6 compared to healthy subjects. O-PMs treatment induced EMT development, fibronectin expression in A549 cells. O-PMs affected the expression of the EMT-related transcription factors NF-κB p65 and ETS-1 in A549 cells. Interference with NF-κB p65 significantly decreased O-PMs-induced fibronectin expression in A549 cells. In addition, O-PMs affected the expression of fibronectin, E-cadherin, and vimentin through modulating ETS-1 expression in A549 cells. ATN-161, an antagonist of integrin α 5β1, decreased the expression of fibronectin and ETS-1 and EMT development in A549 cells. EMT development and the expression of fibronectin and ETS-1 were increased in the lung tissue of mice after exposure to PMs for 7 and 14 days. There was a significant correlation between fibronectin and ETS-1 expression in human pulmonary fibrosis tissue.
Conclusions: O-PMs can increase ICAM-1 expression in in vitro and in vivo through the IL-6/AKT/STAT3/NF-kB signaling pathway and induce EMT and fibronectin expression through the activation of transcription factors ETS-1 and NF-kB in A549 cells. PMs can induce EMT development and the expression of fibronectin and ETS-1 in mouse lung tissues. These findings suggest that the ETS-1 pathway could be a novel and alternative mechanism for pulmonary fibrosis.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB01

支氣管擴張合併慢性阻塞性肺病和慢性阻塞性肺病急性呼吸事件的比較

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Comparison of acute respiratory events between bronchiectasis-COPD overlap and COPD

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Abstract

Purpose The clinical phenotypes of chronic obstructive pulmonary disease (COPD) are related to various outcomes. We investigated the risk of acute respiratory events in patients with bronchiectasis–COPD overlap (BCO) and COPD in Taiwan.

Methods We included 3955 patients who received diagnoses of COPD and bronchiectasis from 2000 to 2007 from the Taiwan Longitudinal Health Insurance Database in the BCO cohort. In the comparison cohort, we included patients with COPD but without bronchiectasis at a ratio of 4:1, frequency matched by age, sex, and index year with each patient with BCO. We followed both cohorts for 5 years to investigate the incidence and risk of acute respiratory events in the BCO cohort relative to the comparison cohort, the incidence rate ratios (IRRs) and corresponding 95% confidence intervals (CIs) were determined using Poisson regression models.

Results The BCO cohort experienced more episodes of acute respiratory events than did the comparison cohort (16.4 vs 5.52 per 100 person-y). After adjustment for potential covariates, the BCO cohort had a 2.20-fold higher risk of pneumonia (adjusted IRR = 2.20, 95% CI = 2.06-2.34), a 3.88-fold higher risk of acute exacerbation (adjusted IRR = 3.88, 95% CI = 3.64-4.13), a 1.74-fold higher risk of acute respiratory failure (adjusted IRR = 1.74, 95% CI = 1.47-2.06), and a 1.99-fold higher risk of cardiopulmonary arrest (adjusted IRR = 1.99, 95% CI = 1.81-2.20) than did the comparison cohort.

Conclusion The patients with BCO had a higher risk of acute respiratory events than did COPD patients without bronchiectasis.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB02

ACO 患者使用乙型交感阻斷劑對急性惡化風險的影響

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Beta-blockers Use and Risk of Acute Exacerbation in Patients with Asthma-COPD Overlap

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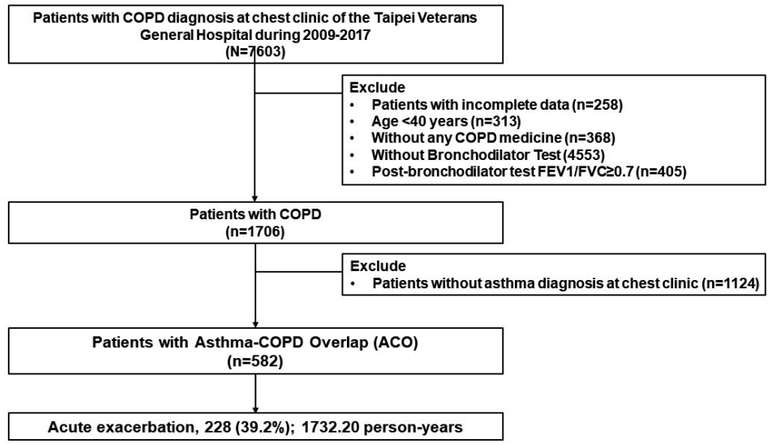
Purpose: Based on current guidelines, the effect of β-blockers on exacerbation in patients with asthma-COPD overlap (ACO) remains unclear.

Materials and Methods: We conducted a retrospective cohort study using data from the claims database of Taipei Veterans General Hospital, Taipei, Taiwan. Patients coexistent with fixed airflow limitation and clinical features of asthma between 2009 and 2017 were enrolled as ACO cohort. β-blockers prescriptions in each 3-month period served as time-dependent covariates. Patients receiving β-blockers ≥ 28 cumulative defined daily dose (cDDD) were defined as β-blockers user. Patients were followed until December 31, 2018. The primary endpoint was hospitalization due to acute exacerbation (AE).

Results: The study included 582 ACO subjects, with a mean follow-up period of 2.98 years. During the study period, 228 (39.2%) ACO subjects had admission due to AE.

A total of 582 ACO patients were enrolled. After adjustments, cardioselective β-blockers use was associated with lower risk of hospitalization due to AE (hazard ratio [HR] = 0.29, 95% confidence interval [CI] = 0.11–0.72, p = 0.008). In contrast, non-selective β-blockers use did not change the risk of hospitalization due to AE.

Conclusions: Cardioselective β-blockers use may lower risk of acute exacerbation in patients with ACO.



A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB03

周邊血液嗜酸性白血球增多症在慢性阻塞性肺病急性發作的角色

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Role of peripheral eosinophilia in acute exacerbation of chronic obstructive pulmonary disease

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Purpose: Eosinophil counts are a promising guide to systemic steroid administration for chronic obstructive pulmonary disease (COPD). To study the role of peripheral eosinophilia in hospitalized patients with acute exacerbation of COPD (AECOPD).
Materials and Methods: From January 2014 to May 2017, patients with AECOPD hospitalized in Taipei Tzu Chi Hospital were retrospectively stratified into two groups according to their peripheral eosinophil count: The EOS group (eosinophil count ≥ 2%) and the non-EOS group (eosinophil count < 2%). Demographics, comorbidities, laboratory data, steroid use, length of hospital stay, and COPD-related readmissions were compared between the groups.
Results: A total of 625 patients were recruited, with 176 patients (28.2%) in the EOS group. The EOS group showed a lower prevalence of infection, lower cumulative doses of prednisolone equivalents, shorter length of hospital stay, and higher number of COPD-related readmissions than the non-EOS group. There were significantly linear correlations between eosinophil percentage and number of readmissions and between eosinophil percentage and length of hospital stay ($P < 0.001$, Pearson's $r = 0.147$; $P = 0.031$, Pearson's $r = -0.086$, respectively). The EOS group and a lower percent-predicted value of forced expiratory volume in one second (FEV1) were associated with shorter time to first COPD-related readmission [adjusted hazard ratio (adj. HR) = 1.488, $P < 0.001$; adj. HR = 0.985, $P < 0.001$, respectively].
Conclusions: The study findings suggest that the EOS group had the features of a shorter length of hospital stay, and lower doses of systemic steroids, but more frequent readmissions. The EOS group and lower percent-predicted FEV1 values were risk factors for shorter time to first COPD-related readmission.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB04

運動功能評估與胸部電腦斷層定量的相關性

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The Correlation among CT Quantification Imaging, Functional Exercise Capacities, Lung Function Tests, Clinical Symptoms and Outcomes in Chronic Obstructive Pulmonary Disease (COPD)

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Objective: This study aimed to evaluate the correlation between lung computed tomography (CT) quantification, functional exercise capacities, lung function tests, clinical symptoms and clinical outcomes in COPD.
Methods and materials: We analyzed chest CT image from 80 COPD patients in National Taiwan University Hospital. Chest CT was quantified using commercially available automatic software, including low attenuation area (LAA) identification, airway and pulmonary vasculature measurement. The association between the automated image quantification, functional exercised capacities, lung function tests, clinical symptoms and clinical outcomes were analyzed.
Results : Total volume and percentage of LAA were highly correlated with the forced expiratory volume in one second (FEV1) (partial r, pr=-0.39 and pr=-0.42, P <0.00091), modified Medical Research Council (mMRC) score (pr=0.38, P<0.05 and pr=0.40 P <0.00091) and airflow obstruction and dyspnea, and exercise capacity (BODE) index (pr=0.46, P <0.00085 and pr=0.48 P value <0.00091), but not chronic obstructive pulmonary disease assessment test (CAT) score. There was no significant association between the six-minute walking distance (6MWD) and chest CT quantification. However, there was significant association between severity of exercise-induced desaturation (EID) during 6MWD and the total LAA volume, LAA percentage and 15% percentile Hounsfield unit value (HU) of whole lung (PI15, P<0.00091). LAA size analysis found the volume and percentage of LAA size between 0 to 10mm showed significant correlation to EID severity (P value <0.00091). We found a trend of correlation between the nadir of oxygen saturation, EID severity, BODE index and the airway measurements, including airway lumen diameter, area, perimeter, wall thickness, lumen volume and wall volume (P <0.05) in the peripheral airway. However, there was no obvious association between the quantification of vessels and clinical parameters. The chest image quantification was not associated with acute exacerbation and disease progression within one-year follow-up.
Conclusion: We found volume and percentage of LAA, as well as PI15 were highly correlated with EID severity during 6MWT but not functional exercise capacities, frequent of acute exacerbation and disease progression.

Keywords: Chest CT quantification, COPD, Functional exercise capacity, LAA, Airway

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB05

肺復原訓練在兩類臨床表型的肺阻塞之長期成效

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Long-term effects of pulmonary rehabilitation in two clinical phenotypes of COPD

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Purpose: Chronic obstructive pulmonary disease (COPD) is complex disease and pulmonary rehabilitation (PR) may improve its lung mechanics, muscle function, symptoms, and exercise tolerance. The aim of the study is to investigate whether a PR program can improve clinical outcomes in 2 phenotypes of COPD.

Materials and Methods: In a prospective study, patients with COPD were enrolled from Chest outpatient department in December 2017, and were followed up for 2 years until December 2019. They performed a complex PR with chest wall-stretching, controlled breathing techniques, and personalized exercise training by cycling and treadmills 1 hour per week. According to initial assessment, these patients were divided into “poor lung mechanics” and “poor muscle function” and others. Those who with “poor lung mechanics” received advanced breathing techniques training and chest percussion as well as intermittent positive pressure breathing (IPPB) therapy. Those who with “poor muscle function” performed advanced treadmill training to reach 60-80% target heart rate.

Results: A total of 8 COPD patients with “poor lung mechanics” (76.0±10.0 years, FEV_1: 79.0±35.7%; n=3) and “poor muscle function” (72.0±4.5 years, FEV_1: 64.2±10.4%; n=5) were enrolled. In the “poor lung mechanics” group, the maximal inspiratory pressure (PImax)/maximal expiratory pressure (PEmax) (56.0±24.2/105.3±43.9 cmH_2O at baseline) increased after PR (74.0±42.6/112.7±41.5 cmH_2O). The 6-minute walk test (6MWT) distance was longer post-PR (476.0±27.0 m) compared with baseline (368.3±72.6 m). The COPD assessment test (CAT) score significantly decreased (9.3±1.2 at baseline, 3.3±0.6 at M24) (p=0.0267). In the “poor muscle function” group, the upper-limb grip-strength (28.8±4.2 kg at baseline) increased after PR (32.1±5.1 kg). The lower-limb 30-seconds chair stand test (30s-CST) showed (13.6±2.4 rises at baseline) significant increase strength and endurance after PR (16.8±2.6 rises) (p=0.0349). The 6MWT was better post-PR (319.4±64.1 m) compared with baseline (288.6±43.6 m). The exercise capacity was significantly increased (2.84±0.33 MET at baseline, 4.20±0.90 MET at M24) (p=0.0141). The CAT score decreased significantly (16.2±4.2 at baseline, 6.8±3.0 at M24) (p=0.0308). With PR, both groups showed decreased exacerbation-related hospital admission.

Conclusions: Planned long-term PR in both “poor lung mechanics” and “poor muscle function” clinical phenotypes of COPD patients will enhance physical activity, improve symptoms, and reduce the risk of hospitalization.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB06

抗嗜中性白血球細胞質抗體陰性之嗜酸性肉芽腫多發性血管炎(EGPA)合併嚴重氣喘、皮膚與腹部症狀之案例報告

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ANCA-negative eosinophilic granulomatosis with polyangiitis (EGPA) with severe asthma, skin and abdominal manifestations: A case report

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Abstract

Introduction: Eosinophilic granulomatosis with polyangiitis (EGPA) is a systemic necrotizing vasculitis of small- to medium-sized vessels. Both vessel inflammation and eosinophilic infiltration are thought to contribute to organ damage, resulting in heterogeneous clinical presentations.

Case Report: A 24-year-old woman had been admitted to a local hospital many times for recurrent cough, wheezing, skin rash, abdominal pain, diarrhea and blood eosinophilia. The highest eosinophil count ever recorded was 8480/μL. In Feb. 2019, her computed tomography (CT) scan of the chest revealed scattered ground-glass opacities and consolidations at the periphery of lungs. In Apr. 2020, her CT scan of the abdomen showed diffuse wall thickening all over the colon. All autoimmune profiles, including ANCA, were negative. Her symptoms and radiological lesions resolved after IV corticosteroid. However, her asthma and other systemic symptoms recurred after discharge, requiring long-term maintenance of oral corticosteroid. Mepolizumab therapy was first initiated in May 2020.

Table 1. Brief summary of course and treatment

Date	WBC (k/μL)	Eosinophil (%)	Eosinophil count (/μL)	Event/setting	Treatments (other than inhalers)	HRCT (2019/02/21)
2018/02/14	16000	53	8480	Hospitalization	IV steroid	
2019/02/27	6000	41.3	2480	Hospitalization	IV steroid	
2019/12/12	7610	35.9	2732	Outpatient clinic	Omalizumab	
2020/03/22	4680	34.4	1609	Hospitalization	IV steroid	
2020/04/22	5070	10.7	542	Outpatient clinic	Prednisolone (OCS)	
2020/05/05	17100	17.1	2924	Outpatient clinic	Mepolizumab + OCS	
2020/09/24	5610	0.9	51	Outpatient clinic	Mepolizumab	

Conclusion: Anti-IL5 therapy may have a role in the management of EGPA refractory to traditional therapies.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB07

探討居家吸氣肌訓練對慢性阻塞性肺疾患者在小呼吸道肺功能與疾病相關症狀之效益

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The effects of home-based inspiratory muscle training on the small airway function and disease-associated symptoms in patients with chronic obstructive pulmonary disease

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Abstract

Purpose

In chronic obstructive pulmonary disease (COPD), airflow limitation occurs mainly in the small airways. Weakness of the respiratory muscles contribute to dyspnea and decreased exercise capacity in COPD patients. The current study aims to investigate the effects of home-based inspiratory muscle training (IMT) on the small airway function and symptoms in COPD patients.

Methods

The study adopted a longitudinal design and repeated measure. The enrolled subjects were COPD patients with at least moderate airflow limitation. Patients were allocated to either the group receiving IMT or the control group. The study period was 12 weeks. Small airway function was assessed by plethysmography on enrollment and at the end of the study. The maximal inspiratory pressure (PI_{max}), 6-minute walking test, the modified British Medical Research Council score (mMRC), and the COPD assessment test (CAT) were recorded at study enrollment and then every four weeks.

Results

After 12 weeks of training, the ratio of the first second of forced expiration to the forced vital capacity (FEV1/FVC%), forced expiratory flow ($FEF_{25-75\%}$), and $FEF_{50\%}$ in the IMT group were better than those in the control group. The IMT group showed significantly lower CAT scores, resting heart rate at week 8 and week 12, and mMRC than the control group at week 12.

Conclusion

Home-based IMT effectively improved post-bronchodilator air flow in the small airways and ameliorated disease-associated symptoms in COPD patients. This training modality may be a good choice of home-based pulmonary rehabilitation programs.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB08

罕見引起吞嚥困難的原因-位於後縱膈腔食道周圍的惡性間皮瘤

A rare cause of dysphagia - Malignant pleural mesotheliomain the Posterior Mediastinum anddiffuse esophageal wall thickening

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A 52-year-old woman patient complained of progressive dysphagia for a long time (since 2018/06) and had body weight loss 7-8 kg (2018/06~2018/10). Meanwhile, the CxR revealed bilateral pleural effusion. But there was no definite diagnosis then. During admission in KMUH (高醫大) 2018/10, High titer of anti-SSA/Ro antibody (20 au/ml) was found and the Schirmer test was positive. She had received systemic steroid therapy under the impression of Sjogren's syndrome.

After discharge from KMUH last November, and she had persistent progressive exertional dyspnea. There was productive cough with yellowish sputum, orthopnea, and bilateral lower legs edema. She also had severe body weight loss around 20kg in recent 6 months. The CxR revealed the massive right pleural effusion and multiple patch consolidation over both lung fields. The Chest CT showed diffuse increase soft tissue infiltration among mediastinum fat with mass effectdisplaced vascular structure, and highly suspect esophageal cancer. The effusion cytology and cell block examination did not show the answer of the mass lesion. She had ever received gastric endoscopic examination twice, but there was no organic esophageal lesion found. (Endoscopic ultrasound was not used due to severe dyspnea). Patient received thoracoscopic surgery in 2019/02. The diagnosis was epithelioid malignant mesothelioma. Reviewing her personal and occupational history, she had never asbestos exposure before.

Malignant mesothelioma is a rare malignance disease in the lining of the lungs, abdomen or heart and usually related to asbestos exposure. The diagnosis of pleural mesothelioma is difficult andoften delayed for 6-8 months after the initial symptoms. Pleural fluidcytology and needle biopsy are limited in value because anumber of benign and inflammatory conditions can producecellular changes confused with malignant disease. It usually develops diffusely along the entire parietal and visceral pleura and tends to cause "inward" contraction of the hemithorax.In our case, the tumorformed a mass in the middle to lower posterior mediastinum andsurrounded the esophagus concentrically without mucosalinvasion. Besides, even repeated cytologic examinationsof the pleural effusions failed to yield a diagnosisof malignant pleural mesothelioma.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB09

初次使用三合一治療肺阻塞的時機：利用 CID 來評估必須增加長效型抗膽鹼劑至吸入性類固醇及長效乙二型交感神經刺激劑的族群

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When to use initial triple therapy in COPD: adding a LAMA to ICS/LABA by clinical important deterioration assessment

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Purpose: Triple therapy versus dual therapy for chronic pulmonary obstructive disease (COPD) can reduce symptoms, limit the risk of acute exacerbations (AEs) as well as improve lung function. Currently, studies that feature clinically important deterioration (CID) as a composite endpoint to assess the need for treatment intensification for patients maintained on dual therapy remained to be scarce.

Materials and Methods: This study is a retrospective analysis (January 2014 to January 2018) of COPD patients that presented with moderate to severe AEs during the previous year with blood eosinophil counts >150 cells/μL. First-line of therapy included a combination of inhaled corticosteroid (ICS) and a long-acting β_2 agonist (LABA). Composite CID was used in assessing the response to treatment after 24 weeks of therapy.

Results: This study included 110 patients, of which 49 patients reportedly experienced CID. The most common events of CID include a decline in forced expiratory volume in 1 second (FEV1) ≥ 100 mL from baseline (25/49, 51%) and an increase in COPD Assessment Test (CAT) scores ≥ 2 (13/49, 26.5%); many of these patients were respond to the addition of a long-acting muscarinic antagonist (LAMA). Seven patients (7/110, 6.3%) experienced moderate to severe exacerbations while undergoing treatment with ICS/LABA. Univariate and multivariate analyses have identified low baseline FEV1 (OR = 0.86, $p = 0.004$) and high CAT score (OR = 1.60, $p = 0.002$) as independent predictors of CID. A baseline FEV1 of ≤ 42% and an initial CAT score ≥ 18 were considered the optimal cut-off values, which were identified via receiver operating characteristics (ROC) curve analysis.

Conclusions: Triple therapy (ICS/LABAs/LAMAs) may be considered as first-line treatment in patients experiencing moderate to severe AEs of COPD in the previous year and who have blood eosinophil counts >150 cells/μL, reduced lung function (FEV1 ≤ 42%), and more symptoms (CAT score ≥ 18).

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB10

慢性阻塞性肺病患者腸內菌相與其肺功能變化的關聯性

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Association between gut microbiota and alteration of lung function in patients with chronic obstructive pulmonary disease

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Objective：Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disease that characterized by persistent airflow limitation. In recent years, the significant differences in the distribution of gut microbiota between healthy individuals and COPD patients and between different levels of COPD patients were found. Gut microbiota closely correlated with inflammation in lung. Our previous study indicated that the microbial ecology of the gut was related to the severity of COPD. However, the gut microbiome study is not performed to lung function decline in chronic lung disease progression. In the study, we evaluated the relationship between gut microbiota and lung function in COPD patients.

Subjects and Methods：A total 55 COPD patients (> 20 years old) was enrolled for this study. After extraction of genomic DNA from stool samples, we performed the next generation sequencing technology to analysis the distribution of gut microbiota in stool samples of COPD patients.

Results：When the whole data were stratified according to the rate of forced expiratory volume in 1 second (FEV_1) decline, our results indicated significant difference in community richness of the microbiome between the initial and the follow-up stool samples in decline group (the rate of FEV_1 decline ≧ 40 ml/yr) but not in control group (the rate of FEV_1 decline < 40 ml/yr and the positive rate of change ≧ 0 ml/yr). In the Matastats analysis, we found the significant differences in distribution of five bacterial genera (*Cetobacterium*, *Ruminococcaceae_NK4A214_group*, *Lachnospiraceae_NK4A136_group*, *Pluralibacter*, and *Tyzzerella_4*) in the control group and five bacterial genera (*Citrobacter*, *[Eubacterium]_eligens_group*, *Weissella*, *[Eubacterium_ventriosum_group*, and *Prevotella_2*) in the decline group between the initial and the follow-up stool samples.

Conclusion：Our results indicated some gut microbiota closely related to changes in lung function of COPD patients. In the future, the mechanism for the alteration of lung function in COPD patients due to the changes in gut bacterial community should be investigated.

Keywords：Chronic obstructive pulmonary disease; Next generation sequencing; Gut microbiota, Lung function

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB11

探討台灣嚴重氣喘病患之病人特性、臨床結果和生物標記之關聯

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Comparing Patient Characteristics, Clinical Outcomes, and Biomarkers of Severe Asthma of Patients in Taiwan

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Purpose: To understand the association between biomarkers and exacerbations of severe asthma adult patients in Taiwan.

Materials and Methods: Data, including demographic, clinical characteristics and biomarkers, were retrospectively collected from the medical charts of severe asthma patients in six hospitals in Taiwan. Exacerbations were defined as those requiring asthma-specific emergency department visits/hospitalizations, or systemic steroids. Enrolled patients were divided into: 1) those with no exacerbations (non-exacerbators) and 2) those with one or more exacerbations (exacerbators). Receiver operating characteristic (ROC) curves were used to determine the optimal cut-off value for biomarkers. Generalized linear models evaluated the association between exacerbation and biomarkers.

Results: A total of 132 patients were enrolled in the study with 80 non-exacerbators and 52 exacerbators. There was no significant difference in demographic and clinical characteristics between two groups. Exacerbators had significantly higher eosinophils (EOS) counts (367.8±357.18 vs. 210.05±175.24, p=0.0043) compared to non-exacerbators. The optimal cut-off values were 292 for EOS counts and 19 for Fractional exhaled Nitric Oxide (FeNO) measure. Patients with EOS count ≥ 300 (RR=1.88; 95%CI, 1.26-2.81; p=0.002) or FeNO measure ≥ 20 (RR=2.10; 95%CI, 1.05-4.18; p=0.0356) had a significantly higher risk of exacerbation. Patients with EOS count ≥ 300 and FeNO measure ≥ 20 had a significantly higher risk of exacerbation compared to those with lower EOS count or lower FeNO measure (RR=2.16; 95% CI, 1.47-3.18; p= <.0001).

Conclusions: Higher EOS counts and FeNO measure were associated with increased risk of exacerbation. Identification of these biomarkers may help physicians identify patients at risk of exacerbations and personalize treatment for asthma patients.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB12

肺阻塞對小細胞肺癌死亡率的影響

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Impact of Chronic Obstructive Pulmonary Disease on the Mortality of Patients with Small Cell Lung Cancer

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Purpose: Chronic obstructive pulmonary disease (COPD) and lung cancer share a common risk factor of cigarette smoking. Previous studies have reported that COPD coexisting non-small cell lung cancer was related to poor prognosis. However, limited studies focused on the impact of small cell lung cancer (SCLC) coexistent COPD. The aim of our study was to examine the impact of COPD on mortality in patients with SCLC.

Materials and Methods: We analyzed data from the Taiwan Cancer Registry Database for patients who were diagnosed with SCLC between January 1, 1997, and December 31, 2015. Definition of COPD population was patients with a COPD diagnosis at least three outpatient claims or at least one inpatient claim coded and also need at least one prescription of bronchodilators at least 3 months before the diagnosis of SCLC. The control group were randomly selected SCLC patients without COPD after propensity score matching with SCLC patients with COPD according to age, gender, index data, cancer staging and comorbidities at a 1:1 ratio. The overall survival and predictors of mortality were analyzed using Cox proportional hazards regression.

Results: There were 9425 patients diagnosed with SCLC and patients were divided into the comorbid COPD group (n = 4235) and the non-COPD group (n = 2334). After matching, there were 1457 SCLC combined COPD patients. Multivariate analysis identified age, old myocardial infarct, congestive heart failure, and diabetes were independent risk factors for overall survival. Comorbid COPD was not significantly associated with poorer survival in SCLC patients.

Conclusions: A diagnosis of COPD did not have an impact on the survival of SCLC.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB13

重症肺阻塞合併社區型肺炎的病人，*Pseudomonas aeruginosa* 及 *Acinetobacter baumannii* complex 的特徵分析

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Factors associated with *Pseudomonas aeruginosa* and *Acinetobacter baumannii* complex isolations in patients with chronic obstructive pulmonary disease and community-acquired pneumonia in an intensive care unit in Taiwan

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Background:
To date, the features of *Pseudomonas aeruginosa* (P.A) and *Acinetobacter baumannii* complex (AB complex) isolations discovered in patients with chronic obstructive pulmonary disease (COPD) and community-acquired pneumonia (CAP) requiring mechanical ventilation and admission to an intensive care unit (ICU) remain unclear. Our study aims were to investigate the characteristics of P.A and AB complex isolations detected in endotracheal aspirates in patients with COPD and CAP in an ICU.
Method:
This retrospective study was conducted in the respiratory ICU (RICU) at Taichung Veterans General Hospital, Taiwan. Patients with COPD and CAP requiring invasive mechanical ventilation who admitted to RICU from January 2005 and December 2015 were included for analysis. Features associated with P.A and AB complex isolations were studied.
Results:
A total of 262 patients were included with 17.2% (45/262) and 11.5% (30/262) had P.A and AB complex isolations in endotracheal aspirates upon endotracheal intubation respectively. Patients with P.A isolates had a lower body mass index (BMI) and poorer lung function while subjects with AB complex isolates had a lower serum albumin level. Furthermore, multivariate logistic regression analysis revealed severe-to-very severe airflow limitation was independently associated with P.A isolation while a poorer nutritional status was a predictor for AB complex isolation in such population.
Conclusion:
Our study provided useful information to help intensivists make better decisions on adequate antibiotic choice in patients with COPD and CAP requiring mechanical ventilation and admission to an ICU.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB14

慢性阻塞性肺病為達文西冠狀動脈繞道手術後肺部相關併發症之獨立危險因子

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Chronic Obstructive Pulmonary Disease (COPD) is an independent risk factor of post-operative pulmonary complication in patients receiving robotic-assisted coronary bypass graft surgery (RA-CABG)

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Backgrounds: Postoperative pulmonary complications (PPC) are common and may cause morbidity and mortality. Risk factors of development of PPC are numerous and most of them are preventable. Chronic obstructive pulmonary disease (COPD) is often neglected and inadequately treated. As smoking is a common risk factor of ischemic heart disease and COPD, we aimed at investigating the relationship between PPC and COPD in patients receiving robotic-assisted coronary artery bypass graft (RACABG) surgery.
Methods: We retrospectively included 298 patients, from January to December 2016, who underwent RAGABG surgery in a tertiary referral hospital in central Taiwan. COPD was defined by obstructive ventilatory impairment (FEV_1 /FVC ≤ 70%) with smoking history greater than 10 pack-year. Major PPC were defined as re-intubation, pneumonia and death during hospital stay.
Results: Totally, two hundred and ninety-eight patients received RACBAG were included for analysis. Among these patients, 19 had major PPC during hospital stay. By univariate analysis (Table 1), patients with major PPC are older (74.8±8 vs 63.5±10.9, p<0.01), lower ejection fraction (40.8±15 vs 52.6±11.7, p<0.01), hemoglobin (10.3±2 vs 11.4±1.8,p=0.01), more blood transfusion (1216.4±1990.9 vs 241.9±429.1, p =0.05), and more diagnosis of COPD (8 (42.1%) vs 29 (10.4%) , p<0.01). Patients with major PPC have longer intensive care unit (ICU) (16.6±20.5 vs 23±2.1 days, p=0.01) and hospital stay (34.2±31.3 vs 9.4±5.8 days, p=0.00). By multivariate logistic regression analysis (Table 2), patients with COPD is an independent risk factor to have major PPC during hospital stay (O.R. 4.38, 95% C.I. 1.17-16.39, p=0.03). Furthermore, patients with COPD were older (71.11 vs 63.14 year-old, p<0.001), lower FEV_1 77.43±25.19% vs 90.05±22.04%, p=0.035), and more blood loss during surgery (617.56 vs 425.04 c.c., p<0.01). Among these patients, those with COPD are associated with pneumonia.
Conclusions: Our results demonstrate that 12.4% patients receiving RACABG has COPD. Among these patients, those with COPD were associated with increased risk of major PPCs and more importantly that some of these patients were unrecognized and under treated. We suggest proper diagnosis and appropriate management of these patients is urgently needed to improve the outcome of patients receiving RACABG.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB15

吸入劑藥物使用的擇定上昇趨勢在真實世界臨床治療肺阻塞的回溯性追蹤

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A real-world COPD management report: focusing on inhaler escalation trend and its effect

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Purpose: We aim to survey the coherence and the difference of our clinical COPD care by guideline and by real-world physician-direct management.

Materials and Methods: A retrospective case series study was conducted. Registered COPD (ICD-10 J44.x) patients, 2017/1/1-2020/9/30, in a regional teaching hospital were initially screened. Exclusion criteria were patients with double registration, patients without spirometry data and error coding for J44. Patients with at least one spirometry tests were registered to be data analysis. At least one annual highest CAT score was recorded, but if the records of CAT score were found in only one year, the highest and next highest values were chosen to record. Every date and types of inhaler medications were recorded as the real-world clinical response. They were labeled as three categories, monotherapy, dual-bronchodilator and combo therapy and triple therapy. If a PDE4 inhibitor was used, it would be recorded also. To survey if escalation or de-escalation of inhaler medications was properly prescribed, we defined an “escalation trending” to reveal a stepwise adjustment in the order of “monotherapy →dual bronchodilator/combo therapy → open triple/one-device triple therapy”. Every individual numbers of in-hospital pulmonary rehabilitation were also recorded. The primary goal of this research is the coherence to the updated GOLD guideline. The secondary goals are the real-world outcome of clinical COPD patients.

Results: N= 105, male/female: 86/19, mean age (SD): 74.3 (9.0) years old and mean BMI: 24.1 (4.2). Mean FEV1/FVC ratio: 0.58 (0.11), post-bronchodilator FEV1%: 66% (23%). Mean days of the initial and the following for spirometry test were 401.6 (71.5) days. Mean eosinophil count in percentage was 3.1% (3.2%). Current smoker: non-smoker: quit smoker: 45:50:10, there was 42.9% of whole COPD patients still smoked. But in the 57 patients of more than 75 years old, a remarkable reduction of current tobacco smoking was noted only 35.1%. GOLD group C had only 2 cases (1.9%) in this series, the age, 87.5 (4.9), was significant older than other groups. Mean BMI, 24.1 (4.2), of each group was not different. 25 cases (23.8%) were with low body weight and their BMI was smaller than 21, however, the percentage of cases with BMI<21 in each group was not different in each group. The “escalation trending” revealed coherence in each group to maintain same class of inhaler medications and the use of triple therapy in group D (52.8%) is noted significantly more than other groups (p-value<0.001). 12 in 21 (57.1%) cases with escalation trending was kept in maintaining use of triple therapy and only 3 (14.3%) was shown de-escalation trend from triple therapy (p-value<0.001). The relative risk to non-survival in escalation of inhaler medications was higher than maintain or de-escalation.

Conclusions: The real-world inhaler use of triple therapy was related to maintain medications in group D COPD patients. Escalation of inhaler medicines might be expected to be a potential factor of survival risk.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB16

手握力對慢性阻塞性肺病急性惡化病患在將來進一步惡化風險的影響

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The impact of handgrip strength on further exacerbation risk in patient admitted due to COPD with acute exacerbation

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Rationale:：
Low handgrip strength (HGS) was independently associated with a higher risk for exacerbations in smokers with stable chronic obstructive pulmonary disease (COPD), but there is no study to examine the relationship between HGS and exacerbation risk in admitted patients due to acute exacerbation of COPD. This study is aim to conduct a prospective study to investigate the impact of HGS on further exacerbation risk in patient admitted due to acute exacerbation of COPD.

Materials and methods：
Adult patients (n=43), admitted due to acute exacerbation of COPD, were enrolled since Jan, 2018 to Jun, 2019. HGS was measured within 3 days after admission and the HGS weakness was defined according to European Working Group on Sarcopenia in Older People (EWGSOP) recommendation. The primary end-point is exacerbations within 12 months of index admission. We analyzed the association of demographics, HGS, pulmonary function parameter and acute exacerbation events.

Results：
Of the enrolled 43 patient, 31 are of HGS weakness (22.1±4.1 Kg). The pulmonary function, forced expiratory volume in one second percentage of predicted value (FEV1 pred%) were significantly lower in the HGS weakness group (0.82±0.20, 1.59±0.77, p=0.018).

Conclusion：
HGS weakness was associated with lower pulmonary function parameters among patients admitted with acute exacerbation of COPD.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB17

肺阻塞合併正常或是低收縮分率心衰竭導致急性惡化發作的不同風險

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Different acute exacerbation outcome in chronic obstructive pulmonary disease patients coexistent heart failure with reduced or preserved ejection fraction

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Purpose: The risk of acute exacerbation in chronic obstructive pulmonary disease (COPD) patients coexistent heart failure with reduced and preserved left ventricular ejection fraction (HFrEF, HFpEF) has not been previously investigated. The aim of this study was to determine whether the risk of exacerbation and respiratory symptom in COPD patients with HFpEF differs from COPD patients with HFrEF.
Materials and Methods: We retrospectively investigated 136 patients with coexistent heart failure and COPD from 2016 to 2018. HFrEF was present in 27 cases (20%) and HFpEF in the remaining 109 cases (80%). All the patients enrolled in this study was followed 1 years.
Results: The mean age of these 136 patients were 73.3 years old and 127 patients (93%) were male. COPD with HFrEF were younger (68±12 vs. 75±10 years; p=0.001), and more frequently had pulmonary hypertension (63 vs. 40%; p=0.028) and atrial fibrillation (33 vs. 15%; p=0.031). They also had lower LVEF (38.2± 11.6 vs. 59.9±5.5%, p<0.001), higher LV mass (116±18 vs. 95±12 g/m2; p<0.001), left atrial size (49±9 vs. 36±5 mm; p<0.001), and mitral E/Ea ratio (15.5±5 vs. 13.1±6; p=0.005) than those COPD with HEpEF. Moreover, COPD with HFrEF had higher CAT score (23±6.3 vs. 19 ±6.8, p=0.003), mMRC score (2.6±0.8 vs. 1.8±1.0, p< 0.001) and more severe acute exacerbation (44.4 vs. 25.7%, p=0.049) than those COPD with HFpEF.
Conclusions: COPD is commonly associated with heart failure in clinical practice since they share the same pathogenic mechanism. Both conditions incur significant morbidity and mortality. From our study, COPD patients with HFrEF had more risk of acute exacerbation and higher CAT and mMRC score than COPD patients with HFpEF.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB18

心肺耦合與慢性阻塞性肺病病人運動能力之關聯性

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Cardiorespiratory Coupling Is Associated With Exercise Capacity In Patients With Chronic Obstructive Pulmonary Disease

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Background: Although comorbidities of cardiovascular disease is common in patients with chronic obstructive pulmonary disease (COPD), the interaction between the heart and lungs in COPD patients has yet to be further elucidated. Synchrogram index is a new parameter that can quantify this interaction and has the potential to apply in COPD patients.
Aim: Our objective in this study was to characterize cardiorespiratory interactions in terms of cardiorespiratory coupling (CRC) using the synchrogram index of the heart rate and respiratory flow signals in patients with chronic obstructive pulmonary disease.
Methods: This is a cross-sectional and a preliminary data from a prospective study, examining 55 COPD patients. K-means clustering analysis was applied to cluster COPD patients based on synchrogram index. Linear regression and multivariable regression analysis were used to determine the correlation between the synchrogram index and the exercise capacity assessed by six-minute walking test (6MWT).
Results: The 55 COPD patients were separated into a synchronized group (median 0.89 (0.64-0.97), n=43) and a desynchronized group (median 0.23 (0.02-0.51), n=12) based on K-means clustering analysis. Synchrogram index was correlated significantly with six minutes walking distance (r=0.42, p=0.001) and distance saturation product (r= 0.41, p=0.001) assessed by 6MWT, and still was an independent variable by multivariable regression analysis.
Conclusion: This is the first result studying the heart-lung interaction in terms of cardiorespiratory coupling in COPD patients by the synchrogram index, and COPD patients are clustered into synchronized and desynchronized groups. Cardiorespiratory coupling is associated with exercise capacity in patients with COPD.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB19

肺阻塞病人從開放式三合一治療至單一裝置三合一治療的效力：真實世界的觀察性研究

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The effectiveness of open triple to closed triple therapy in COPD patient: A real-world observational study

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Purpose: This real-world study evaluated the effectiveness of closed triple therapy shifting from open triple therapy were limited.
Materials and Methods: We conducted this retrospective study at a single medical center from January 2015 to March 2020. Patients with COPD who stepped up to triple therapy were enrolled. We try to indicate the period length from initial COPD management to open or closed triple therapy and identify the clinical predictors of patients who needed triple therapy early. We evaluated the effectiveness of open triple therapy from initial management and closed triple from open triple therapy.
Results: A total 115 patients with COPD who stepped up to triple therapy were analyzed. The length period from initial treatment to triple therapy was 22.4 months. Among patients who early shifted to triple therapy (n=63, less than 22 months) and those lately shifted to triple therapy (n= 52, more than 22 months), their baseline characteristics including the COPD group, airway reversibility, and initial treatment were significantly different. After univariate and multivariate analysis, patient with elderly age, more acute exacerbation (AE) in previous year, asthma and COPD overlap (ACO), and initial dual bronchodilator therapy would be stepped up to triple therapy early. The FEV1 of patients were significantly increased after shifting to open triple therapy. Besides, shifting from open triple to closed triple significantly reduced the incidence of AE.
Conclusions:
COPD patients with older age, more AE last year, ACO, and initial dual bronchodilator therapy were stepped to open triple therapy early to increase FEV1. And shifting to closed triple from open triple therapy can reduce the incidence of AE.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB20

肺阻塞合併骨質疏鬆之處方型態

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Prescription Patterns in Patients with Chronic Obstructive Pulmonary Disease and Osteoporosis

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Purpose: Patients with chronic obstructive pulmonary disease (COPD) have a higher risk of osteoporosis. Fracture is a common complication of osteoporosis, and patients with COPD and fractures have a higher mortality rate than COPD patients without fractures. Few studies have addressed the prescription patterns in osteoporosis patients with COPD. The purpose of this study was to conduct a retrospective study of the prescription patterns in patients with COPD and osteoporosis in Taiwan.
Materials and Methods: The study was conducted with data from the Taiwan National Health Insurance Research Database from January 1, 2003, to December 31, 2016. We selected the COPD population in Taiwan older than 40 years with at least one prescription for a bronchodilator. We excluded patients who had osteoporosis, fracture, asthma, or cancer before the diagnosis of COPD. After the diagnosis of COPD, patients who did not have osteoporosis were also excluded, and the remaining patients were defined as COPD patients with osteoporosis. We followed this COPD and osteoporosis cohort until they had been prescribed medication for osteoporosis.
Results: There were 13,407 patients with COPD and osteoporosis who received osteoporosis treatment. Among the patients who received treatment, the majority were female (n = 9136), accounting for 68.14% of all treated patients. The age distribution across age groups with 15-year intervals was as follows: 6.33% of the patients were 40-54 years old, 15.92% were 55-64 years old, 38.88% were 65-74 years old, and 38.87% were 75 years old or older. The common comorbidities (>20%) included hypertension, cardiovascular disease (including coronary artery disease, peripheral vascular disease, ischemic stroke, hemorrhagic stroke, or heart failure), diabetes and dyslipidemia. A total of 53.4% of the patients had been prescribed steroids least once within the last year before receiving a diagnosis of osteoporosis. A total of 34.61% of the patients received systemic corticosteroids with a daily dose equivalent to 5 mg of prednisolone within the 3 months prior to the diagnosis of osteoporosis. The older the patient was, the higher the probability of the prescription of medication for osteoporosis. Patients with depression had a high probability of receiving medication for osteoporosis.
Conclusions: The rate of prescriptions for the treatment of osteoporosis in patients with COPD was low. Physicians need to be aware of this issue and treat osteoporosis more aggressively in patients with COPD.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB21

台灣氣喘病患短效乙型促進劑處方模式在國際 SABINA 研究中的探討

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An overview of short-acting β2-agonist prescription patterns in asthma in the Taiwanese cohort of the SABINA International study

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Purpose: Asthma is a chronic inflammatory disease of the lung. Understanding the true prevalence of short-acting β2-agonist (SABA) prescriptions for the treatment of asthma in Taiwan may help reveal the full extent of a potential public health issue in the country, as SABAs do not treat the underlying inflammation in asthma. The SABA use IN Asthma (SABINA) studies assess SABA use globally, with an intent to align local practices with global guidelines. Herein, we describe socio-demographics, disease characteristics and treatment patterns in the Taiwanese cohort of the SABINA International study.

Materials and Methods: Patients (aged ≥12 years) with asthma from 10 sites in Taiwan were included in this cross-sectional study. Data on prescriber type, asthma severity and symptom control (per the 2017 Global Initiative for Asthma [GINA] recommendations), severe exacerbation (defined as asthma worsening that required hospitalisation, emergency room treatment, or intravenous/oral corticosteroids for ≥3 days or a single intramuscular corticosteroid dose) history and prescribed treatments in the year before the index date were collected using real-time electronic case-report forms.

Results: Overall, 294 patients were included in the analysis (mean age [standard deviation (SD)]: 57.9 [15.6] years; 69% female). Almost all patients were enrolled by specialists (n=292 [99.7%]) and most patients (n=274 [93.2%]) had moderate/severe asthma (GINA steps 3−5). Overall, 110 (37.4%) patients were overweight and 47 (16.0%), obese per the World Health Organization criteria. Many patients had a negative smoking history (n=234 [79.6%]), high school or university/post-university education (n=182 [61.9%]) and ≤2 comorbidities (n=262 [89.1%]). All patients received fully reimbursed healthcare. The mean (SD) asthma duration was 8.3 (10.0) years, with 111 (37.8%) patients experiencing ≥1 severe exacerbation in the past year. While 183 (62.2%) patients had well-controlled asthma, 77 (26.2%) and 34 (11.6%) patients had partially controlled and uncontrolled asthma, respectively. A total of 56 (19.0%) enrolled patients received SABA prescriptions for ≥3 canisters/year, which suggests potential overuse.

Conclusions: In contrast to other SABINA studies, almost all patients were recruited at specialist centres, as national regulations precluded recruitment from primary care clinics. This Taiwanese cohort may therefore represent the 'ideal scenario', with most patients receiving appropriate asthma management under speciality care and fully reimbursed healthcare. However, our findings indicate room for improvement in asthma treatment practices related to SABA prescriptions in Taiwan. Full results from this study, including SABA prescription data, will be published shortly.

Funding statement: AstraZeneca funded the SABINA programme and was involved in the programme design, study protocol development, study execution and data analysis.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB22

運用心肺耦合以預測慢性肺阻塞病患的急性發作

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Application of cardiorespiratory coupling test in predicting exacerbation in patient with chronic obstructive pulmonary disease

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Running title: Cardiorespiratory coupling in predicting acute exacerbation in COPD patients

Abstract

Background

Factors that could predict acute exacerbation in patients with chronic obstructive pulmonary disease (COPD) including previous exacerbation history, body-Mass Index, airflow obstruction, dyspnea, and exercise capacity Index, (i.e. BODE index). Synchrogram index, a parameter in quantifying the heart lung interaction from cardiorespiratory coupling test, is correlated with performance in six minutes walking test, may has potential application in predicting exacerbation in COPD patients.

Aim

The aim of this study is to evaluate the fluctuation pattern of synchrogram index under 1 year follow up in correlation with acute exacerbation in COPD patients.

Methods

In this observational prospective study, total of 54 patients were followed every 3 months up to one year. Baseline clinical variables, number and severity of exacerbations were recorded. Synchrogram index was analyzed from electrocardioagram and respiratory signals every three months. We investigated the prognostic value of synchrogram index for both the number and severity of exacerbations.

Results

Using receiver operating characteristic curve, dynamic change of synchrogram indicies were categorized into variation group and stable group (area under curve: 0.68, p=0.03). Patients experienced frequent total (moderate and severe) exacerbations in the variation group (50%, total 22 patients, p=0.008). In the multinomial logistic regression model, previous exacerbation history (coefficient: 0.19, p=0.02) and fluctuation synchrogram index (coefficient: 0.32, p=0.02) are independent variables that could predict total exacerbations (adjusted R-squared: 0.29, p=0.002).

Conclusion

This study supports that pattern of dynamic synchrogram indices can predict exacerbations in COPD patients. Further studies are needed to define the heart or lung problem related to fluctuated synchrogram indicies.

Keywords: synchrogram index, acute exacerbation, chronic obstructive pulmonary disease, cardiorespiratory coupling

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB23

慢性阻塞性肺病患者之運動引發支氣管收縮現象

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Exercise-induced bronchoconstriction in chronic obstructive pulmonary disease

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Abstract

Introduction: Exercise-induced bronchoconstriction (EIB) referred to airway narrowing after exercise, and was observed in a proportion of patients with asthma. The EIB phenomenon was also noticed in some patients of chronic obstructive pulmonary disease, but the clinical significance was uncertain.

Methods: We collected data via pulmonary rehabilitation service in a medical center within 18 months retrospectively. We recorded the BMI, baseline lung function tests results, mMRC and CAT score, acute exacerbations (AE) history, comorbidities, serologies (eosinophil count and IgE), 6-minute walking test (6MWT) performance, and changes in oxygen saturation and lung functions after exercise. We defined EIB as 10% decrease in FEV1 after 6-minutes walking tests, and compared the parameters between the groups of the patients with and without EIB.

Results: We collected the data from 186 patients, and 33 of them (17.7%) were with EIB. The patients with EIB had numerically less 6-minute walking distance (6MWD) in meters compared with the patients without EIB (348.36±128.69 v.s. 388.93±102.52, p = 0.051), and also had numerically lower 6MWD %predicted (78.37±25.62 v.s. 83.34±19.36, p = 0.299). The patients with EIB had numerically fewer exacerbation episodes within 1 year (0.58±0.75 v.s. 0.97±1.22, p = 0.073; AE≧2 times in 1 year, 15.2% v.s. 25.5%, p = 0.205), though without statistical significance. The patients with EIB also tended to have numerically higher mMRC score (mMRC≧3, 33.3% v.s. 19.0%, p = 0.068) and higher CAT score (CAT≧10, 42.4% v.s. 28.8%, p = 0.124). In aspects of baseline lung function tests, the patients with EIB had no difference in FEV1 percentage (%) predicted (68.68±25.38 v.s. 64.65±23.14, p = 0.374) and numerically higher proportion of positive bronchodilator response (post-bronchodilator FEV1 +12% & 0.2L, 24.2% v.s. 16.3%, p = 0.281), though without statistical significance. The patients had no difference in eosinophil percentage (%) (3.71±3.05 v.s. 3.54±3.61, p = 0.802) and eosinophil count (260.48±256.10 v.s. 249.12±260.80, p = 0.825). There were no remarkable differences in BMI and comorbidities in between groups. We matched the FEV1 decrease percentage and PEFR decrease percentage after 6MWT, and found a moderate correlation between the two measures (Pearson correlation coefficient = 0.486).

Conclusion: The patients with EIB presented with more prominent exercise limitation and dyspnea symptoms compared with the patients without EIB.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB24

慢性阻塞性肺病病人因急性惡化住院後之一年死亡預測指標驗證與探討

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Predictors of one-year mortality after hospitalization for an exacerbation of COPD

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Purpose: Our previous work provided the consensus of factors associated with high risk of one-year mortality for patients with chronic obstructive pulmonary disease (COPD) required hospitalization. The consensus was concluded by modified Delphi method to obtain the opinions from pulmonologist in Taiwan. We aim to validate the power of predictors of one-year mortality after hospitalization for an exacerbation of COPD (AECOPD).

Materials and Methods: A retrospective cohort analysis conducted in Taichung Veterans General Hospital (TC-VGH) in the period of 2012 to 2018. Patients admitted to the hospital due to AECOPD were enrolled. A total of 9 predictors from modified Delphi method and expert consensus were validated to predict 1-year mortality after discharging. Standard Cox semi-parametric proportional hazards models and the C statistic were applied to model the time-to-death data.

Results: We enrolled 3016 subjects ever admitted due to AECOPD. One year mortality rate was associated with age≧80 (OR=1.61; 95% CI: 1.08-2.41), Body Mass Index (BMI) <20 (OR=1.77; 95% CI: 1.19-2.64), history of AECOPD (OR=1.63; 95% CI: 1.09-2.44), dyspnea score≧3 points (OR=1.99; 95% CI: 1.20-3.29), and Age-Dyspnea-Obstruction (ADO) score≧6 points (OR=2.71; 95% CI: 1.82-4.05). The best predictive model of 1-year mortality was ADO, history of AECOPD and BMI <20 (*C* index=0.662).

Conclusions: For patients with COPD experienced hospitalization due to AECOPD, we found that ADO score plus the medical history of acute exacerbation and BMI <20 has the highest predictive value of 1-year mortality after discharging from hospital. In those patients with these characteristics a more personalized follow-up is mandatory.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB25

肺阻塞的吸入劑使用 – 真實世界研究的系統性回顧與統合分析

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Use of inhaled medicines for chronic obstructive pulmonary disease – a systematic review and meta-analysis of real-world studies

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Background:
Maintenance inhaled medicines are the core treatment for chronic obstructive pulmonary disease (COPD). Adherence to treatment suggestions is critical for disease control. We aimed to assess the gap between evidence-based recommendations and the real-world practice in using inhaled medicines for COPD.
Material and Methods:
We searched Medline, Embase, Cumulative Index to Nursing and Allied Health Literature, Global Health, and Cochrane Database of Systematic Reviews for studies published from 1 January 2000 to 31 December 2018. Observational studies assessing prescription and patients' adherence to inhaled medicines up to 12 months were included. Meta-analysis was done using a non-linear mixed model to obtain the pooled estimates.
Results:
Among 3,381 abstracts screened, 23 full-text articles were included for quantitative assessment. Of 423,358 patients with COPD analyzed, around 6.9% (95% CI 3.3 – 13.8%) of them did not use any inhaled medicine. Those who used only short-acting bronchodilators accounted for 6.3% (95% CI 1.6 – 22.1%) of all patients. Among those who started maintenance therapy, only 32.8% (95% CI 18.0 – 52.1%) were adherent to their treatment in 12 months. Among different types of maintenance therapy, long-acting muscarinic antagonist monotherapy had the highest adherence (43.9%, 95% CI 33.1 – 55.4%).
Conclusion:
More than one in 20 patients with COPD did not use any form of inhaled medicine. Patients' adherence to maintenance inhaler was low even in just one year. Further studies to evaluate and address the underlying causes of poor adherence are needed.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB26

真實世界肺阻塞病患的肺復健順應性 – 系統性回顧與統合分析

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Adherence to pulmonary rehabilitation among patients with chronic obstructive pulmonary disease in real-world – a systematic review and meta-analysis

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Background:
Studies have shown the effect of pulmonary rehabilitation in improving exercise capacity and health-related quality of life across all grades of chronic obstructive pulmonary disease (COPD). The effectiveness of pulmonary rehabilitation depends on patients' adherence to the program. The aim of this systematic review was to assess adherence to pulmonary rehabilitation among patients with COPD in real-world settings.
Material and Methods:
Medline, Embase, Global Health, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Database were searched for observational studies published between 2000 and 2018. We included studies describing recommendations and adherence to pulmonary rehabilitation. Non-linear mixed model was used to perform meta-analysis. Risk factors for non-adherence were also identified from the studies.
Results:
We retrieved 993 abstracts from the database search. After screening, 16 published studies with overall 6,305 patients were included. Among the studies, only one was conducted in low- and middle-income countries. Pulmonary rehabilitation was suggested to only 21.3% (95% CI 13.9 – 31.2%). Among those patients suggested, 95.9% (95% CI 77.2 – 99.4%) of them participated in a pulmonary rehabilitation program. Most studies provided a program ranging from 8 to 12 weeks. The overall adherence to rehabilitation program in the studies was 69.4% (95% CI 62.7 – 75.3%). Five studies assessed risk factors for poor adherence. Current smoking and depression were the only shared risk factors identified.
Conclusion:
In real-world, pulmonary rehabilitation was recommended to only a small proportion of patients with COPD. Data from low- and middle-income countries were scarce. Programs should be designed according to the local context to achieve better coverage and adherence.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB27

肺阻塞病患是否接種疫苗？一個觀察性研究的系統性回顧與統合分析

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Are patients with chronic obstructive pulmonary disease vaccinated? A systematic review and meta-analysis of observational studies

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Background:
Vaccination against influenza can reduce serious illness and death in patients with chronic obstructive pulmonary disease (COPD). Evidence also showed that pneumococcal vaccine provides protection against community-acquired pneumonia and acute exacerbations. The aim of the study was to describe the pattern of vaccine uptake among patients with COPD around the world.
Material and Methods:
We searched five biomedical literature databases for studies published from 2000 to 2018. Observational studies that provided information about influenza vaccine and pneumococcal vaccine in patients with COPD were eligible for inclusion. We applied a mixed-effects approach with binomial distribution for our meta-analysis.
Results:
We obtained 3,128 abstracts from the database search. Following screening, 39 published articles, with 17 of them being population-based surveys, were included for meta-analysis. Among the studies, 38 assessed influenza vaccine coverage and 13 provided data for pneumococcal vaccine. The overall coverage rate for influenza in the past 12 months and pneumococcal vaccine was 57.0% (95% CI 48.5 – 65.0%) and 43.7% (95% CI 23.3 – 66.4%), respectively. Data from only population-based surveys showed lower coverage rates: 47.2% for influenza vaccine in the past 12 months and 26.2% for pneumococcal vaccine.
Conclusion:
The coverage rates for influenza and pneumococcal vaccination were both suboptimal among patients with COPD. Further health policy and patient education should be implemented to increase vaccination.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB28

照護連續性對於慢性呼吸道疾病之醫療資源耗用之影響-以中部一家教學醫院與基層醫療合作模式進行評估

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The impact of introducing care continuity on medical resource utilization in chronic respiratory tract disease among physicians in a teaching hospital and general practitioners in central Taiwan

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Purpose: In Taiwan, the government started to implement the policy of outpatient referral and service volume reductions in medical centers (the two-way referral policy for graded care) in April 2017. Chronic respiratory tract (CRT) diseases, such as asthma and chronic obstructive pulmonary disease (COPD) were thought to be able referral back and care in general practitioners (GP). We aim to investigate the relationship among care continuity, utilization of medical services, and the outcome of care after the implementation of the policy.
Materials and Methods: We analyzed and identified patients refer from GP by electronic medical record (EMR) system in the period of 2018-2019. Demographic data, diagnosis of disease, comorbidity index, and care model after patients were referral from GP were record and analysis. Patients were classified into “coordinated care” and “Non-coordinated care”. The primary outcomes were rate of referral back to GP within 6 months after enrollment. The secondary outcomes were annular rate of emergency room (ER) visits and hospitalization.
Results: A total of 1653 patients were referred from GP to a medical center in Taichung. There were 505 of 1653 (30.55%) patients were classified into coordinated care. The overall rate of referral back to GP in this cohort was 36.72%. However, there were significant difference in the referral pattern between coordinated care group and non-coordinated care group, 67.13% and 23.34%, in respectively. Patients in the coordinated group were significantly more diagnosed as asthma (48.51& 12.80%, $p<0.001$), COPD (23.76% & 15.94%, $p<0.001$) and interstitial lung disease (3.96% & 1.57%, $p=0.005$). The annual ER visits and hospitalization were significant lower in coordinated care group (all $p<0.05$). When we analyzed factors associated with referral back to GP, the results showed younger age and asthma were significantly increased the rate of referral back to GP.
Conclusions: Firstly, we evaluate the real-world situation of care pattern between GPs and a teaching hospital in central Taiwan. Patients with chronic respiratory disease that in the coordinated care group were decreased in the annular numbers of ER visits and hospitalizations and increased the rate of referral back to GPs. Younger age and asthma are two factors associated with increased the possibility to referral back from teaching hospital to GPs.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB29

嚴重氣喘依據血液嗜酸性白血球及血清 IgE 濃度分型之臨床及分子特性探討

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高雄醫學院附設醫院胸腔內科[1]; 台北榮民總醫院胸腔部[2]; 羅東博愛醫院胸腔內科[3]; 亞東紀念醫院胸腔內科[4]; 彰化基督教醫院胸腔內科[5]; 臺灣大學附設醫院胸腔內科[6]

Clinical and molecular characteristics of severe asthma endotypes according to blood eosinophil and serum IgE

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Purpose: Severe asthma is a heterogeneous disease. Successful endotyping can lead to effective treatment. Serum IgE and blood eosinophil are wildly used as biomarkers for severe asthma. The aim of this prospective multicenter study was to investigate clinical and molecular characteristics of severe asthma endotypes, defined by serum IgE and blood eosinophil.

Methods: Adult patients with severe asthma fulfilled the GINA definitions were enrolled and followed for 12 months. Clinical information was prospectively recorded and blood samples were tested for potential biomarkers IL-5, IL-8, IL-13, IL-17, IL-33, TNF-α, TNF-β, TSLP, periostin, and tryptase. Maximal blood eosinophil cutoff of 300 cells/μL and serum total IgE cutoff of 100 KU/L were used to classify severe asthma into 4 endotypes. Comparisons across groups were analyzed by Kruskal-Wallis tests followed by Benjamini-Hochberg multiple-testing corrections.

Results: Among the 126 patients with severe asthma, 53 (42.1%) patients were classified as non-type 2, 34 (27.0%) as allergic, 8 (6.4%) as eosinophilic, and 31 (24.6%) as allergic eosinophilic. In overall analyses, there were significant differences across groups in age (P=0.012), atopy history (P<0.001), pre-bronchodilator FEV_1 (P=0.006), bronchodilator response (P=0.005), while no differences was observed in gender, ACT score, FeNO, and all biomarkers. Interestingly, the post-hoc analysis showed that patients with severe allergic eosinophilic asthma tends to be younger, had more atopy history, better lung function, more bronchodilator response, higher FeNO, higher serum Th2 biomarkers IL-5 and IL-13, and more acute exacerbations.

Conclusions: Allergic eosinophilic endotype represents nearly a quarter of severe asthma cases. This endotype possesses stronger Th2-high characteristics, which may make it more challenging to control. Our study has a limitation of small sample size and therefore is underpowered.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB30

年輕女性反覆性氣胸：一個罕見瀰漫性肺囊腫病例報告-淋巴血管平滑肌肉增生症

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Recurrent pneumothoraces in a young female : A case of rare cystic pulmonary disease – Lymphangioleiomyomatosis

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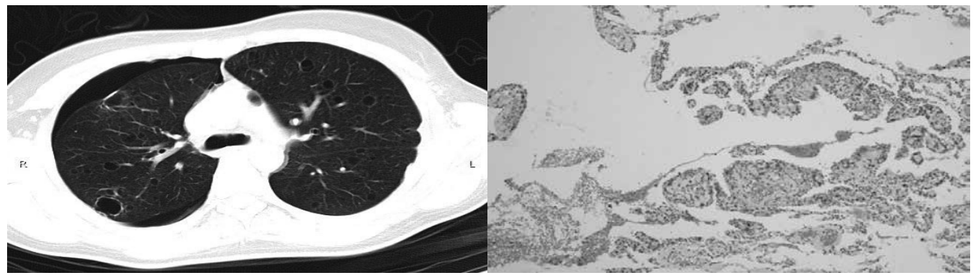
A 41 year-old non-married never smoker Asian female presented to the hospital with right chest pain and breathlessness. She had recurrent episodes of bilateral pneumothoraces in the past one year. Chest computed tomography revealed right pneumothorax and bilateral diffuse distributed thin-walled cysts (Panel A). The patient was treated with oxygen supply and right pigtail drainage that was attached to negative-pressured chest bottle. Due to poor lung re-expansion, the patient received video-assisted thoracoscopic surgery wedge resection of right upper, middle and lower lung blebs followed by abrasion and chemical pleurodesis. Pathology of the resected lung tissues showed cystic spaces surrounded by thicken septa composed of ovoid smooth muscle-like cells with eosinophilic to clear cytoplasm. Immunohistochemistry studies revealed these smooth muscle-like cells were positive for smooth muscle actin, desmin and human melanoma black monoclonal antibody (HMB45) (Panel B) which confirmed lymphangioleiomyomatosis (LAM). About one month after operation, the patient encountered recurrent right pneumothorax treated with chemical pleurodesis via pigtail. Her lung function exhibited near normal spirometry but gas trapping with elevated residual volume (166% of predicted) and decreased of diffusion capacity (77% of predicted). The patient then received sirolimus 1 milligram daily, a mTOR inhibitor, with subsequent improvement of gas trapping and no recurrent pneumothorax to date for at least 4 months.

(Panel A) (Panel B) Immunostain of HMB45



A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB31

兩位肺胸膜實質彈力纖維增生症病患併發長期且穩定自發性氣胸之案例報告

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Prolonged and stable spontaneous pneumothorax complicating pleuroparenchymal fibroelastosis – Report of two case

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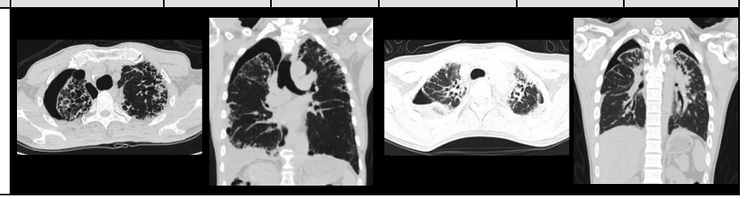
Abstract

Background: Pleuroparenchymal fibroelastosis (PPFE) is a rare interstitial lung disease characterized by fibrosis involving the visceral pleura and fibroelastotic changes predominating in the subpleural lung parenchyma. Pneumothorax is a common complication of PPFE. Prolonged and stable pneumothorax, however, is rarely described in the literature.

Case report: We report two male patients with idiopathic PPFE presenting to our outpatient clinic with spontaneous pneumothorax lasting for more than 6 months in both cases. The physical examination in both patients revealed diffuse crackles over both lungs and slightly decreased breathing sounds over upper lungs. A significant decrease in the anteroposterior diameter of the chest wall (platythorax) was also observed. Both patients could still perform the forced expiratory maneuver during spirometry without the risk of lung collapse, probably due to thickening and adhesion of the fibrotic visceral pleural. Their pneumothorax persisted for more than two years, and remained stable on image follow-up. Unfortunately, both patients died due to progression of lung fibrosis and respiratory failure.

Conclusion: Prolonged and stable spontaneous can develop in patients with PPFE due to its unique pathophysiology.

	Case 1 (67 y/o M)			Case 2 (20 y/o M)		
Time (Month)	Baseline	6M	12M	Baseline	6M	12M
FVC (% predicted)	75.6	74	63.3	21	17.1	9.45
CT						

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB32

電子菸相關肺損傷使用類固醇與低劑量 pirfenisone 治療之案例報告

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臺大醫院內科部[1]

Treatment of electronic-cigarette or vaping product use associated lung injury (EVALI) by corticosteroid and low-dose pirfenisone - A case report

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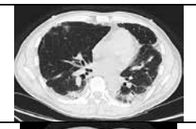
Abstract

Background: Electronic (e)-cigarette or vaping product use associated lung injury (EVALI) is a novel disease defined by the US CDC in response to a multi-state outbreak of severe lung illness that was first identified in August 2019 and is associated with using e-cigarette and vaping products. The pathogenesis, clinical course and optimal management of EVALI remain unclear.

Case Report: A 56-year-old man presented to our hospital with dyspnea and productive cough after taking e-cigarette for 1 week. His past history was notable for a smoking pack year of 50 but he was previously asymptomatic. The physical examination revealed crackles over both basal lungs. The high-resolution computed tomography (HRCT) showed traction bronchiectasis, consolidation, and ground glass opacities over both lungs. The pathology of the video-assisted thoracoscopic surgery (VATS) lung biopsy revealed organizing pneumonia with focal bronchiolitis and fibrous plugs. He was treated with prednisolone and his symptoms and forced vital capacity (FVC) significantly improved. His basal lung crackles disappeared but the recovery of diffusion capacity (DLCO) was slow. Therefore, he also received off-label treatment with pirfenidone (200 mg tid initially with gradual tapering). The follow-up HRCT demonstrated near-total resolution of lung lesions.

Table 1. Serial lung function testing, mMRC score and HRCT results.

	Day 3	1 month	3 months	7 months	HRCT (Baseline)	
FVC	65.7%	70.6%	85.9%	103.6%		
DLCO	63.9%	56.8%	60.5%	64.2%	HRCT (7 months)	
mMRC	2	1-2	0-1	0-1		

Conclusion: To our knowledge, this is the first case of EVALI treated by corticosteroid and low-dose pirfenisone.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB33

以中央型尿崩症為首要表現之蘭格罕式組織細胞增生症

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Central diabetes insipidus as the first manifestation of Langerhans cell histiocytosis

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Purpose: We report the clinical presentation, radiographic features, and physiological findings of two patients with Langerhans cell histiocytosis (LCH) that initially manifested as central diabetes insipidus (CDI).

Materials and Methods: We reviewed the electronic medical records, laboratory and radiographic data of these two patients. Pertinent information and images were collected and presented in a thematic poster.

Results:

Case 1: A 47-year-old man presented with polyuria and nocturia. A water deprivation test confirmed the diagnosis of CDI, and magnetic resonance imaging (MRI) of the pituitary gland showed absence of the normal posterior pituitary bright spot on T1-weighted images, and nodular enhancement at the hypothalamus and the infundibulum after gadolinium contrast. The polyuria and nocturia improved following the treatment with intra-nasal Desmopressin. In addition to the CDI-related symptoms, he had also suffered from chronic nonproductive cough. The chest radiograph and CT scan revealed an extensive mixed nodular and cystic change that was most prominent in bilateral upper lung fields. Pulmonary screening spirometry was within normal ranges. Video-assisted thoracoscopic lung biopsy was done and the histological analysis revealed proliferative Langerhans cell that stained immunohistochemically positive for CD1a and S-100. Chemotherapy with Vinblastine (3 mg/m^2) and Methylprednisolone (32 mg/m^2) began after the diagnosis was established. Shortly into the first course of chemotherapy, the patient died from hospital acquired pneumonia with ARDS.

Case 2: A 35-year-old man presented with polyuria, nocturia, and erectile dysfunction for several months. CDI was confirmed by a water deprivation test; further endocrine analyses revealed pan-hypopituitarism. MRI of the brain showed a thickened pituitary infundibulum and absence the of posterior bright spot on T1-weighted images, and enhancement of the pituitary infundibulum and hypothalamus after contrast. Following intra-nasal Desmopressin treatment, his polyuria and nocturia improved. Chest CT scan showed multiple nodular mixed with cystic lesions mainly in the upper lung regions. Yet, the patient has had minimal airway symptoms. The diagnosis of LCH was made based on the radiographic findings and after a multi-disciplinary discussion. A follow-up CT scan 6 years later showed decrement in the size and number of the nodular lesions, but progression in the extent of the cystic change. Serial pulmonary function tests reported a mild impairment in the DLco and a trend toward obstructive ventilatory deficit. The patient still receives regular follow-up at our hospital.

Conclusions: The aberrant histiocytes in LCH may infiltrate multiple organs simultaneously, including the lungs and pituitary gland. Patients with pulmonary LCH need to be followed for pituitary dysfunction, while patients with unexplained CDI must receive workups to exclude LCH and the concurrent lung involvement.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB34

以經支氣管鏡肺部冷凍切片診斷成人史迪爾氏症合併肺間質性纖維化一個案報告

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[1]臺大醫院新竹分院胸腔內科 [2]風濕免疫科

Progressive interstitial lung fibrosis in adult onset Still's disease diagnosed by transbronchial lung cryobiopsy

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Introduction: Interstitial lung diseases are encountered in our everyday practice, but often unrecognized or underdiagnosed. It is of paramount to exclude infection, lung edema or even neoplasm before making a diagnosis of interstitial lung disease, and performing biopsies of the lung parenchyma can offer crucial information to direct treatment and to predict disease prognosis.

Case presentation: A 64-year-old man presented with fever, arthralgia and maculopapular rash for 2 weeks was diagnosed with adult-onset Still's disease (AOSD). His symptoms was controlled by prednisolone 0.3mg/kg/day. However, he presented with progressive dyspnea and hypoxia 2 months after diagnosis, and he was admitted for impending respiratory failure. Chest HRCT showed diffuse ground glass opacities prominently in upper lung fields, and bilateral lower lung reticular fibrosis with bronchiectasis. Broad-spectrum antibiotics were administered, but dyspnea persisted. Prednisolone 1.6mg/kg/day had limited response. After multidisciplinary discussion, transbrochial lung cryobiopsy (TBLC) was performed and the patient was transferred to ICU for further care. The microbiological studies were all negative, and the pathology of TBLC revealed parenchymal dense interstitial fibrosis with lymphocyte and plasma cell infiltrates. Anti-IL6R Tocilizumab was administered, and his dyspnea improved. He was transferred to the general ward 1 week later.

Discussion: Discrimination of pneumonia, heart failure, pulmonary embolism and interstitial pneumonitis is sometimes challenging among patients having fever and dyspnea, especially in patients with underlying diseases. Taking biopsies from the affected lung is helpful and crucial for making accurate diagnosis. Transbronchial lung cryobiopsy is a comparable measure to surgical lung biopsy with similar diagnostic yield and lower complications if performed by experienced interventional pulmonologists. Adult onset Still's disease is a rare disorder, and pulmonary involvement is seen in about 30-40% of patients, most commonly with pleural effusion and transient radiographic infiltration, but severe injury such as acute respiratory distress syndrome might be encountered. Few pathologic reports exists describing AOSD with pulmonary involvement, and the pathologic patterns include organizing pneumonia, non-specific interstitial pneumonia and diffuse interstitial fibrosis. Although the pathology report of TBLC did not lead to a specific diagnosis in our patient, it helped to exclude infections or malignancies and directed us to administer immunosuppressive agents. It is also important to incorporate multidisciplinary team to patient care, and provide more treatment options to the patient by experienced rheumatologists.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB35

單獨瀰漫融合性 B 線模式是診斷間質性肺炎的獨特胸腔超音波模式：診斷性研究

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Isolated Diffuse Coalescent B-Lines Pattern Is a Unique Lung Ultrasound Pattern for Diagnosing Interstitial Pneumonitis: a Diagnostic Study

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Purpose: Lung ultrasound (LUS) is an important tool to help critical care physicians establish the diagnosis of acute respiratory failure rapidly and accurately. Anterior diffuse B-lines pattern has been shown to be correlated with increased extravascular lung water and is virtually diagnostic for pulmonary edema in several LUS algorithm or procotol, such as the BLUE protocol, with the rare but important differential diagnosis of interstitial pneumonitis (IP), especially in the era of COVID-19. We aimed at reporting a unique B-lines pattern for diagnosing IP, rather than pulmonary edema, and evaluating its diagnostic utility.

Materials and Methods: During the period from May 2014 to Aug 2020, patients who were admitted to the medical intensive care unit and received point-of-care LUS for evaluating the cause of acute respiratory failure were enrolled. The diagnosis of IP was established based on computed tomography-confirmed bilateral ground glass opacites with compatible clinical and/or microbiologic evidence. An isolated diffuse coalescent B-lines pattern without significant pleural effusion or consolidation was identified and its sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in the diagnosis of IP were then calculated.

Results: A total of 66 patients were enrolled. Among them, 30 were diagnosed with IP, with the most common etiologies being infection, acute exacerbation of underlying interstitial lung disease, and drug-induced IP. Among 49 patients with anterior diffuse B-lines pattern, an isolated diffuse coalescent B-lines pattern without significant pleural effusion or consolidation was identified in 30 patients. This LUS pattern changed the diagnosis from pulmonary edema to IP in 28 (57.1%) patients. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in the diagnosis of IP were 93.3%, 94.4%, 93.3%, 94.4%, and 93.9%, respectively.

Conclusions: Isolated diffuse coalescent B-lines pattern is a unique LUS pattern for diagnosing IP with high diagnostic utility. Critical care physicians should be aware of this LUS pattern to facilitate the diagnosis of IP and avoid misinterpretation as pulmonary edema, especially in the era of COVID-19.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB36

Nintedanib 抑制 bleomycin 引起肺纖維化之血管內皮間質轉化作用

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Nintedanib inhibits endothelial mesenchymal transition in bleomycin-induced pulmonary fibrosis

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Purpose: Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, and devastating interstitial lung disease. Pulmonary fibroblasts and myofibroblasts play an important role in the development of IPF. However, the origins of fibroblasts and myofibroblasts are controversial for their heterogeneous phenotypes. Emerging evidence indicates that endothelial cells could be the source of fibroblasts thorough the process of endothelial mesenchymal transition (EndoMT). The aim of this study is to identify that nintedanib inhibits endothelial mesenchymal transition (EndoMT) in bleomycin-induced pulmonary fibrosis and explore its mechanism.
Materials and Methods: Male C57BL/6 mice were treated with bleomycin intratracheal instillation to induce pulmonary fibrosis and then nintedanib was administered via oral gavage once daily, five days per week, for 3 weeks. Mice were harvested on day 7, 14 and 21 to collect lung samples. Human pulmonary microvascular endothelial cells (HPMECs) were treated with bleomycin as an in vitro endothelial mesenchymal transition model. Hematoxylin and eosin staining, immunohistochemistry staining, immunofluorescence staining and western blotting were performed for the experiments.
Results: Masson's trichrome staining of lung sections showed prominent collagen deposition in mice treated with bleomycin, while nintedanib treatment significantly ameliorated collagen deposition and pulmonary fibrosis. Immunohistochemical staining of lung sections and western blotting of lung homogenates revealed that the expressions of collagen-1, α-SMA and vimentin were significantly increased, and the expressions of VE-cadherin were significant decreased after bleomycin treatment. Nintedanib treatment not only significantly decreased the expressions of vimentin and α-SMA but also significantly increased the expression of VE-cadherin. Immunohistochemical staining and western blotting of HPMECs after bleomycin stimulation also showed EndoMT was increased. Furthermore, nintedanib treatment inhibited EndoMT. The FAK activity was significantly increased after bleomycin stimulation, while nintedatinib treatment significantly decreased FAK activation in both in vivo and in vitro study.
Conclusions: Nintedanib inhibited EndoMT and ameliorated pulmonary fibrosis in mice treated with bleomycin via reducing the FAK activity.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB37

SHP-1 活化劑可透過抑制肺泡巨噬細胞減緩博來黴素誘導之小鼠肺纖維化

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A small molecule SHP-1 agonist exerts an anti-fibrotic activity by targeting alveolar macrophages in bleomycin-induced murine pulmonary fibrosis

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Purpose: Idiopathic pulmonary fibrosis (IPF) is a chronic progressive and lethal fibrotic disorder. The commonly used anti-fibrosis drugs in clinics are nintedanib and pirfenidone. Although they can ameliorate the deterioration of the IPF patients' lung function, they have not significantly improved the overall mortality rate. Therefore, new therapeutic invention is urgently needed. A large body of evidence indicates that macrophages produce soluble mediators that regulate fibrotic responses, and recent reports even suggest that monocyte-derived alveolar macrophages are required for the development of pulmonary fibrosis. The SH2 domain-containing protein tyrosine phosphatase 1 (SHP-1) has been identified as a negative regulator of a wide variety of growth factor receptors, including the M-CSF receptor, which plays a pivotal role regulating macrophage survival. Furthermore, mice genetically lacking SHP-1 (me/me) display a profound susceptibility to naturally develop pulmonary fibrosis. Hence, we investigated the therapeutic potential of the SHP-1 agonist on pulmonary fibrosis in the bleomycin-induced murine model.

Materials and Methods: Bleomycin (2.5 mg/kg) was intratracheally instilled in C57BL/6 mice to induce pulmonary fibrosis. After 7 days of bleomycin instillation, the SHP-1 agonist was administered every day by oral gavage at 10 or 50 mg/kg, while the control group was given with vehicle only. The severity of lung fibrosis was evaluated after two weeks of treatment. Histopathological examination, Masson's trichrome staining of tissue sections, and flow cytometry analyses of bronchoalveolar (BAL) fluid were assessed. To further explore its mechanism of action, the effect of the SHP-1 agonist was evaluated in a human monocyte-derived macrophage cell line, THP-1.

Results: Histological examination revealed that treatment of the SHP-1 agonist reduced collagen deposition and lung inflammation. From the cell type analyses of BAL fluid, the percentage of alveolar macrophages stimulated by bleomycin was significantly reduced in the SHP-1 agonist-treated mice. The M-CSF receptor, which critically affects macrophage survival, was significantly downregulated by the SHP-1 agonist treatment. Moreover, the SHP-1 agonist promoted the apoptotic signaling in THP-1 cells, as evidenced by increased expression of cleaved PARP. Multiple pathways including pSTAT3, pNFκB, and pAkt, which are critical for cell survival and inflammation, were also inhibited by the SHP-1 agonist.

Conclusions: The results suggested that the SHP-1 agonist may hold great potential in pulmonary fibrosis resolution, by targeting the alveolar macrophages in patients with IPF.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB38

特發性肺纖維化的臨床特徵與長期預後：台灣 NICEFIT 特發性肺纖維化註冊試驗之結果分析

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Clinical characteristics and long-term prognosis of idiopathic pulmonary fibrosis: results from the NICEFIT idiopathic pulmonary fibrosis registry in Taiwan

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Purpose: Due to the relatively rarity of idiopathic pulmonary fibrosis (IPF), data on the characteristics, course, and treatment outcomes of the disease are limited, underscoring the need for longitudinal registries in studying the condition. In this study, we sought to determine the clinical characteristics, quality of life, and clinical course of IPF patients included in the NICEFIT IPF registry of Taiwan.

Materials and Methods: This was a non-interventional, prospective study of the data of IPF patients treated through routine clinical practice at 10 expert medical centers in Taiwan. Data collection was started at the initial screening assessment for each patient based on their medical records, and was continued prospectively thereafter for those patients deemed eligible for inclusion.

Results: A total of 101 IPF patients (mean age 74.6 years, 83.2% male, 55.4% current or ex-smokers) were recruited from August 2017 through February 2018. Their common comorbidities included COPD and emphysema (54.5%), arterial hypertension (47.5%), GERD (25.7%), diabetes (21.8%), and emphysema (19.8%). Eighty-eight (87.1%) received anti-fibrotic drug treatment and 13 (12.9%) did not. The baseline predicted forced vital capacity (FVC) and predicted diffusion capacity (DL_{CO}) of the treated group vs. untreated group were 69.7 ± 14.06% vs. 97.8 ± 10.97% and 42.7 ± 19.74% vs. 57.5 ± 17.96%, respectively. During mean follow-up periods of 686.0 days and 641.0 days for the treated and untreated groups, respectively, the annual percentages of decline in predicted FVC and the annual percentages of change in predicted DLCO were 0.2 ± 7.74% vs. 2.5 ± 4.52% and -0.5 ± 6.83% vs. 2.6 ± 6.26%, respectively. Besides, the percentage of weight loss gradually improved during the anti-fibrotic agent's treatment (19.3% at baseline vs. 5.7% in second years). Acute exacerbation occurred once in 21.6% and the mortality was 29.5% in the treated group. The percentages of drug-related adverse events was similar to those in previous studies, with diarrhea (28.4%) and liver function impairment (11.3%) being the most frequent adverse event, and most of those adverse events are mild and manageable.

Conclusions: The patients enrolled in the first IPF registry in Taiwan showed characteristics similar to those in other published registries. Most patients were well effective in lung function maintenance and tolerated side effects with anti-fibrotic agents. Moreover, the rate of lung function decline was higher in untreated patients than those with treated groups. Early diagnosis, comorbidity intervention and prompt anti-fibrotic agent treatment will change the unpredictable nature course for IPF.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB39

抑肺纖導致腹瀉與克隆氏症表現相似

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Nintedanib related colitis mimic Crohn's disease

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INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a rapid progressive interstitial lung disease with high mortality rate. Nintedanib is an intracellular inhibitor that targets multiple tyrosine kinases, it significantly reduced the decline of functional vital capacity (FVC) in IPF patients. The most common side effect were diarrhea, and lead to discontinuation of drug in less than 5% of patient. Hematochezia was rarely reported, and only one of the reported cases treated successfully with budesonide. Herein, we reported a case of nintedanib related colitis which mimics Crohn's disease.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB40

Pirfenidone 用於臺灣特發性肺纖維化患者的上市後安全性與療效研究期中報告

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Safety and effectiveness of pirfenidone in patients with idiopathic pulmonary fibrosis in Taiwan – Interim analysis report of a post-marketing surveillance

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a lung disease with a grave prognosis. In Taiwan, pirfenidone was approved for IPF in 2016. The aim of this post-marketing surveillance (PMS) was to assess the safety and effectiveness of pirfenidone for IPF in Taiwan.
Methods: This prospective, 52-week PMS was conducted in six medical centers in Taiwan, with a target study population of 50 patients. The key collected data included adverse events (AEs), symptoms, lung function, the gender-age-physiology (GAP) staging, oxygenation (SpO_2), and 6 min walking distance (6MWD).
Results: Here, we report the results of an interim analysis of the first 28 patients (age 71.6 ± 10.2 years, male 75.0%). Seventy-five percent of patients had been treated for 3 to 6 months, and 42.9% were on a daily dose of 1200–1800 mg pirfenidone. Regarding GAP staging, 53.6%, 35.7%, and 10.7% of patients were stage 1, stage 2, and stage 3, respectively. AEs were reported in 82.1% of patients, including decreased appetite (32.1%), dizziness (14.3%), photosensitivity/rash (10.7%), nausea (10.7%), diarrhea (7.1%), and abnormal liver function (7.1%). Three serious AEs occurred in two (7.1%) patients, all unrelated to the use of pirfenidone, and one of them died. Eleven (39.3%) patients had their treatment dose modified and 25.0% of patients discontinued treatment owing to AEs. Two (7.1%) patients reported acute exacerbation. The effectiveness parameters were generally maintained during the 24-week treatment period.
Conclusion: Our results from this interim analysis suggest that pirfenidone is generally well tolerated by Taiwanese patients with IPF. The safety and effectiveness profiles were consistent with those from previous PMS in Japan.

Effectiveness parameters (n = 17)	Baseline	After 24 weeks	*P*-value
Forced vial capacity (FVC) (pred.%)	75.9 ± 15.5	73.9 ± 22.1	0.663
6 min walking distance (6MWD) (meter)	349.5 ± 150.7	362.6 ± 131.17	0.420
Cough (Azuma et al., 2011) (point)	2.1 ± 0.4	2.1 ± 0.7	1.0
Dyspnea (UCSD SOBQ) (point)	26.7 ± 31.2	36.3 ± 37.5	0.051
SpO_2 (resting), %	95.5 ± 1.9	95.4 ± 2.2	0.896

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB41

具有自體免疫特徵之間質性肺炎病人發生急性呼吸衰竭入住加護病房之後之臨床表徵及預後分析

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Clinical features and outcomes in interstitial pneumonia with autoimmune features patients with acute respiratory failure admitted to the intensive care unit

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Purpose: The clinical features and outcomes in patients with IPAF (interstitial pneumonia with autoimmune features) developing acute respiratory failure (ARF) are not known. We aimed to analyze IPAF patients admitted to the intensive care unit (ICU) due to acute respiratory failure and made comparison with patients with connective tissue disease with interstitial lung disease (CTD-ILD).
Materials and Methods: This is a retrospective observational study conducted in the medical ICU of a tertiary medical center in Taiwan. Patients admitted to the ICU with with ARF needing mechanical ventilation (MV) between January 2014 and December 2016 were screened for eligibility. All patients admitted to the ICU with ARF requiring MV during the study period were enrolled if they had a past history or a new diagnosis of IPAF or CTD-ILD during the ICU stay.
Results: During the study period, 1368 patients were admitted to the ICU with ARF requiring MV. Of them, 1286 patients without a diagnosis of ILD were excluded. Patient with diagnosis of CTD-ILD and IPAF were selected from the remaining 82 patients. There were 13 patients with CTD-ILD and 13 patients with IPAF. Ten out of 13 patients with CTD-ILD were dead at day 28 after acute respiratory failure; three out of 13 patients with IPAF were dead at day 28 after respiratory failure. The 28-day mortality rate was statistically lowered in IPAF patients. The baseline demographic characteristics were similar between survivor and nonsurvivors. However, there are some differences between the two groups. Survivors had lower Acute Physiology and Chronic Health Evaluation (APACHE) II score, and more in patients with IPAF. Critical-ill data, management and outcome were also presented. Survivors had less need of vasopressors. To further elucidate clinical predictors of 28-day mortality, we used univariate and multivariate logistic regression analyses. Significant variables included disease entity per se, vasopressor use, and APACHE II score. After multivariate logistic regression analysis, disease entity per se (OR 22.369, CI [1.462 – 342.353]) remained independent good prognostic factors.
Conclusions: Compared with CTD-ILD patients, IPAF patients had favorable outcome when developing ARF needing MV support.

A. ■原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB42

含 rituximab 和 nintedanib 的雞尾酒療法可快速逆轉與 Sjögren 氏症候群相關的非特異性間質性肺炎

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Rapid reversal of Sjögren's syndrome-related non-specific interstitial pneumonia with cocktail therapy containing rituximab and nintedanib

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Abstract
We reported a 69-year-old female who was diagnosed with Sjögren's syndrome-related non-specific interstitial pneumonia (NSIP) and significant lung function impairment concomitantly during the pre-operational evaluation of papillary thyroid carcinoma. Her initial chest CT showed the canonical "fingernail moon sign" and "straight edge sign," which were common in patients with connective tissue disease-related interstitial lung disease (CTD-ILD). Her serum SSA/Ro antibody was >240 U/mL. Transbronchial lung cryobiopsy at the corresponding CT area of the fingernail moon sign revealed a mixed cellular and fibrosing type of NSIP. Because of upcoming thyroid surgery, it was requisite to provide her a treatment that could definitely slow the decline of forced vital capacity (FVC) in a limited time. We then gave her a combinative regimen containing methylprednisolone, hydroxychloroquine, rituximab, and nintedanib. She well tolerated the regimen and had a drastic improvement in the context of dyspnea score, pulsatile oxygen saturation, and radiographic regression in less than two months. She underwent the scheduled thyroid surgery successfully. This case highlighted the benefit of the early use of antifibrotic in a histology-proven fibrosing ILD, given an unpredictable progressive nature despite standard treatment.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB43

台灣肺泡蛋白質沉積症的流行病學

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Epidemiology of pulmonary alveolar proteinosis in Taiwan

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Purpose: Pulmonary alveolar proteinosis (PAP) is manifested as alveolar macrophage dysfunction and abnormal accumulation of surfactant protein in the alveoli. Its estimated annual prevalence is 5-9 patients per million people in the US. In Asia, only one medium-sized cohort in Japan had been reported and showed much difference in many demographic items compared to western countries. In Taiwan, there is no available literature regarding the epidemiology, disease burden, and prognosis of PAP. In the current study, we aim to investigate the epidemiology of PAP in Taiwan.

Materials and Methods: This project used National Health Insurance Research Database (NHIRD) as data source. We obtained a comprehensive data about all patients having a diagnostic code of PAP (ICD-9-CM code: 516.0) in at least two ambulatory claims or one inpatient claim from the whole population in Taiwan during 1995-2013 in a longitudinal follow-up fashion.

Results: The annual incidence of PAP ranged from 0.5 to 1.3 patients per million people after 2000. The estimated prevalence was 8.7 patients per million people by the end of 2013. In total, 301 patients of PAP were identified during the study period, including 115 female and 186 male patients. The median age of diagnosis was 54.5 years. The median survival was 9.6 years. Male and female patients exhibited similar survival. Twenty-one (7%) patients received whole lung lavage within one year after the diagnosis of PAP, and these patients had better survival compared to others (p=0.009). Only 12 (4%) patients had a hematological malignancy on the diagnosis of PAP, and these patients had poorer survival compared to the others (p=0.003). Multivariable Cox regression analyses, including sex, age, resident area, and comorbidities, showed that elder age and hematological malignancy were independent poor prognostic factors for survival.

Conclusions: In this nationwide population-based study, we determined the epidemiology and some prognostic factors of PAP in Taiwan. To confirm our findings and to provide better patient care, a nationwide registry is warranted.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB44

次發性自發氣胸導致嚴重皮下氣腫: 使用傳統插管無效後採行胸腔鏡手術兩成功案例報告.

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Severe Subcutenous Emphysema Complicating Secondary Spontaneous Pneumothorax: Report of Two Cases Refractory to Tube Thoracostomy and Improved after Video-Assisted Thoracoscopic Surgery.

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Purpose: Subcutaneous emphysema usually occurrs after chest trauma, surgery or medical interventions. Severe subcutaneous emphysema refractory to standard care including chest tube drainage and subcutaneous incision will be high risk for major morbidity or even mortality.

Patients & Methods: Herein two such cases being treated by video-assisted thoracoscopic surgery (VATS) are reported. These two male cases are aged (80 and 75 years old), heavy smoker with underlying emphysema with bullous formation. Chest trauma and Biopsy procedure (due to lung mass) resulted in this attack. The grade of subcutaneous emphysema in this two cases are all grade V (with scrotal/abdominal/lower extremities involvement). Respiratory failure requiring mechanical ventilation, progressive emphysema developed although chest tube drainage and subcutaneous drainage have been administered. Thus they underwent surgical intervention through VATS, including pneumolysis, remove the air leak and bullous lung tissues, chest wall and mediastinal incision/drainage, and re-position the chest tubes.

Results: All of these two patients improved remarkably immediately after operation. Weaning the mechanical ventilation, leave ICU, and remove the drainage tube successfully and discharged 20 and 16 days later.

Conclusion: Using five principles of treatment based on the respiratory pathophysiology of subcutaneous emphysema (will be presented), we have successfully treated more than 10 patients before. We believe that these new principles will provide a good alternative to treat severe and refractory subcutaneous emphysema.

Keywords: Subcutaneous emphysema, Video-assisted thoracoscopic surgery

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB45

探討中年期心肌梗塞病患配偶於加護病房的因應 行為、社會支持與壓力

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An exploration of spouse's coping behaviors,social support and stress of middle aged patient with myocardial infarction in intensive care unit

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Abstract

In the face of myocardial infarction, the life threats, sudden death risks, and unstable disease changes brought about not only affected the patients, but also the closest spouses who lived with each other and faced the danger of losing their families. When the spouse is unable to cope and deal with stress, in addition to causing the spouse's crisis, it may also affect the functioning of family functions, and even cause the patient to lose support and affect their recovery.

The purpose of this cross-sectional study was to explore for spouse's coping behaviors,social support and stress of middle aged patient with myocardial infarction in intensive care unit. A total of 84 spouses with acute myocardial infarction were selected from a medical center of Middle Taiwan. The data were collected using four instruments, including：spouse basic attribute table and disease attribute table, spouse coping behavior scale, social support scale, and spouse stress scale. The spouse stress scale was developed by investigators. The data were analyzed using SPSS for window.The data analysis is mainly descriptive and inferential statistics, including：frequency, percentage, mean, Standard deviation, T test,one-way ANOVA, Pearson Correlation.

Through this study, We hope to understand the stress of myocardial infarction patients' spouses in the intensive care unit, the coping behaviors and social support in the face of stress, as a future nurses to face the patient's spouse, and help to take appropriate actions as soon as possible coping behaviors and social support to help them improve stress.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB46

3-D 列印氣管植體移植入大型動物(豬模式)體內後之新生氣管軟骨

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De novo cartilage growth after implantation of a 3-D-printed tracheal graft in a porcine model

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Purpose: Experiments were conducted on the assumption that vivid chondrogenesis would be boosted in vivo following previously preliminary chondrogenesis in a mesenchymal stem cell (MSC)-rich entire umbilical cord (UC) in vitro.
Materials and Methods: Virtual 3-D tracheal grafts were generated by using a profile obtained by scanning the native trachea of the listed porcine. Although the ultimate goal was the acquisition of a living specimen beyond a 3-week survival period, the empirical results did not meet our criteria until the 10th experiment, ending with the sacrifice of the animal. The categories retrospectively evolved from post-transplant modification due to porcine death using 4 different methods of implantation in chronological order. For each group, we collected details on graft construction, clinical outcomes, and results from both gross and histology examinations.
Results: Three animals died due to tracheal complications: one died from graft crush, and two died secondary to erosion of the larger graft into the great vessels. It appeared that the remaining 7 died of tracheal stenosis from granulation tissue. Ectopic de novo growth of neocartilage was found in three porcine subjects. In the nearby tissues, we detected neocartilage near the anastomosis containing interim vesicles of the vascular canals (VCs), perichondrial papillae (PPs) and preresorptive layers (PRLs), which were investigated during the infancy of cartilage development and were first unveiled in the tracheal cartilage.
Conclusions: 3-D-printed anatomically precise grafts could not provide successful transplantation with stent-sparing anastomosis; nonetheless, de novo cartilage regeneration in situ appears to be promising for tracheal graft adaptability. Further graft refinement and strategies for managing granulated tissues are still needed to improve graft outcomes.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB47

肺阻塞合併心房顫動之處方型態及腦梗塞的風險

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The Prescription Pattern and Hazard of Ischemic Stroke in Chronic Obstructive Pulmonary Disease with Atrial Fibrillation

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Purpose: Patients with chronic obstructive pulmonary disease (COPD) had higher risk of Atrial fibrillation (AF). The treatment of AF includes medicines to control heart rate and reduce the risk of stroke, and procedures such as cardioversion to restore normal heart rhythm. To reduce the stroke, patients with AF may prescribe some type of antithrombotic medication (such as warfarin, one of the new non- vitamin K antagonist oral anticoagulants (NOACs) – dabigitran, apixaban, rivoraxaban or edoxaban) or maybe aspirin. The aim of our study was to exam the prescription pattern in patients with COPD and AF.
Materials and Methods: The study was conducted with data from the Taiwan National Health Insurance Research Database from January 1, 2002, to December 31, 2015.We selected COPD population in Taiwan older than 40 years and less than 90 years old with an COPD diagnosis at least two outpatient claims or at least one inpatient claim coded and also need at least one prescription of bronchodilators. We followed this COPD cohort until they have AF and prescription fill patterns.
Results: We included 267,740 patients with COPD who meet the inclusion and exclusion criteria and 6,582 patient concomitants with COPD and AF. The mean age was 75 years, and about 77% of the patients were older than 70 years. There are three fourths of people are male. The common comorbidities were hypertension (17.58%), diabetes (7.47%), ischemic heart disease (4.66%), dyslipidemia (3.68%). we found that most patients received aspirin which accounting for 31%, followed by coumadin (8.22%) and Clopidogrel.
Conclusions: The prescription in patients with COPD and AF was low and the percentage of NOAC usage also lower than warfarin. The time from AF diagnosis to prescription antithrombotic medication was late.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB48

病例報告: 誤吞油桐花籽窒息致死個案.

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Case Report: A case of tung nut suffocation.

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Introduction: Foreign body suffocation is common in youngsters or adults with or without swallowing function impairment.
Case Summary: A 68-year-old man was sent to emergency room for out-of-hospital cardiac arrest. Asystole was noted on presentation and return of spontaneous circulation was obtained after 2 cycles of cardiopulmonary resuscitation. At the time of presentation to the emergency room, his vitals were temperature 35.1’C, heart rate 109 beats per minute, respiratory rate 18 breaths per minute, and blood pressure 68/55 mmHg. The patient was then sent to the intensive care unit after endotracheal intubation, still in persistent shock despite high dose vasopressors. A history of vascular dementia following several episodes of ischemic stroke was reported by the family. Sudden collapse was witnessed after he presumably swallowed a tung nut planted in his garden. Computerized tomography scan revealed a 3.3 cm x 2.7 cm foreign body behind his tongue, just above the epiglottis, with obstruction of the airway. Bronchoscopy was performed and one large tung nut was extracted. The patient developed persistent metabolic acidosis and expired 4 days later from multi-organ failure.
Discussion: Aspiration is a major concern among the elderly population. It often leads to aspiration pneumonia with high risk of morbidity and mortality, associated with an increased burden on the society in terms of medical resources. Foreign body suffocation, in particular, is often more fatal in the elderly, who often have impaired swallowing function and cognition. Attention should be paid to this issue whenever there are elderly people at home.
Conclusions: Foreign body suffocation is common in youngsters and adults especially with swallowing function impairment. Early prevention and detection is crucial.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB49

進行氣切造口術的醫病共享決策時的困境–由台灣呼吸照護中心發起的問卷的結果分享

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The difficulties encountered in shared decision making for tracheostomy creation - an analysis by questionnaire issued in respiratory care center in Taiwan

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Purpose: Shared decision making (SDM), a more and more popular health care policy, ensures patients to obtain available evidence from clinicians and supported them to face the task of making decisions. To make a more understanding of the difficulties medical staff encounter during SDM program, we issued questionnaire to our stuff in respiratory care center (RCC). In this article, we shared the results of the questionnaire for the difficulties encountered during SDM discussion.
Materials and Methods: We applied tracheostomy SDM program for long-term ventilated patients in our respiratory care center. The patient or his family members were invited for SDM program if the patient had already received ventilator support for more than 21 days. We established a SDM team and hold monthly briefing sessions for tracheostomy creation. We used the public version of the patient decision aids(PDAs) materials by the Joint Commission of Taiwan (JCT), which is an organization established in 1999 funding by the Ministry of Health and Welfare. We issued questionnaire to our medical stuff, patients, and patients' family members. We collectedand analyzed the relevant data.
Results: Total 15 medical staff took questionnaire and 13 patients or his family members took questionnaire. The most benefiting 5 factors facilitating the SDM includes: Providing patients with paper information, Available convenient patient decision aids (PDAs) materials, Patients well-understanding the disease and ready for consultation, Good Doctor-Patient Relationship, and Good communication efficiency. Our stuff mostly concerned about not enough time to discuss and also patients too worried to listen to what the medical staff is saying.
Discussion: The SDM program increased the understanding of the methods of tracheostomy and endotracheal tube treatment to the patients and the patients' family members. To improve the quality of discussion, preparation beforehand is very important including providing patients with paper information and a well-designed PDAs. It is recommended to give medical staff enough time for SDM discussion, and the medical staff must pay attention to whether the patient understands what the medical staff is talking about. We hope that in the future, medical institutions notice these problemsand offered high quality SDM discussing to the patients.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB50

LAMP2 突變引起擴張型心肌病變之病例報告

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Dilated Cardiomyopathy Caused by LAMP2 Mutations – A case report

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Introduction
Danon disease is an X-linked dominant skeletal and cardiac muscle disorder with multisystem clinical manifestations. Lysosome associated membrane protein 2 (LAMP2) was identified as the disease-causing gene. Limited publications were available in women with Danon disease, who are generally described as being at risk for cardiac involvement with milder and later onset of cardiac symptoms compared to men. Cardiac disease in female Danon disease can present with a broad spectrum of clinical features that vary from hypertrophic to dilated cardiomyopathy (DCM).
Case Presentation
A 48-year-old female who had a strong family history of sudden cardiac death, presented with intermittent chest tightness, dyspnea on exertion, palpitation and sometimes legs edema. Physical examination was unremarkable except irregular heart rate. 12-lead ECG disclosed intermittent preexcitation with low voltages. Frequent APCs and VPCs associated with episodes of nonsustained VT were recorded on her Holter ECG. She had a dilated and globally hypokinetic left ventricle with an left ventricular ejection fraction of 47.4% measured by transthoracic echocardiography.
Subsequent cardiac magnetic resonance imaging reported to have transmural myocardial scar in inferior wall and interventricular septum. Due to strong family history of sudden cardiac death, we arranged whole exon sequencing and sanger sequencing which found a splice site deletion mutation, IVS6+3_6delGAGT in the LAMP-2 gene.
Discussions
Danon disease, an X-linked lysosomal and glycogen storage disorder involving a genetic defect in LAMP2 gene, is usually associated with hypertrophic cardiomyopathy in male. About half of the women with Danon disease who develop cardiomyopathy have dilated cardiomyopathy as seen in our patient. The symptoms in male are usually more severe than female. Our patient was found to have LAMP-2 gene mutation and a strong family history of sudden cardiac death involving male family members, it is reasonable to infer that they had a very high possibility of dying from classical Danon cardiomyopathy. Rowin EJ et al. reported anatomic validation of late gadolinium enhancement as evidence of myocardial scarring in LAMP2 cardiomyopathy. CMR imaging of our patient showed transmural myocardial scar in the inferior wall and septum which might be the result of LAMP2 mutation since her coronary arteries were patent. Our case also highlighted the importance of genetic testing in a range of inherited arrhythmia syndromes and cardiomyopathies, which might have great impact on clinical diagnosis, treatment, and prognosis.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB51

自製氣切管內管成功處理困難氣道– 病例報告

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Hand-made Tracheostomy rescuing the difficult airway - A case report

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Introduction：

The formation of tracheal stomas and insertion of tracheostomy tubes is increasing in frequency. Although tracheostomy tube displacement is uncommon, the associated mortality is high. It is an urgent problem for the patients with endotracheal tumor rescuing the airway.

Case Report：

This 58 year-old man was a case of esophageal cancer with multiple metastasis, including the trachea. He received regular chemotherapy but there was acute respiratory failure during admission. Emergent endotracheal tube intubation was performed and the patient underwent tracheostomy due to prolonged ventilator usage. However, there was dyspnea and difficulty ventilation after the tracheostomy creation. Bronchoscopy revealed there was endotracheal tumor obstructing the tip of tracheal tube. We changed the standard tracheostomy tube with an elongated non-kincking tracheostomy tube but there was still migration of the tube causing difficulty ventilation even under fully sedation. After discussing with the chest surgeon, we planned to make a hand-made tracheostomy tube to fit the patient's airway. Initially we checked the endotracheal tumor location and measured the length from tracheostomy across the tumor via bronchoscopy. Then, we made a hand-mand tracheostomy tube using the standard endotracheal tube with inner diameter of 7.5mm and the outer cannula with flange (neck plate) of tracheostomy tube. Finally, we inserted the hand-made tracheostomy tube under bronchoscopy guided. After the replacement of hand-made tracheostomy tube, there was smooth breathing pattern under ventilator and weaning off successfully. Under stable condition, the patient discharged and out-patient department following up.

Conclusion：

There are different types of tracheostomy tubes available and the patient should be given the tube that best suits patients' needs. However, there was still some difficult airways which not fit to current types of tracheostomy tubes. Our hand-made tracheostomy may benefit these patients.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB52

雛型品之功能表現：麩醒球呼吸器

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Functional performance of prototype：Bag-Valve Resuscitator Ventilator

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Purpose: In the outbreak of COVID-19 and the demand for severe illnesses, the development of low-cost respirators has become an option for rapid production and application. The advantage of bag-valve resuscitator ventilator in the application of the equipment design of the bag-valve resuscitator , which can omit oxygen inlet, mixing chamber, exhalation valve, release valve and peep valve design. Most bag-valve resuscitator ventilator use 3D printing and mixing stepping motors Control, this study will explore the performance of the bag-valve resuscitator ventilator in the volume control mode.
Materials and Methods: Galileo ventilator as the measurement, connect the flow sensor between the bag-valve resuscitator ventilator and the test lung to measure, set the motor output and speed, test the change of the volume under different settings, and analyze the change by linear regression. Whether the different positions of the bag-valve resuscitator ventilator affect the volume output, the five-repetition measurement is performed, and the average is expressed.
Results: The R2 value of different motor output settings and output volumes is 0.9872. Under the same settings, the average volume under the motor settings 40~80 is 255.8~740.4ml, and the error of volume is 0.22%~6.25%, deducted after the motor is set to 40, the average volume is 384.2~740.4ml under the motor setting 50~80, and the error of volume is 0.22%~1.35%; under the motor setting 60, 40~80 speed setting, the volume is 490~515ml, and the R2 value is 0.8; Under the setting of motor output 65 and speed 40, the average volume of the three positions of the bag-valve resuscitator is 548.2 mL, 554.4 mL, and 535.8 mL.
Conclusions: Under different motor settings, the lower volume has a larger error; different output speed and position volume will have some changes, but they are all within the error of ideal ventilator volume (<10%), so the future design flow of this type of respirator the feedback mechanism of the sensor is very important. In addition to monitoring the tidal volume, it also needs the function of feedback data for volume control.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB53

近十年胸腔內科醫師所受之醫療訴訟裁判分析

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A ten-year analysis of medical malpractice judgments in chest physicians

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Background: In recent years, with the increase of medical litigation, there is a lack of data on the types of criminal and civil litigation faced by chest physicians.
Methods: Through the judgment search website of Judicial Yuan (https://law.judicial.gov.tw/ FJUD/ default_AD.aspx), using chest medicine, in Chinese, "胸腔內科 or 胸腔科" as keywords, search for the decisions of civil and criminal courts at all levels for nearly a decade from January 1, 2010 to July 31, 2020. Examine and exclude the contents of non-medical litigation cases on a case-by-case basis.
Results: Preliminary search results show that there are 604 and 396 judgments each in the civil and criminal litigation. After excluding non-medical litigation cases one by one, there were 77 civil litigation judgments and 13 criminal judgments. A total of 60 people have been subjected to civil litigation disputes. The longest litigation case time is 9 years. Civil claims of up to $26 million (related to tuberculosis treatment). The maximum award of compensation is 9.47 million (related to bronchoscopy), and finally settled. The types of hospitals where incidents occurred were 49% of medical centers, regional and local hospitals for 47%, and clinics for 4%. Seven persons were subjected to criminal proceedings, which lasted a total of eight years. Two people were sentenced to eight and six months each, while the others were not guilty.
Conclusion: In the past ten years, civil claims are the type of litigation that chest physicians encounter the most, especially at medical center. Although most of the criminal cases were not guilty, two doctors were still sentenced.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB54

利用真空引流瓶及靜脈留置針引流氣胸的安全性及功效

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The Safety and Efficacy of Vacuum Bottle Plus Catheter for Drainage of Pneumothorax

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Purpose: Iatrogenic pneumothorax is one of the morbidities after interventional pulmonology procedures. For pneumothorax larger than 15%, needle aspiration performed through manual air drainage was suggested. However, it is time-consuming. Vacuum bottle plus non-tunneled catheter for air drainage is another option but its safety and efficacy remained to be assessed.
Materials and Methods: Patients over 20 years of age, who developed pneumothorax after lung biopsy were enrolled. Patients were placed in a semi-supine position with the torso at an angle of 60 degrees. A non-tunneled catheter was placed at the intersection of the midclavicular line and the second intercostal space and a three-way stopcock attached. A drainage set and a digital pressure gauge were connected to the other two ends of the three-way stopcock. The stopcock was manipulated to connect pleural space to the digital pressure gauge. Intrapleural pressure was checked at end-expiration before drainage. The stopcock was manipulated again to connect the pleural space to the vacuum bottle and the drainage set was manipulated to drain the pneumothorax with the formation of air bubbles in one straight line. Intrapleural pressure was measured at an interval of 5 seconds in first 60 seconds and then to 30-second intervals until no air could be drained. Chest X-ray was checked immediately and the next day.
Results: From Aug 2018 to Sep 2019, totally 27 patients who developed post-procedure pneumothorax were screened and 15 patients recruited. The mean size of pneumothorax before the procedure was 22.1% by the Rhea method. Pneumothorax improved without persisted air leakage in 9 patients (60%) and the mean size of pneumothorax post-procedure was 8.9%. 6 patients (40%) had persistent air leakage and received pigtail placement. The end-expiratory pleural pressure of all patients remained less than -20 mmH2O during drainage. The median pain scale of ten for pre-procedure, 1 minute after initiation and post-procedure were 1, 1, 1 respectively. The mean duration of hospital stay attributed to pneumothorax was 1.2 days (1-2 days) in vacuum bottle and catheter drainage only group and 6 days (4-8 days) for whom received subsequent pigtail placement. There was no procedure-related complications or mortality.
Conclusions: Vacuum bottle plus catheter drainage of iatrogenic pneumothorax is a safe and efficient procedure. Most patients did not experience procedure-related discomfort and had a short hospital stay. It is an option for iatrogenic pneumothorax.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB55

蒸汽吸入顆粒球巨噬細胞群落刺激生長因子(GM-CSF)治療肺泡蛋白質沉著症的使用經驗: 病例報告

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The experience of treating pulmonary alveolar proteinosis with nebulized recombinant human Granulocyte-macrophage colony-stimulating factor (GM-CSF): A case report

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Introduction: Pulmonary alveolar proteinosis (PAP) is a diffuse parenchymal lung disease characterized by the accumulation of amorphous, periodic acid-Schiff (PAS)-positive lipoproteinaceous material in the distal air spaces. The lipoproteinaceous material is composed principally of surfactant phospholipid and apoproteins. There are mainly three types: hereditary, secondary and autoimmune PAP. Autoimmune PAP accounts for more than 90% in adult cases. Autoimmune PAP is associated with disruption of granulocyte-macrophage colony-stimulating factor signaling and decreased clearance of surfactant by alveolar macrophages.

Case Report: We describe a 46-year-old office lady who was treated with recombinant human Granulocyte-macrophage colony-stimulating factor (GM-CSF) with clinical improvement. She complained of productive cough with scanty whitish sputum and dyspnea on exertion for 3 months. She visited our chest medicine outpatient department due to abnormal chest X-ray in a health checkup. High resolution computed tomography (HRCT) showed multiple patches of ground glass infiltrations and interstitial thickening in both lungs with crazy paving pattern. Blood assays showed no evidence of hematologic malignancy, myelodysplastic syndrome, polycythemia or hypergammaglobulinemia. There was no occupational history with high level dust exposures. Under the impression of autoimmune pulmonary alveolar proteinosis, weekly nebulized recombinant human GM-CSF 300mcg was prescribed. After 2 months course of treatment, 6 minute walking test improved from 485 meters to 518 meters. Image study revealed mild improvement of ground glass infiltrations.

Discussion: The choice of treatment options for patients with autoimmune pulmonary alveolar proteinosis (PAP) depends on the severity of symptoms and gas exchange abnormalities. For patients with minimal symptoms or physiologic impairment, supportive care with supplemental oxygen is suggested. For patients with moderate-to-severe dyspnea and hypoxemia, whole lung lavage is suggested. Recombinant granulocyte macrophage-colony stimulating factor (GM-CSF) administered by inhalation or subcutaneous injection is not approved for use in autoimmune PAP, but may be an option for those who cannot undergo or have not responded to whole lung lavage.

Further studies are needed to define the duration of GM-CSF treatment required for maximal treatment benefit and to evaluate the potential use of differential dosing for induction and maintenance therapy.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB56

$PM_{2.5}$和 NO_2 導致台灣老年人肺功能不同型式的下降

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$PM_{2.5}$ and NO_2 cause different lung function decline patterns in Taiwanese elderly.

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Purpose: Air pollution has been associated with the development of airway disorders and interstitial lung diseases. The effect of air pollution on the pattern of lung function impairment is inconclusive. We evaluated the effect of long-term exposure to ambient air pollution on the change rate of lung function patterns.

Materials and Methods: During 2016~2018, forced spirometry and single-breath helium dilution static lung volume measurement were performed once per year for 543 elderly. Exposure to ambient fine particulate matters ($PM_{2.5}$) and nitric dioxide (NO_2) was estimated using a hybrid Kriging/Land-use regression model. Linear mixed models were used to evaluate the association between air pollution exposure and lung function.

Results: An interquartile range increase in long-term exposure to NO_2 was associated with an additional rate of decline in total lung volume (-1.9% per year), residual volume (-3.4% per year), and the ratio of residual volume to total lung volume (-1.7% per year); whereas $PM_{2.5}$ exposure was associated with an additional rate of decline in the ratio of FEV_1 to FVC (-0.9% per year). The effect of $PM_{2.5}$ and NO_2 remained consistent even with mutually adjustment.

Conclusions: Long-term exposure to ambient NO_2 is associated with a restrictive lung function decline pattern, while $PM_{2.5}$ is associated with an obstructive pattern. The results provide some insights that different air pollutant exposures can cause different lung diseases.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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腫瘤切片後空氣栓塞使用高壓氧之治療經驗: 個案報告

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Hyperbaric Oxygen Therapy in the Treatment of Air Embolism post Biopsy of Lung Tumor - A Case Report

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Introduction: Air embolism is an uncommon complication post lung tumor biopsy, which could result in further coronary or cerebrovascular events. This life-threatening condition usually result from pulmonary barotrauma, accidental intravenous air injection, or some surgical procedures. Hyperbaric oxygen therapy remains the mainstay of treatment, but some complications could take place during the management.

Case report: A 79-year-old male, with colon cancer post concurrent chemoradiotherapy and complete tumor resection 12 years ago, was admitted for biospy of newly developed left upper lung tumor via computed tomography guidance. Air embolism was noted in the left atrium and ascending aorta upon completion of the biopsy. Hyperbaric oxygen therapy (HBOT) was arranged soon after immediate bilateral tympanocentasis. Air bubbles was not visible on chest CT after HBOT, but left side tension pneumothorax was identified. After placement of chest pigtail catheter, full expansion of left lung was noted. Throughout the course, the patient did not have worsen chest pain or any neurological deficit after the biopsy.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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結構性肺復原介入於慢性肺部疾病患者之成效及運動誘發低血氧的影響

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Effect of 8-week Structured Pulmonary Rehabilitation Program in Patients with Chronic Lung Disease and the Impact of Exercise Induced Desaturation

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Purpose: Pulmonary rehabilitation (PR) has been known to improve exercise capacity, pulmonary function and health related quality of life in chronic lung disease patients. However, a portion of patients suffer desaturation during exercise, limiting the effect of PR. We aim to evaluate the clinical impact of an 8-week structured PR program.

Materials and Methods: We retrospectively analyzed 82 chronic lung disease patients who completed structured PR (8-week aerobic and strength training with follow-up evaluation once per month for 2 months) during 2017-2020. We collected baseline characteristics, spirometry, 6-minute walking test (6MWT) from all patients and identified patients with exercise induced desaturation (EID, nadir SpO2 during 6MWT ≤88%). Kruskal- Wallis test assessed difference between groups and Wilcoxon Signed Ranks test assessed improvements of 6MWT parameters.

Results: Among 82 patients, 63 (77.1%) had chronic obstructive pulmonary disease and 34 (41.5%) had EID. The baseline characteristics were similar between two groups. The peak of patients who achieved a minimal clinically important difference (MCID) > 30m occurred at 1st-month follow-up in EID group (50%) and at 2nd-month follow-up in non-EID group (64.6%). At 2nd-month follow up, walking distance during 6MWT (6MWD) increased significantly during PR course with a 56.1% and 45.1% of patients achieving a >30-meter, including 15 patients (44.1%) in EID group and 31 patients (64.6%) in non-EID group (p=0.07), and >50-meter increase compared with baseline. Distance-saturation product revealed a significant improvement compared with baseline in both groups in each follow up evaluation. In the EID group, the nadir spo2 increased significantly (median 1, IQR -1 ~5, p< 0.01) at 2nd-month follow-up with 7 patients (20.6%) relieved from EID status.

Conclusion: In this study, we found EID patients tended to have worse response in 6MWD than non-EID patients during 8-week structured PR program. The severity of EID also reduced after the 8-week PR program and this effect was persistent during 2-month follow-up.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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探討單純性肺炎 (TW-DRGs: 089、090) 疾病嚴重度對於醫療費用支出的影響

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The Impact of Disease Severity on Medical Expenses for Simple Pneumonia (TW-DRGs: 089、090)

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Purpose: In Taiwan，the pneumonia ranks at the third place for all cause of mortality in recent 3 years (from 2016 to 2018). The outcome of pneumonia based on disease severity and patient risk factors. Now the common tools for evaluation pneumonia severity include pneumonia severity index (**PSI**) and **CURB-65**. Medical payment was based on the concept of Diagnosis Related Groups(TW-DRGs) nowadays, including simple pneumonia. Diversity of disease severity was less taken into consideration when talking about the medical expenses. Today，we want to explore the impact of disease severity on medical expenses for simple pneumonia (TW-DRGs: 089、090).

Materials and Methods: We retrospectively analyzed the TW-DRGs (089、090) simple pneumonia data between 2014 to 2018 in our hospital. The demographic data (age, sex, comorbidities…etc.) were recorded. Besides, the medical expenses (total medical fee), pneumonia severity on Day 1 include PSI (pneumonia severity index), CURB-65 score were collected respectively. We used SPSS 22th edition for statistic calculation.

Results: Total 3,281 patients were retrospectively analyzed. The mean age was 70 year-old and length of hospital stay (including emergency room and ward stay) was around 10 days. Male patients was predominant. The median medical expenses was around NT 44,500. Day 1 of pneumonia severity represented by PSI class was class IV predominant (43.7%). Via CURB-65 method，52% patients belong to medium risk group (score around 2~3). After adjusting DRG, sex and hemodialysis，the Day 1 CURB-65 score showed better correlation and prediction of higher medical expenses (OR: 1.38; 95% of CI: 1.29~1.49，P<0.001).

Conclusions: In our preliminary study，we found Day 1 disease severity could predict the medical expenses for simple pneumonia (TW-DRGs: 089、090). As for CURB-65 and PSI, we discovered the better correlation of CURB-65 than PSI for prediction the medical expenses.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

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嚴重睡眠呼吸中止與交通事故的相關性

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Severe sleep apnea related to vehicle accident

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Purpose: Sleepiness at the steering wheel is a major cause of motor vehicle accidents. Sleep apnea (SA) may present daytime sleepiness. Therefore, we investigated the relationship between severity of OSA and vehicle accident.

Methods: We evaluated the patients ≧ 20 years receiving in-lab polysomnography in a sleep center between 2010 and 2015. We collected demographic characteristics, sleep efficiency (total sleep time [TST] / time in bed * 100%), apnea hypopnea index (AHI), and vehicle accident. To grade the severity of sleep apnea, the number of AHI per hour is reported. An AHI of less than 5 per hour is considered normal. An AHI of 5-15 per hour is mild; 15-30 per hour is moderate and more than 30 events per hour define severe SA.

Results: A total, 4351 patients (3284 men and 1067 women) were recruited. Among them, 176 (4.0%) experienced vehicle accident. The participants with SA were likely to experience vehicle accident than that without SA (79.0% vs 71.2%, P = 0.024). Multivariable logistic regression presented that participants with severe SA exhibited 2.29-fold higher risk of vehicle accident than did those without SA (adjusted odds ratio = 2.29; 95% confidence interval = 1.46 – 3.60)

Conclusion: This study indicated that participants with severe SA carried an increased risk of vehicle accident. The government may regulate drivers with severe SA especially for those public transportation drivers.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

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全基因體微矩陣基因表現全貌辨識出調控阻塞性睡眠呼吸中止症的新分子機轉：內皮細胞緊密接合和細胞凋零

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Clinical trial to investigate the titration protocol of intra-oral negative air pressure therapy in obstructive sleep apnea patient.

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Objective:
The intra-oral negative air pressure (iNAP) device was designed to decrease airway obstruction by retaining the tongue and the soft palate forward by providing a constant negative pressure (-40mmHg) within the oral cavity. The lasted studies demonstrate the response rate of iNAP could up to 60%. However, for those OSA patients with very high BMI or AHI, they may need higher pressure to achieve optimal treatment outcome. In this study we hope to select an optimal intra-oral pressure for an OSA patient during iNAP treatment by titration process.
Methods:
All the subjet had received two PSG, one is baseline PSG and the other one is iNAP titration PSG. When conducting the iNAP titration PSG, the initial treatment pressure is -40mmHg. iNAP presure should be increased by at least 10mmHg. with an interval no shorter than 15 min, with the goal of eliminating obstructive respiratory events iNAP presure should be increased if(1) at least 2 obstructive apnea. (2) at least 3 hypopnea. (3) at least 3 min of loud or unambiguous snoring. The recommended maximum iNAP pressure should be -150mmHg.
Results:
18 subjects were consented and enrolled into the study. The mean age of all subjects was 47.45±13.34 years old and the mean BMI was 28.74±5.64 kg/m^2. The baseline AHI was 53.92±22.10, which decreased to 38.41±24.14 (p=0.001) at initial pressure (-40mmHg). Comparing to baseline AHI, the AHI reduction without titration is 28.76%. After iNAP titration, the final tereatment AHI is 5.43±6.17 (p=0.0001). Comparing to baseline AHI, the AHI reduction with titration is 89.93%.
Conclusion:
This study is a First-in-human clinical trial to investigate the titration of intra-oral negative pressure in treating the patient with obstructive sleep apnea. The result show that titration could improve the efficacy of iNAP treatment, especial for the non-responder. The titration result was only available in 18 subjects, but even in this small sample we saw signifcant differences between baseline AHI and titration AHI. We believe further iNAP titration studies need to be performed to understand the side effect of higher pressure and the optimal pressure exploring process.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

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總睡眠時間對慢性阻塞性肺部疾病的影響-臺灣阻塞性肺部疾病亞型之世代分析

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The impact of total sleep time on COPD - subgroup analysis of the Taiwan obstructive lung disease cohort

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Purpose: Patients with chronic obstructive pulmonary disease (COPD) have been reported to have poor sleep quality. However, total sleep time, which is an important parameter of sleep quality, has not been evaluated in detail among patients with COPD.
Patients and Methods: This retrospective, observational, multicenter research study was performed across six participating hospitals in Taiwan with a total of 421 adult patients enrolled from outpatient pulmonary clinics. Pulmonary function, the Modified British Medical Research Council (mMRC) Dyspnea Scale, the COPD Assessment Test (CAT) and basic clinical data were assessed in patients who had completed these measures within the past year. The Pittsburgh Sleep Quality Index (PSQI) was also administered to patients, and the total sleep time was extracted for further analysis.
Results: The patients whose total sleep time was between 6 and 7 hours had better pulmonary function, and the patients who slept less than 5 hours had worse comorbidities, such as diabetes, dyslipidemia and osteoporosis. There was a significant increase in total sleep time in Global Initiatives for Chronic Obstructive Lung Disease (GOLD) group B compared to GOLD group A. COPD patients who sleep between 5 and 6 hours used fewer oral steroids and were less likely to use triple therapy (long-acting beta-agonist (LABA), long-acting muscarinic antagonist (LAMA), inhaled cortical steroid (ICS)).
Conclusion: Sleep duration is an indicator of disease status in COPD patients. COPD patients sleeping 5 to 7 hours had better outcomes than those sleeping less than 5 hours in terms of pulmonary function, comorbidities and medication usage.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB63

使用智慧床墊感測睡眠呼吸中止症

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Detection of Sleep Breathing Disorder By an Unconstrained Mattress Sensor

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Introduction: Sleep breathing disorder (SDB) are highly prevalent but a considerable portion of patients remain undiagnosed. Various research groups had made effort on developing unconstrained and accurate sleep monitoring devices. Among these innovative sensors, bed/mattress-based devices can give the best sensitivity overall as well as moderate to severe cases. In this study, we evaluated the accuracy of an unconstrained mattress based on piezo-electric (PE) sensor system in measuring physiological signal and detection rate of SDB.
Materials and Methods: Seventy adults, including 58 males and 12females (mean age: 39.4 ± 10.6 years, mean BMI: 26.2 ± 4.0, mean AHI: 41.8 ± 28.9) with suspected sleep apnea was recruited to our study. The subjects went to our sleep center, undergoing examination of full night PSG and PE sensor-based mattress simultaneously. The PE sensor was placed under the mattress near thoracic area, which can measure physiological signal including respiratory rate, snoring rate and heart rate without discomfort. These extracted features can further used to determine whether SDB occurred or not by a machine learning algorithm. The data was compared to PSG with manual scoring by sleep specialist according to AASM guidelines, so the accuracy of the PE sensor can be assessed.
Results: Boxplots were used to compare the accuracy of measuring physiological signal between PE sensor and PSG in each patient. In 85% subjects, the overall difference of respiratory rate between PE sensor and PSG located in ±3 bpm, and the difference of snoring rate located in ±7 bpm. As for the heart rate, the result showed that 80% subjects' overall difference located in ±3 bpm. SDB, including obstructive sleep apnea (OSA), central sleep apnea (CSA) and mixed sleep apnea (MSA) was detected respectively by the machine learning algorithm, and result was compared to PSG as well.
Conclusions: This mattress type sleeping device based on PE sensor can predict physiological signal with acceptable accuracy, especially in respiratory rate and heart rate. However, the sensitivity of this PE sensor and algorithm in detecting different type SDB ranged from 43% to 64.4%, and there is still room for improvement. In the same time, new sensor should be applied to distinguish the difference between normal breathing and hypopnea, and the AHI can be measured consequently.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

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多睡眠中心技師可靠性研究：睡眠階段分期

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Multiple sleep center inter-scorer reliability study: sleep stage scoring

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Purpose: This program provides a rare opportunity for technicians from multiple medical sleep centers to study the reliability and to determine the consistency of sleep stage scoring. The purpose is to use the results as the ground truth being the training basis for artificial intelligence to development computer-assisted automatic scoring of polysomnograms, hoping to increase the efficiency and accuracy of sleep technician in sleep study scoring.
Material and Method: The sample included whole night sleep study data of 58 patients from 6 sleep centers with 4 different polysomnography systems and got 44782 epochs. Six technicians from different medical centers, most of whom have 4 or more years of experience, have undergone rigorous three-stage scoring to obtain the final result.
Results: The total agreement rate was 72.6% in the first stage across all sleep stage. The consistency of N2 was the highest, at 78.7%. The agreement of REM, wake, and N3 was 77.4%, 76.9%, and 53.7%, respectively. The sleep stage with the lowest consistency is N1, only 24.4%. After the second stage modification, the consistency of N2 is the highest, which is 91.6%. The agreement of REM, wake, and N3 was 91.3%, 91.0%, and 83.8%, respectively. The N1 stage was still the lowest but increased to 62.6%. After face-to-face discussions in the third stage, the REM stage had the highest consistency at 99.8%. The agreement of wake, N2, and N3 were 99.6%. The N1 stage increased significantly to 98.4%.
Conclusion: After three stages of discussion and revision, the consistency can be significantly improved all above 98%, especially the N1 with the very low agreement rate in the first stage.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

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使用睡眠內視鏡協助調整陽壓呼吸器的結果：一個隨機對照交叉試驗

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The outcome of CPAP titration under drug-induced sleep endoscopy: A randomized controlled crossover trial

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Purpose: The titration pressure of continuous positive airway pressure (CPAP) is important for patients with obstructive sleep apnea (OSA). This study aimed to understand the impact of drug-induced sleep endoscopy (DISE)-guided and doctor-guided CPAP pressures on OSA patients.
Materials and Methods: In this randomized controlled single-blinded crossover trial, we compared the effects of 1-month CPAP treatment in OSA patients. Twenty-four OSA patients were recruited for this study. All patients underwent polysomnography, DISE-guided CPAP titration, and accommodation. Patients were randomly assigned to receive either DISE-guided or doctor-guided CPAP pressure treatment for 1 month. They then switched to the other treatment for another month. Epworth sleepiness scale (ESS) was recorded at baseline, 1 month, and 2 months.
Results: The DISE-guided and doctor-guided CPAP pressures had no significant differences (13.9 ± 0.7 cm H_2O vs 13.5 ± 0.5 cm H_2O; P = 0.92). Residual apnea-hypopnea index (AHI) and compliance were also not significantly different between the groups. The ESS significantly improved from baseline to 1-month post CPAP treatment in both groups. There was a significant association between epiglottis (anterior-posterior collapse) and AHI (P < 0.001, Spearman correlation). Both epiglottis (anterior-posterior collapse) and tongue base collapse were significantly associated with 95% CPAP pressure (P = 0.031 and 0.038). After multivariate regression analyses, epiglottis (anterior-posterior collapse) was the independent factor for 95% CPAP pressure.
Conclusions: There was no significant difference between the DISE-guided and doctor-guided CPAP pressure on the improvement of ESS. Epiglottis (anterior-posterior collapse) was the independent factor for AHI and 95% CPAP pressure.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB66

肥胖合併睡眠呼吸中止症病人接受內視鏡袖狀胃切除術後的呼吸中止低通氣指數變化之預測因子

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The factors predicting resolution of apnea hypopnea index in obese patient with obstructive sleep apnea received laparoscopic sleeve gastrectomy

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Purpose: Bariatric surgery via laparoscopic sleeve gastrectomy (LSG) was the main surgery in obesity patient which associated with significant reduction in apnea hypopnea index (AHI). However, even after receiving surgery, there were still nearly half of the patients who met the OSA diagnosis criteria needed to be treated. We aimed to identify the factors predicting good obstructive sleep apnea (OSA) response in these patients.
Materials and Methods: From April 2016 to December 2018, 22 obese patients who underwent PSG before and after bariatric surgery at the obesity center, National Taiwan university Hospital were retrospectively studied. The simultaneously nocturnal transcutaneous CO2 (TcCO2) monitoring was applied. Demographic, anthropometric characteristics, Epworth sleepiness scale (ESS), Pittsburgh Sleep Quality Index (PSQI), PSG parameters were reviewed. Treatment success was defined as AHI reduction ≥50% and residual AHI< 10/hour.
Results: Postoperative PSG was performed in 22 patients [13 men and 9 women, median age 38 (32.8-46.5), median body mass index (BMI) 44.5(32.8-46.5) kg/m2] a median of 405 (330-520) days after LSG while the median BW loss was 27.8 (23-33.6) %. Median AHI decreased from 51.9 (23.1-87) to 8.4 (1.3-16.4) events/h (p<0.01). Median average TcCO2 decreased from 51.1 (43.9-55.4) to 46 (41.9-51.3) mmHg (p<0.05). Of 22 patients, treatment success was achieved in only 10 people (45%). Multivariate logic regression showed baseline AHI was associated with treatment success adjusted by baseline WC. (odds ratio: 0.913(0.839-0.994), p=0.036)
Conclusions: We identified the baseline AHI was the most important factor for treatment success.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB67

阻塞性睡眠呼吸中止症之日間嗜睡與主觀睡眠時間減短之相關性

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Short habitual but not objective sleep duration is associated with excessive daytime sleepiness in patients with sleep apnea

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Background: Excessive daytime sleepiness (EDS) is a common symptom with prevalence up to 60% in OSA population. EDS increases OSA patients' risk of cardiovascular events, and cognitive impairment. Sleep duration in OSA patients is associated with increased risks of cardiovascular events and metabolic disturbances as well, and impair quality of life in patients with EDS. However, current literature provided limited data on the interaction between OSA, EDS and sleep duration. We hypothesize that habitual but not objective sleep duration was associated with the EDS in patients with different OSA severity. This study aimed to test if habitual and objective short sleep duration would further increase risk of EDS in large cohort of patients with sleep disordered breathing (SDB).

Materials and Methods: Information prospectively collected from 7,834 adult patients who underwent initial overnight polysomnography (PSG) for the first time in the Center of Sleep Disorder of National Taiwan University Hospital between January 2009 and December 2017 were reviewed. Subjective sleepiness was assessed with Epworth Sleepiness Scale (ESS) and EDS was defined as ESS≥10. Depression was assessed with Hospital Anxiety and Depression Scale Depression. Short sleep duration was defined as sleep duration <6h while extreme short sleep defined as sleep hr <5h. Logistic regression was applied to clarify the association between habitual and objective sleep duration, OSA severity, and EDS with adjustment of age, gender, anthropometrics, co-morbidities, smoking, and depression.

Results: In 7,834 patients, 75.5% was male, median age was 47 y/o, body mass index 26.5 kg/m^2, and apnea-hypopnea index 21.8/h. EDS was observed in 46.9% patients and up to 47.9% in male <65 y/o. 22.5% of patients had habitual short sleep and 7% extreme short sleep. Compared to patients without EDS, patients with EDS had higher percentage of man, smoking, obese, co-morbidities, short sleep, and depression. Patients with EDS also had higher OSA severity, longer objective duration, and higher %REM. Compared to no OSA, severe OSA was associated with increased risk of EDS. Compared with sleep hour ≥6 hr, sleep 5-6 hr was associated with EDS across all severity of OSA while the sleep <5hr was associated factor in severe OSA .

Conclusions: In patients with OSA, EDS are associated with higher BMI, co-morbidities, and depression. Short habitual sleep is associated with EDS.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PB68

尋找適合的面罩使用於連續性陽壓呼吸器治療：網絡統合分析

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In search of a better interface for CPAP therapy: A network meta-analysis

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Purpose: Up to date, no known articles have described the different impacts on continuous positive airway pressure (CPAP) therapy for patients with obstructive sleep apnea (OSA) among the nasal masks, nasal pillows, and oronasal masks. This study aimed to compare the impact of three interfaces on effectiveness and adherence in a network meta-analysis (NMA).

Materials and Methods: PubMed, EMBASE, CENTRAL, and ClinicalTrials.gov were systematically searched from inception to December 2019 for studies which compared the different interfaces on adult OSA patients with CPAP treatment. The outcomes were residual apnea-hypopnea index (AHI), CPAP pressure, and adherence. A multivariate random effect network meta-analysis in a frequentist framework was used for estimations. Three interfaces were ranked using surface under the cumulative ranking (SUCRA) probabilities.

Results: Twenty-nine studies comprising 5948 participants were included. Patients who used nasal masks have lower residual AHI (mean difference (MD) -3.97/hr, 95% CI, -6.20 to -1.74), lower CPAP pressure (MD -0.95cmH_2O, 95% CI, -1.45 to -0.44), and higher adherence (MD 0.43 hr/night, 95% CI 0.25 to 0.60) compared to patients who used oronasal masks. Nasal pillows also appeared better performance than oraonasal masks, which the MD in residual AHI, CPAP pressure, and adherence were -3.42/hr (95% CI, -6.75 to -0.09), -1.22cmH_2O (95% CI, -1.90 to -0.55), and 0.26 hr/night (95% CI, 0.04 to 0.49). There were no differences between nasal pillows and masks. The SUCRA rankings confirm that nasal mask was most likely to result in the lowest residual AHI and highest adherence (SUCRA 1.4 and 1.1 respectively) while nasal pillow was most likely to result in the lowest CPAP pressure (SUCRA 1.2).

Conclusions: Oronasal masks were associated with the highest residual AHI and CPAP pressure, and lowest adherence compared to nasal masks and pillows while nasal masks and nasal pillows have similar impacts.

Respiratory Tract Infections

Critical Care Medicine

Tuberculosis

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) □海報競賽 (Post)

OC01

急性呼吸窘迫症候群病患使用體外膜氧合下的機械功率和住院死亡率相關性之探討

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Mechanical power during extracorporeal membrane oxygenation and hospital mortality in patients with acute respiratory distress syndrome

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Purpose: Our objective was to assess the potential impact of consecutive changes of normalized mechanical power (MP) on hospital mortality among acute respiratory distress syndrome (ARDS) patients receiving extracorporeal membrane oxygenation (ECMO).

Materials and Methods: We performed a secondary analysis of patients with severe ARDS receiving ECMO in a tertiary care referral center in Taiwan between May 2006 and October 2015. Serial changes of MP during ECMO were recorded.

Results: A total of 152 patients with severe ARDS rescued with ECMO were analyzed. Overall hospital mortality was 53.3 %. There were no significant differences between survivors and nonsurvivors in terms of baseline values of MP or other ventilator settings. Cox regression models demonstrated that MP alone, MP normalized to predicted body weight (PBW), and MP normalized to compliance during the first 3 days of ECMO were all independently associated with hospital mortality. Higher MP normalized to compliance (HR 2.289 [95% CI 1.214-4.314], $p = 0.010$) was associated with a higher risk of death than MP itself (HR 1.060 [95% CI 1.018-1.104], $p = 0.005$) or MP normalized to PBW (HR 1.004 [95% CI 1.002-1.007], $p < 0.001$). The 90-day hospital mortality of patients with high MP (> 14.4 J/min) during the first 3 days of ECMO was significantly higher than that of patients with low MP (≦ 14.4 J/min) (70.7 % versus 46.8 %, $p = 0.004$), and the 90-day hospital mortality of patients with high MP normalized to compliance (> 0.53 J/min/ml/cm H_2O) during the first 3 days of ECMO was significantly higher than that of patients with low MP normalized to compliance (≦ 0.53 J/min/ml/cm H_2O) (63.1 % versus 29.5 %, $p < 0.001$).

Conclusions: MP during the first 3 days of ECMO was the only ventilator setting independently associated with 90-day hospital mortality, and MP normalized to compliance during ECMO was more predictive for mortality than was MP alone.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC02

成功利用短期二氧化碳吸入治療策略於不同肺損傷動物模式

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Therapeutic applications of short-term carbon dioxide inhalation therapy (stCO2-IT) in different animal models of experiment lung injury.

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Purpose: In patients with acute respiratory distress syndrome (ARDS), there is still controversial information regarding the effect of hypercapnia on outcomes. We found the duration of carbon dioxide inhalation may be the key to the protective effect of hypercapnia. Last year, we had demonstrated that pre-treatment with 10-min carbon dioxide inhalation can ameliorate LPS-induced lung injury. Furthermore, in this study, we used three different animal models of lung injury to evaluate the protective effects of short-term carbon dioxide inhalation therapy before clinical trials.
Materials and Methods: Rats or mice were exposed or not to short-term carbon dioxide inhalation therapy (stCO2-IT) for 30 min before or after lung injury. Three different animal models of lung injury. (1) Hyperoxia-induced lung injury (HO-ILI) in mice. (2) Ventilator-induced lung injury (VILI) in rats. (3) Ischemic-reperfusion induced lung injury (IR-ILI) in rats.
Results: In these three different animal models, stCO2-IT significantly attenuated the lung injuries such as lung edema (LW/BW), permeability (protein in bronchoalveolar lavage fluid; BALF), lung injury (LDH activity in BALF), inflammatory cells infiltration (total cell counts in BALF), and lung tissue damage (pathology). To investigate the molecular mechanisms, we used lung tissues from HO-ILI model for further analysis. Hyperoxia (exposure to 100% oxygen for 72 hours) induced the lung apoptosis and stCO2-IT significantly attenuated the pulmonary apoptosis (TUNEL assay). Moreover, stCO2-IT significantly suppressed hyperoxia-induced NF-κB activation. Furthermore, stCO2-IT suppressed hyperoxia-induced endoplasmic reticulum stress (ER Stress) such as ATF6, CHOP, PERK, and XBP1 protein expressions. The protective may be associated with stCO2-IT induced the increased expressions of stress proteins such as HO-1 and HSP70.
Conclusions: Follow our previous LPS-induced lung injury, we have demonstrated the protective effects of stCO2-IT in another three animal models of lung injury. Further clinical trial of application of stCO2-IT in lung injury is on-going. In the future, stCO2-IT have the potential to be used in the treatment of lung injury.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC03

電子菸透過加強 p38 MAPK 調控嗜中性球活化與內皮功能失常，進一步惡化內毒素所引起的急性肺損傷

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E-cigarette enhances endotoxin-induced ALI through p38 MAPK pathway to regulate neutrophil activation and endothelial dysfunction

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Background: The mechanism of e-cigarette or vaping product use–associated lung injury (EVALI) remains unclear. We investigated the effect of e-cigarette in moderating neutrophil chemotaxis in endotoxin-induced acute lung injury (ALI).
Methods: Male C57BL/6 mice at 8 to 12 weeks of age were studied. Vegetable glycerin (VG) is the major component of e-cigarette liquid. Mice received intratracheal administration of PBS or 30% VG at the day 1 – day 4. At the day 5, each mouse will receive an intratracheal instillation of LPS or PBS. Lung histopathological findings, expression of chemokine receptors, and regulatory signaling pathways were analyzed after 24 hours.
Results: Intratracheal administration of VG significantly not only induced the histopathological changes of ALI in control mice but also amplified the histopathological changes in LPS-induced ALI mice. Masson's trichrome stain revealed aspiration of VG increased fibrotic change in LPS-induced ALI mouse lungs. The immunohistochemical staining and western blots both revealed that aspiration of VG increased neutrophil recruitment and endothelial to mesenchymal transition (EndoMT) in LPS-induced ALI mouse lungs. The aspiration of VG mediated a up-regulation of the chemotactic response (VCAM-1 and VLA-4) and EndoMT (α-SMA and TGF-β), and a down-regulation of endothelial marker (VE-cadherin) to endotoxin by increasing p-p38/p38 expression in mouse lungs. Importantly, p38 inhibitors can reduced these harmful changes of VG aspiration in ALI mice.
Conclusion: VG, a major component of e-cigarette liquid, enhances neutrophil chemotaxis and EndoMT in endotoxin-induced ALI. These effects are mediated, at least in part, by the enhancement of p-38 MAKP activity.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC04

控制不佳之糖尿病患者之潛伏結核篩檢及治療--一個前瞻性多中心之觀察性研究

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The intervention of latent tuberculosis infection in poorly diabetic controlled patients, a prospective, multicenter, observation study

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Background: Diabetic Mellitus (DM) has been identified as a risk factor for tuberculosis (TB) disease and poorly-diabetic-controlled (pDM) status may accelerate the endogenous reactivation of latent TB infection (LTBI). To understand the predictors of LTBI and the optimal treatment regimen for LTBI treatment among pDM patients is essential.

Methods: Patients with pDM, defined as glycated hemoglobin (HbA1c) ≥9% within recent one year were enrolled from two medical centers for LTBI screening by using QuantiFERON. Three-month weekly isoniazid plus rifapentine (3HP) or nine-month daily isoniazid (9H) were offered. This study aimed to investigate the factors associated with LTBI status, completion rate, and adverse drug events under different regimens among pDM patients.

Results: Overall, 980 of 1057 (92.7%) pDM patients received LTBI screening from endocrinologists, with 26.6% (261 of 980) had positive results of Interferon-Gamma Release Assay (IGRA) test, and 76.6% (200 of 261) among them received preventive therapy under programmatic follow-up by pulmonologists. The completion rate was 82.5% in overall. Of them, 62 and 138 received 9H and 3HP regimen, with 49 (79.0%) and 116 (84.1%) completing treatment, respectively. In the 3HP group, 9 (6.5%) suffered from systemic drug reactions. Age with per-year increment, DM period, chronic kidney disease, stage ≥3, and use of DDP4 inhibitor were associated with IGRA-positivity, whereas the use of metformin was protective. Post-treatment QFT follow-up was subsequently assessed in 81 cases, and the overall negative conversion rate was 26.7%.

Conclusion: The current study demonstrated prompt LTBI intervention should be applied to pDM patients with the above risk factors, and an excellent treatment completion rate can be achieved under a collaborative framework.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC05

T 細胞上增加的免疫調節 TIM3 受器在非結核分枝桿菌肺病的角色: 從免疫細胞失能到臨床嚴重度

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The role of increased TIM3 on T cells in patients with nontuberculous mycobacterial lung disease: from immune cell dysfunction to clinical severity

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Background: Nontuberculous mycobacterial lung disease (NTM-LD) is increasing in recent decades worldwide but the nature remains unclear. The immune exhaustion has been reported before but only limited to programmed death-1, which cannot explain the whole picture. In contrary, T cell immunoglobulin and mucin domain- containing protein 3 (TIM3) is reported as a new “co- inhibitory” or “checkpoint” receptor, shown to suppress CD4+ and CD8+ T cells. However, there are scarce studies investigating the role of TIM3 in NTM-LD.

Methods: We prospectively recruited patients with NTM-LD from December 2014 to June 2019 in three tertiary referral centers in northern Taiwan. NTM-LD was diagnosed according to American Thoracic Society guideline. Patients with human immunodeficiency virus infection were excluded. We also enrolled healthy population as the control group. We examined the TIM3 expression on the T cell using flow cytometry. The Agena MassARRAY platform was applied to investigate single nucleotide polymorphism (SNP) of *TIM3* gene. We analyzed the impact of TIM3 on of NTM-LD.

Results: Among enrolled subjects (48 patients and 46 controls), TIM3 on CD4 cells (6.39% vs 4.12%, p=0.028) and CD8 cells (19.80% vs 9.74%, p=0.007) were significantly expressed higher in patients with NTM-LD than that in the controls. The Galatin-9, ligand of TIM3, on CD14 monocyte was not different between the patients and the controls. The TIM3 level on CD4+ and CD8+ T cells were significantly associated with T cell apoptosis (Pearson correlation: 0.534 and 0.316, respectively, both p<0.001). In-vitro stimulation of peripheral blood mononuclear cells using heat-killed *Mycobacterium avium* bacilli, TIM3 were induced to increase both CD4+ and CD8+ T cells. In addition, the post-stimulation TIM3 level was negatively correlated with tumor necrosis factor-alpha (TNF-α) on CD8+ T cells, indicating the effect on T cell dysfunction. In regard to clinical manifestation, TIM3 on CD4 cells was associated with low body mass index (BMI), radiographical fibro-cavitary pattern and positive sputum acid-fast smear (all p<0.05). We examined the SNPs of *TIM3* gene and found a SNP “X” was associated NTM-LD significantly (odds ratio: 1.63, 95% C.I.:1.07-2.49 by additive model).

Conclusions: In patients with NTM-LD, TIM3 over CD4+ and CD8+ T cells were increasing and correlated with cell apoptosis and attenuation of TNF-α expression. In addition, TIM3 correlates with low BMI, cavitary pattern and high bacilli burden. We found a *TIM3* SNP might involve its role in NTM-LD and needs further investigation.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC06

吸入性類固醇與非結核分枝桿菌肺病的相關性:一醫學中心的 10 年資料及統合分析

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The association between inhaled corticosteroid and nontuberculous mycobacterial lung disease: from 10-year database of a Taiwan medical center to meta-analysis

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Background: Inhaled corticosteroids (ICS) is one of important medication used in patients with chronic airway diseases including asthma and chronic obstructive pulmonary disease (COPD). Recent studies have demonstrated ICS use was associated with an increased risk for pneumonia and tuberculosis. Concerning the increasing global burden of nontuberculous mycobacterial lung disease (NTM-LD), the impact of ICS on NTM-LD was rarely investigated.

Methods: We retrospectively review a 10-year database from a medical center in northern Taiwan. Under microbiological criteria for NTM-LD by American Thoracic Society, we identified NTM-LD patients and matched 1:4 as a control group by age, sex and index date of NTM-LD diagnosis and their enrolled date. We reviewed the ICS use within 12 months before the index date and analyzed the odds ratio (OR) on NTM-LD using conditional logistic regression model. The adjusted factors included underlying comorbidities as well as oral corticosteroid (OCS) within the same period. Meta-analysis was performed by DerSimonian-Laird random-effects approach.

Results: Among 6,235 patients with respiratory specimen positive for NTM, we finally recruited 1,235 NTM-LD patients after excluding those with tuberculosis and matched a comparing cohort in a four-fold number (n=4,932). Patients with NTM-LD were thinner (BMI 21.3 vs 23.0 Kg/m^2, p<0.001) than the control group. The cumulative duration of ICS was associated with NTM-LD comparing with those without ICS use and had dose response in the duration <1 year and ≥2 year (aOR: 1.6 [95% C.I.: 1.2–2.2] vs 2.6 [1.4–6.1], respectively). In regard to the daily dose of ICS, the aOR for NTM-LD was 3.5 (2.1–6.0) for high dose, 2.1 (1.2–3.7) for moderate dose, and 2.5 (1.4–4.2) in low dose ICS. For recency of ICS use, we found that the aOR was highest while ICS use within 60 days prior to NTM-LD (aOR: 3.4 [2.3–5.0]), and decreased in ICS use 60–120 days prior to NTM-LD (aOR: 2.4 [1.0 – 5.8]) and insignificant for >120 days prior to NTM-LD (aOR: 0.9 [0.6–1.5]). The pooled results of the current study as well as additional two studies in the meta-analysis showed that NTM-LD was associated with ICS use within 30 days (pooled OR: 2.4 [1.4–4.1]), and ICS use within 120 days (pooled OR: 2.7 [2.1–3.6]), and within 1 year (pooled OR: 2.1 [1.4–3.3]). Higher dose of ICS use in 1 year showed prominent association with NTM-LD (pooled OR: 3.5 [1.9–6.4] for high dose, 1.9 [1.3–2.6] for moderate dose, and 1.6 [0.9 – 2.9] for low dose).

Conclusions: In this large-scale study, using ICS was associated with a higher risk of NTM-LD, supported by positive dose response even after adjusted by OCS. The impact was most significant within 4 months of ICS prescription. Clinicians need to be alert for NTM-LD if clinical suspicion of pulmonary infection for patients using ICS recently.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) ☐海報競賽 (Post)

OC07

生物膜在 *Acinetobacter baumannii* 肺炎合併菌血症的病人上的臨床觀察

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***Acinetobacter baumannii* isolated from the patients with pneumonia and bacteremia: biofilm production in clinical observation**

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Introduction: *Acinetobacter baumannii* has been among the most important nosocomial pathogen last ten years, only because of its increasing isolation in clinical culture, but also its increasing rate of drug resistance. *A. baumannii* infection which included bacteremia, urinary tract infection, pneumonia and wound infection and usually led to mortality. It had been reported that biofilm-forming ability was one of the main virulence factors in *A. baumannii* infection.

Materials and Methods: We enrolled the 68 patients who were diagnosed as both pneumonia and *A. baumannii bacteremia* from 2014-01 to 2018-10 at China Medical University Hospital. Forty patients received the blood test for biofilm detection. Biofilm formation was determined by a microtiter plate assay

Results: The mean age was 65.8 years old and 49 patients were female. 48 patients were multi drug resistance *Acinetobacter baumannii* (MRDAB).The infection related mortality was 69.1% (n=47). Compared with the survival groups, the non-survivor groups had more underlying disease of liver cirrhosis and chronic kidney failure. However, the rate of biofilm had no significant difference among the survival and non-survival group, (41.7% vs. 31.7%, *p*=0.563). Compared with non-MDRAB patients, MDRAB patients had higher incidence of acute respiratory failure(n=47, 97.9%) and hospital-acquired pneumonia(n=46, 95.8%). However, the patients with MDRAB had lower rate of biofilm formation (23.3% vs 70%, p=0.007).

Conclusions: The relationship between biofilm producers and drug susceptible had been reported before. In this study, biofilm producers were not relate to high mortality. Morever, biofilm producers were seen more in patients with community-acquired pneumonia and the patient infected with non-MDRAB. Biofilm producers maybe the factor that influenced the choice of antibiotics.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. ■口頭報告 (Oral Presentation) □海報競賽 (Post)

OC08

多重抗藥革蘭氏陰性菌肺炎重症患者中克痢黴素與急性腎損傷之關聯

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Association between colistin and acute kidney injury in critically ill patients with pneumonia caused by multi-drug resistant Gram-negative bacteria

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Purpose: Colistin is one of the most important antibiotics for the treatment of multi-drug resistant (MDR) Gram-negative bacteria (GNB) infections. However, the concerns of nephrotoxicity largely limit its clinical use. The aim of this study was to investigate the epidemiology and risk factors of colistin-associated acute kidney injury (AKI).

Materials and Methods: This multicenter, retrospective study was conducted in five medical centers. A total of 727 critically ill patients with hospital-acquired or ventilator-associated pneumonia caused by MDR GNB were enrolled. We excluded patients already on hemodialysis and those survived for less than 48 hours, leaving 455 patients for analysis. Serial serum creatinine levels in the first 14 days were used to define AKI, according to the KIDGO criteria. We used multivariable logistic regression to analyze risk factors of AKI.

Results: Among the 455 study patients, 120 (26.4%) received intravenous colistin for > 48 hours. The incidence of AKI was higher in colistin group than in non-colistin group (73/120, 60.8% vs 94/335, 28.1%, $P < 0.001$). In multivariable analysis, colistin was an independent risk factor of AKI (aOR= 3.23, 95% CI= 2.06-5.07, $P < 0.001$). Among the 120 patients receiving colistin, we did not identify any specific risk factors associated with AKI. However, higher daily dose (median 6 MU) tended to be associated with higher risk of AKI (aOR= 1.12, 95% CI= 1.01-1.31, $P = 0.098$) than low daily dose (median 4 MU). Among the 73 patients with AKI, 37 (55.2%) were in Stage I, and only 6 (8.2%) required hemodialysis. AKI was associated with a higher hospital mortality in both colistin group (61.6% vs 42.6%, $P = 0.041$) and non-colistin group (63.8% vs 28.6%, $P < 0.001$).
Conclusions: Intravenous colistin is an independent risk factor for AKI in critically ill patients with pneumonia caused by MDR GNB. Higher daily dose of colistin might be associated with higher risk of AKI. The risk factors of colistin-associated AKI need future larger studies to identify.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC01

The exploration of patients with planned extubation
計畫性拔管病人的探討

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The Exploration of Patients with Unplanned Extubation—the predictive factors of re-intubation and mortality

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Purpose: In the care of critically ill patients, liberation from mechanical ventilation (MV) is an essential and universal element. Our study is to exam the outcome of PE and predictors of weaning failure (re-intubation within 72 hours) and hospital mortality in patients with planned extubation (PE).
Materials and Methods: We reviewed the medical records of patients (n=1771) who experienced PE in intensive care units (ICUs) from 1 January, 2019 to 31 Dec, 2019 in a medical center in south Taiwan. The baseline data before and after extubation, length of stays, mortality and expenditure at hospital discharge were collected to compare between each group.
Results: The overall weaning rate was 95.8 % (1696/1771) and the in-hospital mortality rate was 7.5% (132/1771). The weaning failure group showed significantly higher ICU and hospital mortality rate (6.7% vs. 2.0% and 32.0% vs. 6.4%), longer ICU and hospital stays (18.8 vs. 8.1 and 46.2 vs. 25.2 days) and higher hospital costs (46.2 vs. 25.2 x 10^4 New Taiwan Dollars) as compared with the weaning success group (p all <0.05). Those who expired during hospitalization also had prolong stays on ICU and hospital (16.4 vs. 8.0 and 39.9 vs. 25.0 day). After multi-variate analysis, some predictive factors of weaning failure included: intubation due to post operation [Odds Ratio (OR), 0.481], PaO_2/FiO_2 (P/F ratio) after extubation (OR, 0.993) and maximal expiratory pressure (MEP) before extubation (OR, 0.993). The predictors of hospital mortality included: medical patients (OR, 2.937), weaning failure (OR,13.119), albumin (OR, 0.333) and renal comorbility (uremia) (OR, 3.295).
Conclusions: Our study presented that weaning failure was associated with a significantly poor prognosis as higher mortality rate and increased hospital expenditure. Surgical patients, higher P/F ratio after extubation and higher MEP predicted weaning success. Mortality predictors included: medical patients, weaning failure, lower albumin and patients with uremia. To facilitate the optimal management and the accreditation of medical care quality of MV patients, we have to focus on those prognostic factors to prevent unnecessary expenditure and mortality.
Key words: mechanical ventilation, planned extubation, weaning, outcome, predictors

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC02

72 小時之 NEWS2 及合併 SOFA 在預測敗血症預後和風險分組之應用

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Application Of 72-Hour National Early Warning Score And Incorporation With Sequential Organ Failure Assessment For Predicting Sepsis Outcome And Risk Stratification

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Purpose: We investigated the best timing for using the National Early Warning Score (NEWS) 2 for predicting sepsis outcome and whether combining the NEWS2 and the Sequential Organ Failure Assessment (SOFA) is applicable for mortality risk stratification in intensive care unit (ICU) patients with severe sepsis.
Materials and Methods: All adult patients who met the Third International Consensus Definitions for Sepsis and Septic Shock criteria between August 2013 and January 2017, who did not die within 3 days of ICU admission, and had complete clinical parameters were enrolled. The primary outcomes were the 7-, 14-, 21-, and 28-day mortality.
Results: We included 699 consecutive adult patients. The 72-hour NEWS2 had good discrimination for predicting 7-, 14-, 21-, and 28-day mortality (AUC: 0.780, 0.724, 0.700, and 0.667, respectively) and was not inferior to the SOFA (AUC: 0.740, 0.680, 0.684, 0.677). With the new combined NESO tool, the hazard ratio was 1.854 (1.203–2.950) for the intermediate-risk and 6.810 (3.927–11.811) for the high-risk relative to the low-risk group.
Conclusions: The 72-hour NEWS2 was non-inferior to the admission-SOFA or day-3 SOFA for predicting sepsis outcomes. The NESO tool is useful for 7-, 14-, 21-, and 28-day mortality risk stratification in patients with severe sepsis.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC03

運用超保護性通氣策略及靜脈靜脈葉克膜治療高劑量鈣離子通道阻斷劑中毒併多重器官衰竭

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Ultra-Protective Ventilation With Venovenous Extracorporeal Membrane Oxygenation Support For Prolonged Extremely High-Level Calcium Channel Blocker Intoxication

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Abstract

Herein, we describe a 58-year-old woman presented with hypotension lasting one day after taking 40 amlodipine tabs. Upon transfer to our hospital, a confused status with blood pressure of 106/67 mm Hg; heart rate of 94 beats/min; respiratory rate of 16 breaths/min; and pulse oximetry of 90% under oxygen mask, norepinephrine, and vasopressin infusion were noted. Blood sampling showed metabolic acidosis and a high concentration of amlodipine (303 ng/mL).

Resuscitation with saline, inotropic agents, glucagon bolus and insulin infusion was started. Her SVRI was extremely low (556 dynes/sec/cm^{-5}/m^2) despite increasing the insulin dose to 10 units/kg/hour. Lipophilic emulsion (750 mL) was administered for refractory shock; however, oliguria with frank pulmonary edema developed. She was then intubated and CVVH was started; however, her hypoxemia and shock progressed and vv-ECMO support was initiated on the 7^{th} day of intoxication. Ultra-protective ventilation (UPV) with fixed low driving pressure (10 cm-H_2O) was started: PEEP of 10 cm H_2O; RR of 10-20/min with the Vt limited to 6 mL/kg of ideal body weight and FiO_2 of 40%. The sweep gas and blood flow were titrated to maintain a partial arterial CO_2 pressure of 30–35 mmHg and arterial O_2 pressure of 50-80 mmHg. Even she experienced one episode of propofol infusion syndrome and hospital-acquired pneumonia, the vv-ECMO, hemodialysis and ventilator were successfully discontinued after 30 days and she was discharged with totally independent status.

To our knowledge, this is the first report of using an UPV strategy with vv-ECMO to minimize the VILI in a case with prolonged CCB intoxication.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC04

身體質量指數對不同改良 NUTRIC 分數之敗血症病患存活率之影響

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Impact of Body Mass Index on Survival of Septic Patients with Different Modified NUTRIC Score

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Background: Sepsis is a life-threatening condition, and outcome of septic patients are associated with their nutrition status. The Nutrition Risk in the Critically Ill (NUTRIC) score is verified for nutrition evaluation for critical patients. Body Mass Index (BMI) is also commonly used to indicate nutrition status for general population. However, previous studies showed controversial results of sepsis outcome among different BMI groups. To examine how nutrition affects the survival of septic patients, this study analyzes impact of BMI and modified NUTRIC (mNUTRIC) score on survival of septic patients.

Methods: This study was a retrospective cohort study. Data were extracted form 799 septic patients who were admitted to medical intensive care unit (MICU). The mNUTRIC score greater than or equal to 6were allocated to high mNUTRIC score group (n=513), and those less than or equal to 5 were allocated to low mNUTRIC score group (n=285). According to WHO criteria, BMI <18.5 was underweight (n=149), 18.5<=BMI<25 was normal weight (n=405), and BMI>=25 was overweight (n=245). The outcome measures were mortality, length of stay, ICU days and survival curve of 90-day mortality. We used logic regression analysis to examine risk factors of mortality. Besides, we also analyzed cytokine and biomarkers from 165 participants.

Results: Septic patients with low mNUTRIC scores had higher 90-day survival than the high mNUTRIC score group (63.9% vs. 54.9%, p=0.002). The results were consistent in subgroup analysis of underweight (70.8% vs. 54.2%, p=0.005).However, the overweight (66.2% vs. 55.2%, p=0.059) only showed tendency. 90-day survival of the underweight group with low mNUTRIC was significantly better than the normal weight group with low mNUTRIC (70.8% vs, 58.3%, p=0.048), whereas such difference didn't exist in high mNUTRIC group. In regression model analysis of low mNUTRIC group, cancer significantly increased nearly 4 times the mortality (odd ratio (OR)=3.921, p<0.001), whereas underweight (OR=0.557, p=0.082) and HbA1C (OR=0.792, p=0.078) had a trend of decrease in mortality. In biological analysis of low mNUTRIC groups, the normal weight with low mNUTRICsignificantly had the lowest HLA-DR on day1 (Underweight/normal weight/overweight: 94.3 vs. 82.1 vs. 94.3, p=0.007) and day 3 (91.8 vs. 91.0 vs. 93.2, p=0.047).

Conclusions: Among septic patients with low mNUTRIC scores, normal weight patients had higher mortality compared to underweight ones. Cancer was an independent risk factor associated with mortality. Underweight and HbA1c tend to be protective factors. The HLA-DR were the lowest in the high mortality group. Besides, among septic patients with normal weight, mNUTRIC score was not an effective evaluation tool to predict mortality.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC05

分節嗜中性球與單核球比例的變化量為加護病房嚴重肺炎病患28天死亡率的良好預測工具

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The dynamic segmented neutrophil-to monocyte ratio is a good predictor for 28-day mortality in patients with severe pneumonia admitted to intensive care unit

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Background: Inpatients with pneumonia and needing intensive care have a high mortality rate. Although there are many scoring systems and markers that may help clinicians to predict the patient's outcome, they are usually complex to use and sometimes clinicians may miss some information to fulfill the scoring system calculation. Segmented neutrophil-to monocyte ratio (SeMo) has been proposed recently and we found that dynamic SeMo [SeMo(Day3-Day1)] was associated with outcomes of septic patients admitted to intensive care unit (ICU). In this study, we thought to determine the relationship between dynamic SeMo and mortality in patients with severe pneumonia admitted to ICU.

Materials and Method: This post hoc analysis enrolled adult patients with severe pneumonia and in need of ICU admission. Baseline characteristics and scoring systems, such as sequential organ failure assessment (SOFA) score, qSOFA, pneumonia severity index (PSI) score, Charlson comorbidity index, CURB-65 score, APACHE II score were analyzed. SeMo ratio on admission day1 and day3, and dynamic SeMo ratio (SeMo(day3-day1)) were calculated. The relationship between dynamic SeMo ratio and 28-day mortality were also analyzed.

Result: A total of 456 patients with severe pneumonia admitted to ICU were enrolled in the study, with 357(78.3%) survived. Significant differences in comorbidities were found between survivors and non-survivors, such as cancer (18.5% v.s. 37.4%, P<0.001), liver cirrhosis (4.8% v.s 10.1%, P=0.046) and chronic kidney disease (29.9% v.s 19.2%, P=0.034), respectively. There were significant differences between groups in Charlson index [2.0(1.0-2.0) v.s 2.0(2.0-6.0), P=0.001], SOFA score(day1) [8.0(6.0-11.0) v.s 10.5(7.0-14.0), P=0.007], O_2 index(day 1) [6.9(3.9-14.3) v.s 6.1(3.2-12.6), P=0.015], SeMo(day3) [17.8(11.7-29.4) v.s 22.7(12.1-48.0), P=0.003] and dynamic SeMo [-0.8(-14.4-8.7) v.s. 0.4(-6.6-15.6), P=0.014], respectively. Multi-variable analysis of the odds ratio between dynamic SeMo≥7 and <7 groups revealed significant difference in mortality [OR: 2.843(1.691-4.778), P<0.001], and Kaplan-Meier plot showed separated curves (log-rank P<0.001).

Conclusion: Dynamic SeMo may be a simple and good predictor for 28-day mortality in patients with severe pneumonia that admitted to ICU.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC06

運用尖峰血糖及糖尿病狀態預測重症敗血症之預後

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Association of peak glucose range and diabetes mellitus status with mortality risk in critically ill septic patients

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Background
We evaluated whether peak glucose range or diabetes mellitus (DM) status was associated with mortality in septic patients admitted to the medical intensive care unit (ICU).
Methods
This retrospective study enrolled consecutive septic patients, including a subpopulation of 148 patients with immune profiles.
Results
The 722 septic patients were analyzed according to each of six combinations (6-group tool), when stratified by categories of DM status (DM+: n=386, DM-: n=336) and peak glucose level (3-group tool)(P1 [n=121]: ≤ 140 mg/dL, P2 [n=262]: 141 - 220 mg/dL, P3 (n=339): >220 mg/dL) in the first 3 days. The DM group had lower crude and adjusted hazard ratios (HRs) for 7-day and 14-day mortality compared to non-DM patients, although the 28-day and 90-day adjusted HRs were comparable. The P3 group had a lower human leukocyte-antigen-D related (HLA-DR) expression on day 3 and a higher mortality (14-day and 90-day) than that in the P1 and P2 groups. The 6-group tool discriminated mortalities and HRs (crude and adjusted) (7-day, 14-day, 28-day, and 90-day). Kaplan–Meier survival curves and Cox regression revealed the worst 90-day survival in non-DM patients with P3 peak glucose level (DM-, P3) among 6 groups.The 3-group tool and 6 group-tool were useful for predicting 90-day mortality in patients without DM (both p<0.001 in logistic regression and Cox regression). Mortality was possibly associated with lower HLA-DR expression and relatively higher Sequential Organ Failure Assessment (SOFA) scores among the six groups.
Conclusions
Peak glucose level and diabetes status can be used as easy adjunctive tools for mortality risk stratification in critically ill septic patients.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC07

運用糖化血色素及尖峰血糖預測糖尿病重症敗血症之預後:一回溯性多醫學中心研究

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Application of glycated hemoglobin and peak glucose level in mortality risk stratification for critically ill sepsis patients with diabetes mellitus: a retrospective multicenter cohort study

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Background
We evaluated whether glycated hemoglobin (HbA1c) level and/or peak glucose level in the first three days post-admission were associated with mortality in sepsis patients with diabetes mellitus (DM) admitted to the intensive care unit (ICU).
Methods
This retrospective, observational, multicenter cohort study evaluated critically ill diabetic patients with sepsis admitted between 2012 and 2017.
Results
The 15887 sepsis patients were analyzed according to the following six combinations, stratified by HbA1c level (L [n=15303]: HbA1c≤7, H [n=584]: HbA1c>7) and peak glucose level (P1 [n=1002]:<140 mg/dL, P2 [n=1751]: 141–220 mg/dL, P3 (n=2660): >220 mg/dL) in the first three days; (A [n=977]: L+P1, B [n=1683]: L+P2, C [n=2526]: L+P3, D [n=25]: H+P1, E [n=68]: H+ P2, F [n=134]: H+P3).
The HbA1c level and/or peak glucose level in the first three days post-ICU admission were associated with differences in mortality rates (28-day mortality: L [16.6%], H [19.9%], p=0.039; P1 [16.4%], P2 [10.3%], P3 [15.1%], p<0.01; A [16.4%], B [10.3%], C [14.7%], D [16.0%], E [10.3%], F [23.1%], p<0.001). The underlying diabetes complications severity index (DCSI) or sequential organ failure assessment (SOFA) scores were different between or among groups. Both the SOFA and DCSI scores had a positive crude hazard ratio (HR) (28-day mortality: HR, 1.264 [95% Confidence Interval (CI), 1.22-1.31] and 1.03 [1.01-1.06], respectively) for predicting 28-day mortality and 90-day mortality. Patients with peak glucose levels between 141 and 220 mg/dL in the first three days had better survival (multivariable logistic regression for 28-day mortality: HR P1=1 (reference), P2=0.679 [95% CI=0.47-0.98], P3=0.910 [0.66-1.25]) after adjusting for age, sex, SOFA, and DCSI. Kaplan–Meier survival curves and the Cox proportional hazard model showed different mortality rates between and among groups
Conclusions
Both HbA1c and the peak glucose levels, and their combination are useful for mortality risk stratification in critically ill diabetic patients with sepsis.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC08

無阻塞性冠狀動脈的心肌梗塞－A 型胸腺瘤引起非 ST 上升型心肌梗塞之病例報告

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Myocardial infarction with non-obstructive coronary arteries –A case report of non-ST-segment elevation myocardial infarction due to a type-A thymoma

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Introduction: Myocardial infarction with non-obstructive coronary arteries (MINOCA) has become an increasingly recognized subgroup in patients with acute myocardial infarction (AMI), with a recent cohort study reporting a prevalence of 8.8% out of all AMI cases. We reported a patient presenting with non-ST-segment elevation myocardial infarction (NSTEMI) due to an incidental anterior mediastinal mass.

Case Presentation: An 80-year-old woman presented to our emergency department with the chief complaint of progressive shortness of breath associated with retrosternal chest pain for one day. An anterior mediastinal mass was observed upon computerized tomography (CT) angiogram of the chest. An acute episode of recurrent severe chest pain was found in chest ward and was diagnosed as NSTEMI. Emergent cardiac catheterization was performed because of unstable vital signs, yet results showed no evidence of atherosclerotic changes in the major coronary arteries, compatible with the diagnosis of MINOCA. The mediastinal mass was later confirmed as type A thymoma upon CT-guided biopsy.

Conclusions: This case illustrates a rare presentation of a thymoma resulting in myocardial infarction with unobstructed coronary arteries. We highlight the fact that mediastinal neoplasms may masquerade as acute coronary events, especially if the mass lesion closely abuts relevant coronary structures. We also call attention to the importance of increased awareness of MINOCA, and for the need of additional studies to address potential etiologies and management in such cases.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC09

馬偕醫院治療嚴重低血氧病人的呼吸器策略與拯救療法

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Setting the pace: The mechanical ventilation strategy and rescue therapies for refractory hypoxemia patients at Mackay Memorial Hospital

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Acute respiratory distress syndrome (ARDS) is the inflammatory process involving the lungs that induce non-cardiogenic pulmonary edema. The clinicopathological features included the injury to alveolar-capillary barrier of the lungs, surfactant dysfunction, activation of the immune systems and dysregulation of blood clotting. The application of PEEP is a prerequisite in mechanical ventilation of ARDS patients. However, how much PEEP is adequate remains extremely variable. We proposes the survey of the quasi-static respiratory system pressure-volume (P/V) curve to evaluate the recruitment potential of patient's lung, therefore to individualize setting of initial PEEP in patients with ARDS. The presence of lower inflection point (LIP) on the lung P/V curve indicates the pressure at which to prevent alveolar re-collapse because it is the point of significant compliance change. Once determined, PEEP at LIP + 2 cmH2O combined with low tidal volume is used to provide lung volume recruitment and avoid overdistention.

Another approach is to maintain patients spontaneous breath to induce lung recruitment and reduce global stress/strain. The potential benefits of airway pressure release ventilation (APRV) include: 1.better patient-ventilator synchrony ; 2.improvement in ventilation/perfusion matching; 3. a potential decrease in sedation, analgesia and neuromuscular blockade. In our protocol, when patients' condition fulfills the criteria of moderate or (above) degree of ARDS, whether of maintaining spontaneous breathing is open for clinician to choose APRV first or perform P/V curve survey. In patients were assigned for P/V curve measurement, if there was the presence of LIP (recruitable) , patients would be managed by PEEP titration, prone positioning and optional recruitment maneuver. In patients who were not "recruitable " , inhaled vessels dilators may be tried before extracorporeal membrane oxygenation (ECMO) was available. After initial stable condition was achieved, right ventricle protection would be considered for avoiding acute cor pulmonale. We would try to minimize lung stress by limiting plateau pressure< 25-28 cmH2O and driving pressure < 18cmH2O. Artial carbon dioxide concentration was strictly maintained below 60mmHg.Prone positioning is also for this purpose. Patients with the most severe form ARDS have mortality rates exceeding 50% despite optimal supportive care provided. ECMO was considered as the last resort. Because the late crossover may be futile, the decision to start ECMO should be evaluated early. In our protocol, all managements can be completed within 8-24 hours before they were thought to be ineffective. ECMO was a option for ultra-protective low tidal volume ventilation In summary, our protocol offered a structured, timely and resource saving approach for ARDS. Implementing this protocol-based management of severe ARDS has been regarded as feasible and safe practice. It offers a convenient, flexible, appropriate strategy for individualized ventilation setting.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC10

『RALE』CXR 評分系統在急性呼吸窘迫症候群嚴重度之應用

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The Radiographic Assessment of Lung Edema (RALE) Scores are Associated with Clinical Outcomes in Patients with ARDS

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Purpose: Despite the improvement of clinical care and treatment, the mortality of acute respiratory distress syndrome (ARDS) remains high. There is no accurate, non-invasive measurement to estimate the degree of pulmonary edema on chest radiograph and clinical severity in ARDS**.** The Radiographic Assessment of Lung Edema (RALE) score has been proposed to evaluate the extent and density of alveolar opacities on chest radiographs in sepsis patients with ARDS. We want to assess whether RALE score are associated with clinical outcomes of patients with ARDS.

Materials and methods: All consecutive patients with age ≥18 years and ARDS as defined by American-European Consensus Conference (AECC), admitting at Taipei Veterans General Hospital between 2007 and 2011, were enrolled. To calculate RALE scores, each radiographic was divided into 4 quadrants. Each quadrant was scored for the extent of consolidation (0–4) and density of opacification (1–3). The product of the consolidation and density scores for each of the four quadrants was summed. RALE was scored by two independent reviewers.

Result: 48 patients were enrolled in the retrospective study. Agreement between these two independent reviewers for RALE scores was excellent (intraclass correlation coefficient=0.96, 95% CI: 0.95–0.97). 28-day ventilator free days were significantly lower in patients with higher RALE scores at day 2 (p=0.033), day 7 (p=0.014) and day 14 (p=0.001). Patients with higher RALE scores at day 2(p=0.043), day 7(p=0.012) had significantly lower ICU free days. The RALE scores at day 2 (p=0.06), day 7 (p=0.008) and day 14 (p=0.024) were significantly higher in ARDS patients died in the hospital compared to those who survived.

Conclusion: The RALE scores can be used to assess the severity of ARDS, and is associated with clinical outcomes.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC11

流感重症患者的臨床特徵及影響預後的危險因子

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Clinical characteristics and predictors of mortality in patients with severe complicated influenza infection

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Purpose: Patients with influenza infection may complicate with pneumonia or acute respiratory distress syndrome(ARDS), associated with high mortality. The use of ECMO is a successful rescue treatment for ARDS. However, some of the patients with ARDS under ECMO support died of infectious complications leading to multiple organ failure. The aim of this study was investigate risk factors affecting clinical outcome in severe complicated influenza infection.
Materials and Methods: We retrospectively reviewed medical records of adult patients with laboratory-confirmed severe influenza infection from January 2006 to May 2016 at the Kaohsiung Veterans General Hospital in Taiwan. Patients were excluded if no endotracheal tube intubation and mechanically ventilation or no use of non-invasive positive ventilation or did not have any one of organ dysfunction.
Results: We found severe complicated influenza patients, who presented with ARDS(P: 0.004, OR: 8.054, 95% CI: 1.975-32.855), high APACHE II score(P: 0.008, OR: 1.102, 95% CI: 1.025-1.184), or high PEEP(P:0.008, OR: 1.259, 95% CI: 1.061-1.493) had a risk to receive ECMO support. Patients under ECMO support had longer ventilator days(P: 0.038) and ICU stay days(P: 0.001). Influenza A(P: 0.037, OR: 0.105, 95% CI: 0.013-0.876) and multiple organ failure (P: 0.007, OR: 0.056, 95% CI: 0.007-0.457) were significantly associated with high mortality rate in patient with severe complicated influenza infection.
Conclusions: We identified clinical predictors of mortality and tendency to use ECMO in severe complicated influenza patients. Influenza A and multiple organ failure were associated with higher mortality rate.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC12

一個 COVID-19 患者困難插管的窘境: 病例報告和文獻回顧

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Dilemma of difficult airway management in a patient with COVID-19: Literature review and case report

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Abstract: Aerosol and fomite transmission of SARS-CoV-2 is possible, since the virus can remain infectious in aerosols for hours. The dangerous situation was notable especially during the procedure of intubation and extubation of patients with COVID-19. However, many modality for difficult airway management were not suitable during the pandemic. Herein, we report the dilemma and experience of difficult airway management in a patient with COVID-19.

Case report: A 63-year-old man traveled to Turkey between March 4 to March 13. He was quarantined to our airborne infection isolation rooms by Taiwan Centers for Disease Control (TCDC) guidance because of close contact with COVID-19 confirmed cases. The patient tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time reverse-transcriptase-polymerase-chain-reaction (rRT-PCR) on oropharyngeal swab after admission. His body mass index is 29 and had a short neck. The patient had been well until 4 days after admission. He then presented with fever off and on, fatigue, and malaise. Dyspnea progressed rapidly despite with nonrebreather oxygen mask support on day10. Chest radiography and arterial blood gas confirmed acute respiratory distress syndrome. He was tried intubated by an experienced anesthesiologist with full personal protective equipment including N95 mask with face shield. Rapid sequence intubation was performed with video assisted laryngoscope and avoidance of Ambu bagging for possible aerosol spreading. However, intubation attempts were failed due to anatomical difficult airway accompanied by severe laryngeal edema. During 4 times failed attempt, each hypoxia period has been partially corrected using laryngeal mask to support oxygen temporarily. Laryngeal mask airway (LMA) were instituted for bridging until further airway management established (tracheal intubation or tracheostomy). Finally, we decided to get Fiber-Optic Bronchoscope for assistance of intubation, although it was not suggested by guideline for intubation in COVID19 pandemic for fear of aerosol producing during the procedure. Due to severe laryngeal edema, and severe hypoxemia in this patients with LMA in situ, a 6.5-mm ID endotracheal tube was then inserted via nose with Fiber-Optic Bronchoscope guidance successfully.

Conclusions: We must prepare well in advance for difficulties during tracheal intubation and extubation. Supraglottic airway device can be used for bridging and flexible bronchoscope-assisted intubation may be helpful for difficult airway management in patients with COVID-19.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC13

長期使用人工呼吸器且成功脫離呼吸器病患的長期存活分析

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The long-term survival of successfully weaned prolonged mechanical ventilation patients

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Background: Over six years, five hundred and seventy-four patients were admitted to the respiratory care center. Three hundred and ninety-one patients were successfully weaned from the ventilator. How is the long-term outcome of these successfully weaned prolonged mechanical ventilation patients? We will explore this issue in depth in this article.

Methods: We analyzed retrospective data from successfully weaned prolonged mechanical ventilation patients to investigate the clinical variables, discharged status, long-term survival, the cause of death, end-of-life decisions.

Results: The factors between patients who died in the ward and those who survived ≥1 year revealed the poorer survival of patients who died in the ward was due to a higher percentage of end-stage renal disease comorbidity, a higher percentage of malignant comorbidity, higher percentage of ≥ four comorbidities and a higher percentage of signed do-not-resuscitate / do-not-intubate orders. The factors between patients who survived <1 year and those who survived ≥1 year revealed the poorer survival of patients who survived <1 year was due to older age, a higher percentage of signed do-not-resuscitate / do-not-intubate orders.

Conclusion: The end-of-life decision is one of the major influence factors of long-term survival of successfully weaned prolonged mechanical ventilation patients.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC14

敗血症病患合併早期癌症之死亡率並不高於無癌症之敗血症病患

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The survival of septic patients with early stage cancer was not inferior to septic patients without cancer

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Objectives. We aimed to determine whether survival of septic patients with cancer are worse than patients without cancer. We also investigated the survival of septic patients with early stage cancer and late stage cancer.
Methods. This study enrolled consecutive 799 adult patients with sepsis admitted to medical intensive care units in a tertiary referral hospital. 23 patients were excluded due to re-admission and 17 patients with hematologic cancer were excluded. Survival rate (7-day, ICU, and hospital mortality) were further analyzed on septic patients with early stage cancer, late stage cancer and septic patients without cancer.

Results. Of the 776 septic patients in the study, 444 (57.2 %) patients survived. 186 (24.0 %) septic patients presented with cancer disease and 17 patients with hematologic cancer were excluded. 169 septic patients with solid cancer were divided into two groups: earlystage cancer(n=57) and late stage cancer(n=112). The survival of septic patients with solidcancer had worse outcome than septic patients without cancer disease. (7 days mortality: 19.5% vs. 10.3%, p=0.001, ICU mortality: 36.1% vs. 23.4%, p=0.001, and hospital mortality: 61.5% vs 36.6%, p<0.001) However, the survival of septic patients with earlystage cancer was not inferior to septic patient without cancer. (7 days mortality: 10.5% vs. 10.3%, p>0.05, ICU mortality: 24.6% vs. 23.4%, p>0.05, and hospital mortality: 47.4% vs 36.6%, p>0.05)
Conclusions. Septic patients with cancer disease had higher mortality compared to patients without cancer. However, we found the survival of septic patients with earlystage cancer was not inferior to septic patients without cancer.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC15

以血球分型及生化數值變化探討 COVID-19 患者產生急性呼吸窘迫之危險因子

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Dynamic laboratory data and leukocyte differential count ratios for acute respiratory distress syndrome (ARDS) development risk in patients with COVID-19

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Background

COVID 19 caused by SARS-CoV-2 is a pandemic disease, which lead to acute respiratory distress syndrome and mortality. We thought to determine whether dynamic laboratory data and serial leukocyte differential count ratios be useful for predicting ARDS development in patients with COVID-19.

Methods

This prospective observational study analyzed data from consecutive COVID-19 infected patients between March 2020 and April 2020 at Kaohsiung Chang Gung Memorial Hospital, a tertiary hospital in Southern Taiwan. COVID-19 was confirmed by reverse-transcriptase–polymerase-chain-reaction assays for SARS-CoV-2 via throat or nasal swab. The day after diagnosis was set as day 1, and all patients received serial laboratory data including leukocyte differential count ratios and viral load on day 1, 4, 8, 12 and 16. We used one sample t test to examine the difference between ARDS and non-ARDS patients.

Results

Nine patients were enrolled for study, and one (11.1%) of nine was diagnosed ARDS on day 7. The C-reactive protein (ARDS: 82.99 vs non-ARDS: 11, p<0.001), Lactate dehydrogenase (390 vs 177.5, p<0.001), NLR (3.43 vs 1.57, p<0.001) and MLR (0.44 vs. 0.2, p<0.001) were significantly elevated on day 4 in ARDS patient. The viral load of SARS-CoV2 isolated from ARDS patient was fluctuated during the following period, and there were no difference between those of ARDS and non-ARDS patients.

Conclusions

In addition to elevated CRP and LDH, both segmented neutrophil to lymphocyte ratio and monocyte to lymphocyte ratio on day 4 after disease onset may be predictors for ARDS development in patients with COVID-19 infection.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC16

一位呼吸器患者產生氣縱膈合併心臟壓迫：電腦斷層下扁平的心臟

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Pneumomediastinum with cardiac compression in a mechanically ventilated patient: radiographic finding of heart flattening on CT scan

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Purpose: Pneumomediastinum can result from mechanical ventilation-related barotrauma. In severe case, it may further lead to cardiac compression that is difficult to be detected through plain chest radiography. Here, we present a case of pneumomediastinum with radiological finding of heart flattening on chest CT scan.

Case Report: A previously healthy 51-year-old woman presented with fever and productive cough for two weeks. She received intubation and mechanical ventilation for hypoxic respiratory failure. Subsequently, she developed pneumothrox and received left-side tube thoracostomy but her clinical condition deteriorated with tachycardia. Chest plain film disclosed a continuous diaphragm sign, indicating pneumomediastinum. A chest CT demonstrated bilateral pneumothorax, severe pneumomediastinum with cardiac compression, resulting in flattening of the heart contour, and air dissection along the bronchovascular sheath in the perihilar area. Ventilator setting was adjusted to pressure-controlled mode(24cmH2O) with zero PEEP and additional right-side tube thoracostomy was performed. Her tachycardia subsided gradually. Five days later, the CT scan revealed that the pneumomediastinum resolved and the cardiac contour returned to a normal shape. Finally, she was weaned from mechanical ventilation and discharged six weeks after presentation. A follow-up chest radiograph before discharge showed no continuous diaphragm sign.

Discussion: The first important finding in our case was that the CT scan demonstrated an image of pneumomediastinum with cardiac compression and heart flattening, which indicated the necessity for immediate decompression. The second finding was that there was air dissection along the bronchovascular sheath, suggesting barotrauma with air migrating back to the mediastinum, which is known as the Macklin effect. Notably, our case did not receive decompressive procedure directing to pneumomediastinum, the pre-tamponade condition resolved following chest tube thoracostomy for right-side pneumothorax. However, direct decompressive intervention for tension pneumomediastinum should be considered in patients with cardiac compression and hemodynamic instability.

Conclusions: In mechanically ventilated patients with barotrauma, pneumomediastinum should always be suspected and evaluated for cardiac compression, which warrant early management for successful resolution.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC17

預測嚴重社區型肺炎病患臨床預後的臨床預測因子分析

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Clinical prediction rules for predicting clinical outcomes in patients with severe community acquired pneumonia

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Purpose: This study aim to survey which clinical prediction rule would be the independent factor for predicting clinical outcomes in patients with severe community acquired pneumonia

Materials and Methods: We prospectively enrolled patients with severe CAP in a multicenter setting. Clinical prediction rules for pneumonia, such as Charlson comorbidity index, pneumonia severity index, Curb-65 score, APACHE II score, SOFA score, qSOFA score as well as other clinical factors were calculated and recorded. Clinical outcomes such mortality status, treatment outcome, and antibiotics effectiveness were addressed after patient discharged. We use ROC curve method and multivariate logistic regression analysis to see which scoring data will be the independent factor for predicting clinical outcomes.

Results: In this study, we enrolled 815 patients with severe pneumonia. We found that 137 patients were non-survivors and morality rate was 16.8%. We also found that high CCI sore, PSI score, Curb-65 score, Apache II score and female gender, bacteremia status had higher mortality rate. High CCI sore, PSI score, Curb-65 score, Apache II score and female gender also had higher opportunity for treatment failure and antibiotics ineffectiveness. By ROC curve analysis, we found that Apache II score had more strength to predict every clinical outcome and had highest AUC value. The cut-off value for predicting mortality is 22.5. We also found that Apache II score is the independent factor for predicting clinical outcomes such as mortality, treatment outcome and antibiotics effectiveness in patients with severe CAP.

Conclusions: In this study, clinical prediction rules as CCI score, Curb-65 score, PSI score, Apache II score, SOFA score and qSOFA sore were effectively predicting clinical outcomes. And we also found that Apache II score is the independent factor for predicting clinical outcomes in patients with severe pneumonia.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC18

高維度呼吸變異和呼吸器脫離的相關分析---一個前瞻性的研究

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Higher order respiratory dynamics correlates with the ventilator weaning outcome – a prospective study

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Abstract

Background: We developed an index called WIN, which quantifies variability of breathes, aimed at improving the accuracy of the traditional indexes.

Method: Patients who have been intubated for >24 hours with mechanical ventilator and able to check the spontaneous breathing test in a medical center were recruited. The volume change per cycle (VEC) was calculated from dividing instantaneous respiratory rate and instantaneous volume exchange from the recorded flow signal of 3 minutes long. The WIN index is defined as the standard deviation of the time series of VEC. The prediction of WIN for successful weaning, defied as free from ventilator ≥48hr, was compared to rapid shallow breathing index (RSBI).

Results: 150 patients were recruited and the 128 patients (85.3%) succeeded ventilator weaning. Among the data before extubation, patient characteristic and respiratory indices were comparable between success and failure group, except patients of failure group had older age (p=0.05) and lower systolic blood pressure (p<0.01). WIN (median with range, 3.25 (0.59-0.73) vs. 2.32 (0.73-6.86), p=0.001) and RSBI (52.0 (13.0-131.0) vs. 59.5 (22.0-240.0), p=0.042) were significant different in success and failure groups, respectively. The area under curve (AUC) of WIN is 0.696, with the confidence interval [0.591, 0.783]. The AUC of RSBI is 0.623, with the confidence interval [0.512, 0.75]. Based on the analysis of the ROC curve, we obtained a cut-off value of the WIN index, which is 2.96 with a sensitivity of 0.541 and specificity of 0.821.

Conclusion: The predictor capability for successful weaning of WIN is higher than RSBI, in terms of AUC.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC19

台灣單一醫學中心於亞急性呼吸照護病房內洗腎對於脫離呼吸器之影響

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The Impact of Renal Replacement Therapy on Prolong Mechanical Ventilation Patients in Subacute Respiratory Care Center-Single Medical Center Experience in Central Taiwan

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Backgrounds: In the subacute respiratory care center (RCC), patients with prolong mechanical ventilation (PMV) have high cost and poor outcome. However, there are limited information about patients with renal replace therapy (RRT) and PMV. Thus, the purpose of this study is to investigate the clinical characteristic, survival and weaning outcome for patients with PMV and RRT.

Material and Methods: We retrospectively screened patients who admitted to RCC of Taichung Veterans General Hospital (TCVGH) during January 2014 to December 2018 and collected clinical data for further study. We further defined RRT patients into two groups: one which already received regular RRT before index admission and the other group belong to RRT initiated during index admission (started in intensive care unit, ICU).

Results: Totally, 1079 patients admitted to RCC were enrolled for analysis. Among these patients, the rate of overall mortality and weaning failure were 13.3% and 39% respectively. Nighty-three patients (8.6%) had RRT and their mean APACHE II score was around 25. Patients under RRT was associated with higher proportion of type 2 diabetes mellitus (T2DM), coronary artery disease (CAD) and chronic kidney disease (CKD) compared with those without RRT. Patients under RRT had higher rate of weaning failure (53.8% vs 37.8%, P=0.006) and mortality (53.8% vs 37.8%, P=0.003) compared with those without RRT. The rate of weaning failure for patients already received regular RRT before index admission and those initiated during index admission (started in ICU) was 49.0% and 59% respectively. The group of RRT initiated during index admission had trend of higher mortality rate (29.5% vs. 16.3%) than those already received RRT before index admission.

Conclusion: Patients admitted to RCC who had PMV and RRT had higher rate of mortality and weaning failure compared with patients without RRT. Also, patients with RRT had higher proportion of T2DM, CAD and CKD. Besides, patients initiated RRT during index admission (in ICU) had trend of higher rate of mortality and weaning failure compared with those already received regular hemodialysis before index admission, though no significant change. The odds ratio(OR) of mortality and weaning failure were 2.149 (95% confidence interval, 0.793-5.823; P=0.132) and 1.505 (95% confidence interval, 0.662-3.421; P=0.330) for patients whose RRT initiated during index admission (started in ICU) compared with patients already under regular RRT before index admission.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC20

台灣單一醫學中心急性呼吸窘迫症候群的流行病學與治療經驗

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Epidemiology, management, and mortality for patients with acute respiratory distress syndrome in intensive care units of a tertiary referral medical center in central Taiwan (TCVGH LUNG SAFE study)

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Background: Acute respiratory distress syndrome (ARDS) is common in intensive care unit (ICU) and often these patients are associated with high mortality. There are substantial progresses, from basic pathophysiology to clinical management of ARDS in the past few decades, however, adherence to current available evidence remains unsatisfactory in real-life practice. It is especially important that epidemiologic data about ARDS in Taiwan is limited. Thus, the purpose of this study is to investigate the incidence, clinical characteristics, modalities of management and outcome of ARDS in a tertiary referral medical center in central Taiwan.

Method: This is a retrospectively analysis of prospective acquired study which was conducted in a tertiary referral hospital in central Taiwan. These data are collected from clinical audit program for quality improvement of critical care. Patients with acute respiratory failure needing invasive mechanical ventilation were screened from October 2018 to September 2019. Those who met the criteria of ARDS by Berlin Definition were included for analysis.

Results: Totally, 1954 patients needing mechanical ventilation admitted ICUs were screened. Among these patients, 351 patients met the criteria of ARDS and eligible for analysis. The incidence of ARDS was 18% (including mild 25.6%, moderate 55.6%, and severe 18.8%, respectively). The overall mortality rate among these patients was 41.6% (mild 32.2%, moderate 45.1% and severe 43.9%, p=0.110). For mechanical ventilation setting, the mean tidal volume was 7.4 ml/kg (mild 7.8, moderate 7.4 and severe 7, p=0.005). The mean plateau pressure was 21.6 cmH_2O (mild 19.8, moderate 21.8 and severe 23.3, p<0.001). The mean driving pressure was 12.6 cmH_2O (mild 12.6, moderate 12.5 and severe 12.8, p=0.883). The overall adherence to low-tidal volume ventilator strategy was 67.5% (mild 62.2%, moderate 66.2% and severe 78.9%, p=0.077). Prone positioning was used in 15.1% in patients with severe ARDS. The most common risk factors of ARDS was pneumonia (74.6%). After multivariate analysis, APACHE II score (OR 1.076, p<0.005), driving pressure (OR 1.112, p=0.039), underlying with malignancy (OR 2.336, p=0.003) and aspiration of gastric content (OR 2.833, p=0.021) were associated to ICU mortality in patients with ARDS.

Conclusion: The incidence of ARDS in patients with respiratory failure was high in the tertiary care center, Taiwan. APACHE II score, driving pressure, underlying with malignancy, and aspiration of gastric content were factors to predict mortality in patients with ARDS. Mortality in patients with moderate ARDS was similar to patients with severe ARDS. Although not significant, adherence to low tidal volume ventilator strategy was better in patients with severe ARDS in this study. Improvement in the ventilator strategy may potential improve mortality in patients with ARDS.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC21

心臟手術後使用非侵入性陽壓呼吸治療惡化吸入性肺炎

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NIPPV associated pneumonia after cardiac surgery

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Purpose: Cardiac surgery usually leads to the deterioration of the respiratory function postoperatively. And the application of noninvasive positive air pressure ventilation (NIPPV) is beneficial to restore lung function more quickly in short term use, especially vital capacity and safety during the execution of respiration therapy. However, NIPPV associated pneumonia after cardiac surgery is not well documented.

Case: A 75 -year-old female was admitted because of persist chest discomfort and shortness of breathing on exercise for a couple of years. Patient had been diagnosed as a case of severe mitral regurgitation caused by ruptured chordae tendineae in the posterior leaflet of the mitral valve by echocardiography. Patient had undergone percutaneous coronary intervention (PCI) with stent deployment for her stenotic LAD lesion one year ago. Therefore, the patient had undergone mitral valve replacement (MVR) with an uneventful postoperative course. The patient was extubated on the second postoperative severe wound pain made the patient breathing shallow, cough ineffectively that resulted in poor ventilation with O_2 saturation down to 90-92% with O_2 mask of FiO_2 10 L/min. A follow up chest x-ray also revealed increased infiltration with small patches in both lungs. Biphasic Intermittent positive air pressure (BIPAP) was required on the 3rd to 6th postoperative days that exaggerate pneumonia on the 7th postoperative day. Frequent chest percussion with vibrating jacket and high flow O_2 nasal cannula inhalation therapy was applied. Cardio-pulmonary rehabilitation in addition to vigorous antibiotics IV were also administered to improve pulmonary hygiene.

Results: Bilateral pneumatic patches on the chest x-ray resolved slowly on 9th postoperative day, and the patient was discharged from the hospital in good condition.

Conclusions: Non-invasive positive pressure ventilation (NIPPV) is used in postoperative patients with aims of improving oxygenation, clearing secretions and to restore lung function more quickly and safely after cardiac surgery. However, if worsening oxygen at 1 hour of therapy and worsening x-ray infiltration 24 hours after onset of therapy, it is better to change NIPPV to high-flow O_2 nasal cannula. Carefully selected patients and use of high flow cannula is necessary to avoid unexpected NIPPV associated pneumonia encountered after cardiac surgery.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC22

多處致命性頸部刀傷穿刺，呼吸道維持評估與外科介入的時機點

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Emergent Airway management of life threatening open penetrating neck injury

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Background: Open penetrating neck injury (PNI) is a relatively uncommon trauma presentation with the potential for significant morbidity and possible mortality. Surgical intubation is considered instead of traditional rapid sequence intubation (RSI) if airway is threatened and the anatomic structures are not preserved. We present a severe open penetrating neck injury (PNI) case with alternative treatment modality.

Case (# 2477775): A 38-year-old female with a past history of ankylosing spondylitis and asthma, was assaulted by a cutting knife that resulted in severe open neck injury on 2018/05/24. Patient was sent to the emergency room of Chung-Shan Medical University Hospital immediately. She developed a hypovolemic shock with massive bleeding and resulted in cardiac arrest on arriving (OHCA). There were six cutting wounds; including one 7cm in length wound over the low chin, one 3cm in length of open wound involved the left anterior wall of middle cervical trachea, 6 cm in length wound over right subclavian area and 1 cm, 3 cm, 4cm in length open wounds over her left upper limb ,respectively. Cardiopulmonary cerebral resuscitation (CPCR) was performed. With blood flooding in the field, air bubbles emanated from the transected tracheal opening and a size of 7.0 endotracheal tube (ETT) was readily inserted through the neck wound via the opening of transected trachea. Return of spontaneous circulation (ROSC) was noticed 30 minutes after CPCR. After surgical repair of the lacerated right subclavian vessels and cutting wounds in sequence, then retrograde stylet -guided endotracheal tube was conducted and followed by the debridement and wound closures of the injured trachea. Patient was send to intensive care unit with clear consciousness (E1M1Vt, E4V5M6). Later patient was discharged from hospital on 2018/06/13.

Conclusion: Patients with open penetrating neck injury (PNI) whose condition was unstable should undergo immediate operative exploration. Endotracheal tube insertion through the open transected trachea is superior to the traditional rapid sequence intubation(RSI) to avoid misplacement endotracheal tube during CPR.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC23

流感肺炎相關急性呼吸窘迫症候群患者使用葉克膜的死亡預測因子

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The predictors of mortality for extracorporeal membrane oxygenation in influenza related acute respiratory distress syndrome patients

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RATIONALE: The extracorporeal membrane oxygenation is one of the rescue therapies for severe gas exchange impairment is severe acute respiratory distress syndrome (ARDS) patients. In the previous studies, the timing of ECMO usage and the severity score are survival predictors in these patients, but the ventilator settings or gas exchange condition are seldom to be evaluated. In this study, we analyze the influenza related ARDS patients who were treated with ECMO, and the purpose is to define the predictive factors of mortality.

METHODS: This is a retrospective observational study which was conducted by Taiwan Severe Influenza Research Consortium (TSIRC) that enrolled subjects admitted to eight tertiary referral centers in Taiwan due to severe complicated influenza between Oct 2015 and March in 2016. All patients who were ARDS and treated with ECMO were included for analysis.

RESULTS: A total of 336 subjects with severe complicated influenza were screened, and 263 subjects met the Berlin definition of ARDS. Totally 53 subjects had been treated with ECMO (veno-venous ECMO: 40; veno-arterial ECMO: 13), and the in-hospital mortality rate was 62.3%. The significant predictive factors for the in-hospital mortality included timing of ECMO usage, APACHE II, pre-ECMO $PaCO_2$, post-ECMO $PaCO_2$, post-ECMO HCO_3, post-ECMO peak airway pressure, and post-ECMO positive end expiratory pressure (PEEP) (*p* value are 0.043, 0.014, 0.034, <0.001, 0.003, 0.022, and 0.045 respectively). In the multivariate Cox regression analysis, the timing of ECMO usage (Hazard ratio: 1.537 [1.047-2.256], p value = 0.028) and post-ECMO $PaCO_2$ (Hazard ratio: 1.182 [1.033-1.353], p value = 0.015) have significant correlation to mortality.

CONCLUSIONS: The timing of ECMO usage and post-ECMO $PaCO_2$ are 2 of most important predictive factors of mortality for influenza pneumonia related ARDS patients with ECMO usage.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC24

秋水仙服用過量導致多重器官衰竭

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Colchicine Overdose Leading to Multi-Organ Failure; A Case Report

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Colchicine is usually a safe drug if taken according to therapeutic recommendations (maximum 1.2mg/day). However, ingesting colchicine that exceeds the recommended amount can cause serious systemic side effects and can even be life-threatening. Here we report a rare case of colchicine overdose caused by inappropriate self-medication. Gastrointestinal symptoms and acute kidney injury developed, and hemodialysis was initiated. Acute respiratory failure and profound shock with acute heart failure were noted, along with hepatitis and pancytopenia. Various modes of treatment were implemented, and the patient had gradually recovered from the multi-organ dysfunction and was eventually discharged. The pharmacology of colchicine, the clinical features associating with overdose, and options for treatment are discussed.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC25

Pendelluft 現象與自發性呼吸力道之正向相關－在一急性呼吸窘迫症候群患者之觀察

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The Positive Correlation between Pendelluft and Breathing Effort in a Case of Severe Acute Respiratory Distress Syndrome

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For patients with moderate to severe acute respiratory distress syndrome (ARDS), sedation and paralysis are often required. Daily interruption of sedation and paralysis is a standard of care in current concept. However, physicians may concern that excessive breathing effort generated by the patients themselves could be harmful. The phenomenon of pendelluft is hypothesized to be associated with such hazards, while the association of pendelluft and breathing effort has not been well established.

Here we report a case of severe acute respiratory distress syndrome who received electrical impedance tomography (EIT) recording with simultaneous esophageal manometry monitoring during daily spontaneous breathing trial. A positive correlation between the volume of pendelluft and the breathing effort, global inhomogeneity (GI) index and the breathing effort were noted.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC26

加護病房中血液系統惡性腫瘤患者的結局及預後因素

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Outcomes and prognostic factors in patients with hematological malignancy admitted to the intensive care unit

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Background: Patients with a hematologic malignancy (HM) have one of the highest mortality rates among cancer patients admitted to the medical intensive care unit (ICU). The objective of this study was to identify outcomes and risk factors predicting the prognosis of critically ill HM patients in the ICU.
Methods and materials: A retrospective observational study was conducted in a tertiary referral hospital in Taiwan for over 40 months (January 1, 2017–April 30, 2020). All adult patients with HM admitted to medical ICU were enrolled. Clinical data upon hospital and ICU admission were collected. Predictors for ICU mortality were evaluated using multivariate analysis.
Results: Totally 233 HM patients met the inclusion criteria. The median age was 59.3 years [Standard deviation (SD) 15.1]. Seventy-six percent of the HM diagnoses were high-grade and 28.7% post-hematopoietic stem cell transplantation (HSCT). Eighty-nine percent of patients required mechanical ventilation (MV). Median Sequential Organ Failure Assessment (SOFA) score at ICU admission was 11 [Interquartile range (IQR) 9-15], median SAPS (Simplified Acute Physiology Score) II was 64 (IQR 51-80), and median Acute Physiology and Chronic Health Evaluation (APACHE) II score was 28 (IQR 23-34). The most common reasons for ICU admission were acute respiratory failure (63.1%) and septic shock (19.7%). ICU and hospital mortalities were 54.1% and 67.8%, respectively. Multivariate analysis revealed that the initiation of renal replacement therapy in ICU (OR 3.88; 95% CI 1.66-9.08) and SOFA scores (OR 1.16; 95% CI 1.03-1.31) were independently associated with ICU mortality.
Conclusions: With better general ICU care, a trend of decreased ICU mortality could be observed. Factors including performance status, disease severity, MV, severe neutropenia, and transplantation status were not predictive for ICU outcome. Initiation of renal replacement therapy in ICU and SOFA score upon ICU admission were independently associated with ICU mortality. This result helps clinicians for triage decisions for a time limit trial for this patient group.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC27

台灣首例 SFTS 病毒引發發熱伴血小板減少綜合症與心肌病變死亡之案例

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First Case of Severe Fever with Thrombocytopenia Syndrome Virus Infection in Taiwan

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Severe fever with thrombocytopenia syndrome (SFTS) is a tickborne infection caused by the SFTS virus (SFTSV, also known as *Huaiyangshan banyangvirus*), which was identified in China in 2009 and afterward in Korea, Japan, and Vietnam. Since then, the number of SFTS cases in East Asia has risen rapidly. In November 2019, a 70-year-old man who lived in northern Taiwan was admitted to the hospital with a 9-day history of high fever, chills, nausea, vomiting, and malaise. At admission, we noted a generalized rash over the trunk and both feet. Laboratory examinations showed that the patient had leukopenia; thrombocytopenia; abnormal prothrombin time; elevated levels of aspartate transaminase, alanine transaminase, creatinine kinase, and C-reactive protein; and diagnostic disseminated intravascular coagulation. Chest radiography and chest computed tomography showed patchy consolidations and ground-glass opacities of both lungs. A few hours after admission, the patient experienced a general tonic–clonic seizure, with worsening consciousness and dyspnea. He was transferred to the intensive care unit for ventilator support. He also received massive blood transfusions for severe thrombocytopenia, active mucosal (oral, nasal, and gastrointestinal tract) bleeding, and disseminated intravascular coagulation. Then the patient, who was originally suspected of having dengue or rickettsial infections, was laboratory confirmed SFTS by Taiwan CDC. Unfortunately, his condition continued to deteriorate progressively. The patient died on day 40 after illness onset as a result of multiorgan dysfunction syndrome and cardiomyopathy, confirmed by the heart biopsy. Thus, the SFTS virus infection should be included in the differential diagnosis of sepsis with liver function impairment and thrombocytopenia.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC28

急性人類免疫缺陷病毒感染出現皮疹，急性肝炎和無菌性腦膜炎一案例報告

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Acute Human Immunodeficiency Virus Infection Presented with Skin Rash, Acute Hepatitis, and Aseptic Meningitis

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Acute or early Human Immunodeficiency Virus (HIV) infection may present as a retroviral syndrome with nonspecific symptoms. Without a high suspicion, the diagnosis could be missed frequently by clinicians. An estimated 10 to 60 percent of patients with acute HIV infection will not experience symptoms. In patients who have acute symptomatic HIV infection, the usual time from HIV exposure to the development of symptoms is about two to four weeks. It had been reported that the most common findings are fever, lymphadenopathy, sore-throat, skin rash, tired feeling, diarrhea, weight loss, and headache. Headache related to acute HIV infection, often described as retroorbital pain exacerbated by eye movement. More serious neurologic manifestations of acute HIV infection, for example of meningitis, have also been reported but are unusual.

We report a case of 23-year-old male without any underlying disease except hearing impairment. He suffered from intermittent fever for one week. At beginning , he got sore-throat and had been to Local Medical Department for help about 10 days ago but in vain. Subsequence of fever occurred since one week ago. Consciousness disturbance, limbs stiffness, poor appetite, general weakness and headache in recent 2 days were noted, so he was brought to our emergency room for help. At there, his GCS showed E4V4M5 and initial vital signs showed blood pressure of 147/72 mmHg and TPR of 39.4/116/20. Physical examination revealed kernig's sign negative, clear breathing sounds, no abdominal tenderness, but skin rash over trunk and limbs. Lab data showed no leukocytosis, no electrolyte imbalance, normal renal function, mild elevated CRP (26.3 mg/L), and abnormal liver function (GPT : 351 U/L : GOT: 245 U/L). Brain CT was arranged and showed mild dilatation of bilateral frontal horns, suspected of mild communicating hydrocephalus. Lumbar puncture was performed and CSF study showed high protein level (439.9 mg/dL), elevated RBC (1133 /uL) and WBC (83 /uL) with lymphocyte predominant (81/uL). Acute aseptic meningitis was impressed and Rocephin and Acyclovir were prescribed, then he was admitted to the intensive care unit (ICU) .

During admission at ICU, Anti HIV 1/2 showed positive and Confirmatory assay revealed inderterminant (only GP41 peptide showed positive). CD4+ lymphocyte count decreased to 171 /uL and CD4+/CD8+ ratio decreased to 0.1. Blood XpertHIV viral load was detected (3,481,715 copies/mL). Blood HBsAg and Anti-HCV all showed negative. Throat secretion and urine Measles virus PCR revealed negative. CSF HSV-PCR, Cryptococcus Ag, MTB PCR, and aerobic culture also showed negative. Triumeq 1 TB QD was prescribed immediately for acute HIV infection.
His Consciousness became clear and liver function improved, then he was transfer to ordinary ward.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC29

呼吸器設定對於體外循環維生系統在流感合併急性呼吸窘迫症候群之影響

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Effect of ventilator settings during venovenous extracorporeal membrane oxygenation on outcomes in influenza-associated acute respiratory distress syndrome

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Purpose: Patients with influenza-associated acute respiratory distress syndrome (ARDS) requiring venovenous extracorporeal membrane oxygenation (vv-ECMO) support have high mortality. However, the optimal settings of mechanical ventilation during vv-ECMO are still uncertain.
Materials and Methods: We retrospectively investigated the association between six-months mortality and variables of mechanical ventilator settings, baseline characteristics and intensive care unit (ICU) management among patients with influenza associated ARDS treated with mechanical ventilation and vv-ECMO support.
Results: A total of 65 patients with influenza-associated ARDS receiving vv-ECMO support were included. Among them, 26 (40%) died within six months. Survivors and non-survivors had similar tidal volume (5.2 vs. 5.4 mL/kg predicted body weight, P=0.89), dynamic driving pressure (15 vs. 15 cm H2O, P=0.51), mechanical power (10.9 vs. 11.2 J/min, P=0.26), and positive end-expiratory pressure (PEEP) (10 vs. 12 cm H2O, P=0.97). In contrast, survivors had a lower respiratory rate setting compared with non-survivors (12 vs. 14 breaths/min, P<0.001). After adjustment for age, severity index and other important confounders, lower respiratory rate of <12 breaths/min during vv-ECMO support still had significant effect on mortality (Adjusted hazard ratio = 3.229, 95% confidence interval, CI =1.226-8.499, P=0.018).
Conclusions: In influenza-associated ARDS receiving vv-ECMO support, we found that a higher respiratory rate setting was associated with higher mortality. Respiratory rate might be a modifiable factor in addition to tidal volume setting during vv-ECMO support.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC30

以人工智慧預測訓練脫離呼吸器與拔管的時機

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Using artificial intelligence to predict the timing of ventilator weaning and extubation

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Purpose: Mechanical ventilation is one of life-sustaining treatments. However, prolonged ventilator use causes a lot of complications including acute lung injury, pulmonary infection and airway injury and also spends a lot of medical expenses. The patient should be liberated from ventilator as soon as possible when mechanical ventilation is not necessary. We use artificial intelligence (AI) to assist physicians in making decisions of ventilator weaning trial and extubation aiming to reduce the duration of ventilator use and ICU stay.

Materials and Methods: During 2016 and 2019, we collected 7,019 patients using ventilator in our ICU. After extraction, transformation, loading and validation, the innumerable data from automatic data transmission of ventilators composes big data. In addition to the patients' vital signs, anthropological and laboratory data, we have integrated more than 20 features to predict the success rate of ventilator weaning trial and extubation at the 11 time points we selected with half an hour intervals. This predicting program of ventilator weaning is already online on the ICU and respiratory therapist's operating system.

Results: In the preliminary data analysis, we compared the data from May to July last year and the same duration this year. The mean duration of ventilator use was reduced from 162 hrs to 142 hrs. The 48-hr ventilator weaning rate was increased from 96.2% to 98.4% and 72-hr ventilator weaning rate from 95.3% to 98.4%. Because each patient spends an average of NT$15,000 per day in ICU and there are about 2,500 patients using ventilator in our hospital each year, we can reduce medical expenses by more than NT$30 million per year in our hospital via decreasing the ventilator days of 0.82 days (20 hrs) per patient.

Conclusions: We use AI to develop a program that can assist critical care physicians in judging that patients can start weaning from mechanical ventilation and extubation. This program can predict the success rate of switching into the next step in ventilator patients. It may reduce the ventilator complications and medical expenditure by decreasing the duration of mechanical ventilation. Especially in the era of the COVID-19 epidemic, critical care resources can be used more efficiently to avoid the collapse of the medical system.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC31

在高手術風險病人以保守性治療氣管裂傷

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Treat tracheal rupture with conservative treatment in high surgical risk patient

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Iatrogenic tracheal rupture is a rare and severe complication of endotracheal tube intubation. Surgical repair is often required for a large rupture. We present a case of 67 year-old woman with long history of heart failure, aortic valve stenosis s/p aortic valve replacement. She was diagnosed tracheal rupture after emergent intubation. Due to hemodynamic unstable, She received conservative treatment instead of surgical repair for a large tracheal rupture. And result a significant improvement at 15th day after intubation.

The treatment standard of tracheal rupture is still uncertain. Therefore, we recommend conservative treatment maybe suitable in cases with high risk of surgical intervention.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC32

通氣比對於需機械通氣之急性呼吸衰竭的預後意義

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Prognostic implication of ventilatory ratios in acute respiratory failure requiring mechanical ventilation

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Introduction: Ventilatory ratio (VR) is a simple surrogate index of pulmonary dead space fraction, which has been shown to be a good outcome predictor in acute respiratory distress syndrome (ARDS). However, the prognostic role of VR in respiratory failure other than ARDS setting remains unclear.
Materials and Methods: This retrospective cohort study included adult patients who newly received invasive mechanical ventilation between October 01, 2014 and May 22, 2017 at the National Taiwan University Hospital in Taiwan. VR on the first day of mechanical ventilation was calculated according to the following formula: [minute ventilation (ml/min) × PaCO2 (mm Hg)] / (predicted body weight × 100 × 37.5). The primary outcome was 30-day mortality. Logistic regression was used to evaluate the association between VR and mortality. Discriminatory power for mortality was determined by the area under the receiver operating characteristic curve (AUROC).
Results: A total of 2854 mechanically ventilated patients were included. The median age was 66 years (interquartile range [IQR], 56-78), 63% were male and 79% were intubated for non-surgical reasons. The median VR and PaO2/FiO2 (P/F) ratio on day 1 were 1.28 (IQR, 1.01-1.68) and 246 (IQR, 148-382), respectively. VR was significantly higher in non-survivors compared with survivors (1.57 vs 1.38, p <0.001). There was a significant association between VR and mortality (Odds ratio [OR], 1.54, 95% CI, 1.36-1.75, p <0.001). The association remained robust after adjusting for P/F ratio (adjusted OR, 1.28, 95% CI, 1.12-1.46, p <0.001). The AUROC for discrimination of mortality was 0.60 (95% CI, 0.58-0.62) for VR and 0.63 (95% CI,0.61-0.65) for P/F ratio.
Conclusions: Initial VR during the acute phase of respiratory failure was well correlated with subsequent outcome and had acceptable discrimination capacity for mortality compared with P/F ratios.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC33

雙腔靜脈導管使用肝素固定對活化部分凝血活酶時間的影響

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The Effect of Heparin Lock of Double Lumen Catheter to Activated Partial Thromboplastin Time.

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Purpose: Heparin lock for double-lumen catheter (DLC) is common procedure to prevent blood clot inducing catheter obstruction. However, small amount heparin leakage from heparin lock would happen but there are only limited data about it. We want to evaluate the effect caused by heparin leakage.
Materials and Methods: We analyzed the data from the patients who received intermittent hemodialysis at Intensive care unit (ICU) of National Taiwan University Hospital, HsinChu branch retrospectively. The analyzed data including the activated partial thromboplastin time (aPTT) after dialysis (Before heparin lick/ 30 minutes / 1 hours/ 2hours / 3 hours/ 4 hours after heparin lock), coagulopathy related complications, and the patency of the DLC during ICU admission.
Results: There were total 14 sets of data from 9 patients included. The heparin lock dosage was pure heparin (5000 IU/mL) 1.5mL/ 1.6mL at each lumen of DLC. The results of followed aPTT showed significant increasing till 3 hours later after heparin lock (*p*-value: 0.000/ 0.000/ 0.001/ 0.012/ 0.141). The peak of aPTT happened at 30 minutes (150 seconds) after heparin lock. Among the 9 patients, 5 patients suffered from gastrointestinal bleeding. For severe coagulopathy, heparin lock dosage was decreased (1.3mL/ 1.4mL) at 3 patients and 9 sets aPTT were followed. After adjusting heparin dosage, the aPTT significant prolongation condition kept till 1 hour after heparin lock only (*p*-value: 0.000/ 0.012/ 0.363/ 0.989/ 0.141) and the peak still happened at 30 minutes after (139.7 seconds). The patency of all the 3 sets DLC was kept till discharge from ICU.
Conclusions: We confirmed that heparin lock will induce coagulopathy and has the risk of GI bleeding. Decreasing heparin lock dosage could decrease duration of coagulopathy but not affect the patency of DLC.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC34

肝膿瘍破裂引發膿胸-案例報告

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Pleural Empyema secondary to Ruptured Liver Abscess–A Case Report and Interesting Image

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Introduction

Parapneumonic effusions and empyema are relatively common complications of pneumonia. Rarely, empyema results from trans-diaphragmatic translocation from a rupture liver abscess. Herein, we report a case of a liver abscess due to *Klebsiella pneumoniae* causing right pleural empyema.

Case presentation

A 74-year-old woman, with a past history of hepatocellular carcinoma, liver cirrhosis, chronic hepatitis C and hypertension, visited the emergency department complained of progressive dyspnea for days. She has general malaise, poor appetite, right flank pain but denied fever, chills, severe cough, diarrhea. Desaturation developed followed by intubation with ventilator. The initial CXR showed right lower lung pneumonia with pleural effusion. The CT revealed right pneumonia, empyema and suspected right subphrenic emphysematous abscess crossing right posterior hemidiaphragm to the right pleural space. Then she was admitted to ICU. The Video-assisted thoracoscopic surgery was done which found right pleural empyema, right lower lung abscess, diaphragm ruptured and much pus trans-diaphragm from liver abscess. The sputum culture and abscess culture yielded *Klebsiella pneumoniae*. After antibiotics treatment and abscess drainage, the conditions got improving. But recurrent hospital-acquired pneumonia developed. Even the interval improvement of hospital-acquired pneumonia after antibiotics treatment, it was difficult of ventilator weaning. Finally, she was transferred to subacute respiratory care center.

Discussion

Patients with a *Klebsiella pneumoniae* liver abscess have often accompanying metastatic complications, most concurrent infections in the lungs. There are rare reports of *Klebsiella pneumoniae* liver abscess, in which pleural empyema is caused through a direct invasion of the thoraces. The rate of *Klebsiella pneumoniae* infection is increased in individuals with impaired host defenses, such as diabetes mellitus, alcoholism, hepatobiliary disease, malignancy, glucocorticoid therapy, and renal failure… Besides, in this case, the liver abscess is hidden behind empyema in CT which might be missed.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC35

以機器學習模型來預測重症病人的住院死亡率

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A Machine Learning Model for Predicting Hospital Mortality in Intensive Care Units

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Purpose: The aim was to establish machine learning model to predict hospital mortality of ventilated patients in the intensive care units (ICU).

Materials and Methods: From January 1, 2019 to May 31, 2019, data from 674 patients who had undergone planned extubation in the ICU at the Chi-Mei Medical Center were used to train (70% dataset) and test(30% dataset) with random forest (RF)machine learning algorithm-one of machine learning algorithms used for supervised learning, this means for learning from labelled data and making predictions based on the learned patterns. RF can be used for both classification and regression tasks. This analysis and evaluation-related parameters were included basic personal information (age, BMI, gender, etc.), on the first day of illness severity (APACHE II), the total number of intubation, the original disease (comorbidity), spontaneous breathing trial (SBT) status and vital signs before and after extubation . The feature variables were 24 clinical risk factors, and the output variable was a prediction of hospital mortality.

Results: According to the results, the survival rate was 93.2%, which medical admission, APACHE II, renal comorbidity, BUN, ICU length,ICU mortality and medical costs, were obviously much lower than the death group ($p < 0.05$). The variable analyses showed that failure was positively associated with APACHE II scores (odds ratio [OR]: 1.099; 95% Confidence Interval [CI]: 1.057–1.114), medical admission (OR: 1.912; 95% CI: 1.047–3.490), b*lood urea nitrogen* (BUN) (OR: 1.012; 95% CI: 1.001–1.023).The overall performance of this RF model with testing dataset was Accuracy: 0.92, Precision: 0.91 and F1: 0.92. The Specificity was 0.97, which is better than any one of the following predictors: APACHE II >21.5: 3.437;(95% CI: 1.802–6.553, $p<0.001$);ventilator hours >144.5: 2.787;(95% CI: 1.498–5.186,$p=0.001$).

Conclusions: The RF performed well when predicting hospital mortality of ventilated patients in ICUs.

Keywords: intensive care unit ;predictor; hospital mortality ; machine learning; random forest

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC36

探索定義急性呼吸窘迫症候群的最佳 PaO_2/FiO_2 比值的分界值

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Cut-offs of PaO_2/FiO_2 Ratios for Defining Acute Respiratory Distress Syndrome

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Purpose: PaO_2/FiO_2 (P/F) ratios are used to define and categorize the severity of acute respiratory distress syndrome (ARDS). However, these cut-off values of P/F ratios were mainly determined by consensus but not high-level evidence. We aimed to evaluate the association between P/F ratios and two key features of ARDS, namely, reduced respiratory compliance and poor ventilator outcome.
Materials and Methods: This retrospective cohort study included adult patients who received mechanical ventilation for ≥12 hours from October 2014 to July 2020 in a medical center in Taipei, Taiwan. The P/F ratio on day 1 of mechanical ventilation (MV) was calculated along with static respiratory compliance. The primary outcome was a composite of death or MV dependent at ICU discharge. Logistic regression was used to evaluate the association between P/F ratios and the composite outcome and risks of having reduced respiratory compliance with different predefined levels.
Results: A total of 4105 mechanically ventilated patients were included and 2760 (67%) of them had static respiratory compliance measured. The median age was 67 years (Interquartile range [IQR], 56-78) and median P/F ratio was 234 mm Hg (IQR, 142-360). At ICU discharge, 1187 (28.9%) were dead and 1653 (40.3%) patients experienced the composite outcome events. Probabilities of the composite outcome at P/F ratios of 400, 300, 200 and 100 mmHg were 35.1%, 36.1%, 38.5% and 53.1%, respectively. The change of probabilities of the composite outcome was significant below the P/F of 200 mmHg (p = 0.002) but not for the P/F of 300 mmHg (p = 0.73). Probabilities of reduced respiratory compliance at P/F ratios of 400, 300, 200 and 100 mmHg were 34.7%, 44.9%, 49.0% and 53.6%, respectively. The change of probabilities of reduced respiratory compliance was significant below the P/F of 300 mmHg (p = 0.004).
Conclusions: A P/F ratio of 300 mmHg was an appropriate cut-off for identifying patients with reduced respiratory compliance, whereas a P/F ratio of 200 mmHg was a better cut-off for both reduced respiratory compliance and poor ventilator outcome.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC37

碳青黴烯類抗藥性鮑氏不動桿菌肺炎重症病人院內死亡危險因子探討

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Predictive factors of hospital mortality in critically ill patients with Carbapenem-resistant *Acinetobacter baumannii* (CRAB) pneumonia

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Purpose: Carbapenem-resistant Acinetobacter baumannii (CRAB) is a common pathogen of pneumonia in the ICU, and is usually associated with high mortality. Although some studies report possible factors affect mortality, limitations such as small sample size or without appropriate adjustment for confounders make it difficult to reach definitive conclusions. The aim of this study was to clarify risk factors influencing hospital mortality in CRAB pneumonia patients in the ICU.
Methods: This multicenter, retrospective study was conducted in three hospitals during 2010-2015 in southern Taiwan. Adult ICU patients with CRAB pneumonia and receiving appropriate antibiotics covering the CRAB isolates for more than 2 days were included. Enrolled patients were followed until death or loss of follow up. Baseline characteristic, clinical, microbiological, laboratory data, and treatments were assessed as risk factors of hospital mortality by univariate and multivariate logistic regressions.
Results: Among the 305 critically ill patients with CRAB pneumonia, the overall ICU mortality rate was 30.8%, hospital mortality rate was 58.4%, and long-term mortality rate was 65.6%. In multivariable analysis, hospital length of stay prior to ICU admission (OR= 1.03, 95% CI= 1.01-1.05, P = 0.001), sequential organ failure assessment (SOFA) score on pneumonia diagnosis (OR= 1.13, 95% CI= 1.04-1.22, P = 0.003), and presence with CRAB bacteremia (OR= 3.67, 95% CI= 1.18-11.42, P = 0.025) were independent predictors of hospital mortality.
Conclusions: The hospital mortality rate almost doubled the ICU mortality rate in ICU patients with CRAB pneumonia. Nearly 40% of patients who survived the ICU finally died in the hospital. Longer hospital stay prior to ICU admission, higher SOFA score on pneumonia diagnosis, and presence with CARB bacteremia were independent risk factors of hospital mortality. These epidemiological data may help clinicians to make more appropriate decisions of treatment and monitoring for such patients.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC38

高頻胸壁振盪治療於顱內出血術後病人之安全性及成效分析

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Safety and effectiveness of high frequency chest wall oscillation in postoperative patients with intracranial hemorrhage

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Purpose: HFCWO (High-Frequency Chest Wall Oscillation) has been increasingly used in post-operative patients facilitate airway clearance. However, the safety and therapeutic effects of HFCWO in patients following brain surgery has never been studied. The aim of this study was to investigate the safety and effectiveness of HFCWO in postoperative patients with intracranial hemorrhage.

Materials and Methods: This retrospective study was conducted in a medical center during Jan 2016 and Dec 2018. A total of 30 patients with brain surgery for intracranial hemorrhage and receiving postoperative HFCWO (twice daily) for increased pulmonary infiltrations on the chest radiograph were included. Clinical information and hourly physiological data were extracted from the electronic medical records for the first 7 days after HFCWO. Changes of intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP), and heart rate (HR) after HFCWO were analyzed to evaluate the safety, and changes of pulmonary infiltrations on the chest radiograph were analyzed to evaluate the effectiveness. All data were analyzed using nonparametric tests.

Results: A total of 310 HFCWO treatment events were collected and analyzed. Compared to the pre-HFCWO baselines (Hour 0), the physiological data measured one hour (Hour 1), two hours (Hour 2), and three hours (Hour 3) after HFCWO showed no significant changes, except for CPP on Hour 2 (difference= 2.0 [-5.0 to 8.0] mmHg, P= 0.032) and MAP on Hour 3 (difference= 2.0 [-5.7 to 8.7] mmHg, P= 0.027). Considering that the physiological conditions might change over time, we further stratified the analysis by days after HFCWO. The results showed that HFCWO only cause minimal physiological changes, including ICP on Day 1 (difference= -2.5 [-4.0 to 0.0], P= 0.023), CPP on Day 5 (difference= 4 [1.5 to 11.5], P= 0.044), MAP on Day 6 (difference= 8.7 [2.3 to 15.7], P= 0.016), and HR on Day 7 (difference= 4.5 [1.0 to 10.5], P= 0.07). Evaluation of pulmonary infiltration on the chest radiograph showed significant improvement after 7 days of HFCWO use (3% vs 20%, P< 0.001).
Conclusions: HFCWO caused minimal and not clinically significant physiological changes in postoperative ICH patients. Pulmonary infiltrations on the chest radiograph improved after HFCWO treatment. Our findings suggest that HFCWO is safe and effective in patients following brain surgery.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC39

類似乳房腫瘤之原發性胸壁膿瘍：病例報告與文獻回顧

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Primary Chest Wall Abscess Mimicking a Breast Tumor: Report of a Case and Review of Literature.

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Purpose: Chest wall abscess can be categorized as primary and secondary, with the former arising spontaneously and the latter occurring in response to preexisting disease. Chest wall abscess can be mimicking breast tumor if located behind the breast tissue.
Patients and Methods: A 74 year woman presented with progressive painful swelling in her left breast. She has hypertension and diabetes mellitus history with regular control, and no trauma or other systemic infection history were noted before this attack. She has intermittent fever, with her left breast being swollen, painful, with local redness/heat and a point of impending rupture. Chest CT revealed an ill-defined, huge infiltrative lesion over left chest wall.
Results: She underwent surgical debridement through local small incision and wound culture was performed (Staphylococcus aureus was identified. No malignancy was found from the necrotic tissue. Local wound drainage with wet dressing and systemic antibiotics were administered postoperatively. Her conditions got improved and discharged 14 days later uneventfully.
Conclusion: For patients with chest wall abscess mimicking breast tumor, accurate diagnosis and adequate surgical drainage timely will remarkably improve the outcome, and teamwork cooperation will be needed.
Keywords: primary chest wall abscess, surgical debridement.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC40

比較 cefoperazone-sulbactam 與 piperacillin-tazobactam 對院內肺炎的療效

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Cefoperazone-sulbactam versus piperacillin-tazobactam in the treatment of nosocomial pneumonia

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Objectives: To compare the clinical efficacy of cefoperazone-sulbactam to that of piperacillin-tazobactam against hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP).
Methods: Baseline demographic and clinical response data were extracted from a clinical study on the efficacy and safety of Brosym® (the BATTLE study). The BATTLE study was conducted in nine hospitals in Taiwan from March 1, 2018 to May 30, 2019. We compared the clinical outcomes of patients who received either cefoperazone-sulbactam or piperacillin-tazobactam for more than 5 days for HAP/VAP.
Results: Data from 410 patients were analyzed, including 345 HAP patients and 65 VAP patients; 209 and 201 patients received cefoperazone-sulbactam and piperacillin-tazobactam, respectively. Patients who received cefoperazone-sulbactam had higher Charlson and APACHE II scores than patients receiving piperacillin-tazobactam. The clinical cure and failure rates of patients receiving cefoperazone-sulbactam were 80.9% and 17.2%, respectively, comparable to those of patients receiving piperacillin-tazobactam (p = 0.943). The cefoperazone-sulbactam group had clinical effectiveness and ineffectiveness rates of 80.9% and 17.7%, respectively, comparable to those of the piperacillin-tazobactam group (p = 0.711). The overall mortality of the cefoperazone-sulbactam group was 23.9%, similar to that of the piperacillin-tazobactam group (p = 0.480). The similarities between cefoperazone-sulbactam and piperacillin-tazobactam in terms of clinical outcomes remained unchanged after adjusting for disease severity and comorbidity status.
Conclusions: The clinical efficacy of cefoperazone-sulbactam is similar to that of piperacillin-tazobactam in the treatment of HAP/VAP.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC41

克雷伯氏肺炎菌在社區型及健康照護相關膿胸的發生率及風險分析

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The incidence and risk analysis of Klebsiella pneumoniae in community-acquired and health-care associated pleural infection

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Purpose: *Klebsiella pneumoniae* leads into a high mortal community acquired pneumonia. We aim to identify the influence of *Klebsiella pneumoniae* in community-acquired and health-care associated empyema, including incidence, risk factors and clinical outcome.
Materials and Methods:
Patients with empyema were identified by pleural effusion analysis and surgical results. We collected their medical record, clinical presentation, laboratory analysis, bacterial culture and clinical outcome. Patients were divided into *Klebsiella* empyema (KE) and Non- *Klebsiella* empyema (NKE) groups according to the results of pleural effusion culture. We used univariable and multivariable statistical analyses to realize risk factors and clinical outcomes in *Klebsiella* empyema.
Results:
Most of 477 recruited patients (mean age:61.2 years old) were male (78.4%). 70.8% patients had ≧ 1 comorbidity. Hypertension (39%) and diabetes mellitus (30.9%) were the highest incidence. Fever (37.9%) was the most common initial discomfort. The top two bacterial isolates in order were *Viridans streptococcus* (73, 21.6%) and *Klebsiella pneumoniae* (49, 14.5%). 49 patients were grouped into *Klebsiella* empyema. Old age, diabetes mellitus, coronary artery disease, cancer history, lung cancer, less frequency of fever, and lower pleural effusion protein were significant risk factors for pleural infection with *Klebsiella pneumonia*. KE group pretended to high 90-day mortality, comparing with NKE group (18.37%: 10.28%, p=0.088), but the difference was not significant in statistics. In the multivariate analysis, diabetes mellitus, cancer history, and lower pleural effusion protein were significant risk factors for *Klebsiella* empyema.
Conclusions:
Klebsiella pneumoniae is an important and high-incidence pathogen of patients with community acquired and health-care associated empyema in Taiwan. Diabetes mellitus, cancer history, and lower pleural effusion protein are the strong risk factors and may take into consideration when choosing initial antibiotics.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC42

流感嗜血桿菌相關社區型肺炎的結果預測因子和產生 β-內醯胺酶的流感嗜血桿菌的臨床意義

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Outcome predictor of Haemophilus influenzae related community-acquired pneumonia and the clinical significance of β-lactamase producing Haemophilus influenzae

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Introduction: *Haemophilus influenzae* (*H. influenzae*) is the second most common cause of community-acquired pneumonia (CAP). Depending on geographic location, approximately 20 to 35% of strains produce β-lactamase, which mediates resistance to amoxicillin, and β-lactamase was hypothesized as a predictive factor for antibiotics treatment failure but the results were inconclusive. Outcome predictors for *H. influenzae* isolated CAP and the clinical significance of β-lactamase producing strains were not clear.
Materials and methods: A retrospective study was conducted in one of the largest medical centers in Taiwan over a 5-year-period (January 2014 to December 2018). Patients with *H. influenzae* related CAP, proven by either sputum or blood culture were enrolled. Clinical information was collected and outcomes were analyzed.
Results: Seventy-one patients with *H. influenzae* isolated CAP were retrospectively enrolled in our study. The mean age was 67.8 years and fifty-one patients (71.8%) were male. The most common underlying disease was cardiovascular disease (58%) and malignancy (28%). The in-hospital mortality was 19.7%. Multivariate analysis demonstrated that risk factors for mortality included *H. influenzae* bacteremia (OR 4.45, 95% CI 1.01-19.73; p = 0.049) and underlying disease with malignancy (OR 7.48, 95% CI 1.08-51.82; p = 0.042). Among the isolated *H. influenzae*, forty-two stains (59%) had β-lactamase production, which was related to lower bacteremia incidence (n=4, 9.5%). However, no direct correlation with the mortality rate was observed.
Conclusion: *H. influenzae* bacteremia and underlying disease with malignancy were the risk factor for *H. influenzae* isolated CAP. Although β-lactamase producing *H. influenzae* caused less bacteremia, there was no correlation between the mortality rate and β-lactamase production.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC43

膿瘍分枝桿菌肺感染致胸痛

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Pectoralgia caused by Mycobacterium abscess infection of lung

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Introduction: Common causes of chest pain in the general population include chest wall pain; GERD; and costochondritis pulmonary, and psychological anxiety even cardiovascular illness. Physician considered patient related risk factors to **identify causes**.
Materials and methods: Brief description of the case
This 34 years old man past history of GERD. He visited OPD because of angina for year. He came from Vietnam and stayed in Taiwan as foreign worker. He complained of cough with yellowish sputum and Sore throat not improve. Denied fever, nausea, vomiting running nose. Then, he visited OPD for help. Due to clinical needs, HRCT was arranged for the surveying to find Lt lingular lobe lesion as few effusion from Chest U.S. So he was admitted to our ward for further evaluation and management.
Results:
BAL over Lt lung AFS culture was M. abscess. After medical treatment with amikacin plus Clarithromycin his uncomfortableness relived. The following CXR also improved over lesion site.
Discussion: About NTM disease group, observed symptoms of thoracic pain had reported form other study. As NTM is increasing worldwide, sputum smear is the main tool available to diagnose and differentiate between TB and NTM disease.
Conclusion: HRCT and BAL combined with molecular methods is the best combination in dealing with this kind of patients.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC44

肝移植病患肺結節合併檸檬酸桿菌感染

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Citrobacter koseri in patient s/p liver transplantation with solitary pulmonary nodule

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Introduction:
Citrobacter koseri is a seldom known to be a pathogen leading infection in individuals with significant comorbidities and immunocompromised status. Community-acquired infections were rarely reported. Citrobacter koseri may cause infection including UTI, pneumonia even bacteremia. Most commonly infected individuals with severe comorbidities or immunocompromised hosts . We report a liver transplantation patient who took *anti-rejection medication* presenting with C. koseri infection in a recent diagnosis of pulmonary nodule scenario.
Materials and Methods: case brief description
A gentle man in his 67 y/o with past history of liver transplantation taking *anti-rejection medication* was arranged bronchoscope for Lt lingual lobe nodule from LDCT .He denied any symptoms included dyspnea cough or other S/S . Investigating the cause of Lt lingula lobe lesion by BAL was successfully performed.
Results:
Citrobacter koseri was isolated from BAL culture. He was safely treated with antibiotics. He is well until now.
Discussion:
Intrapulmonary pathology shoulder be invested aggressively in immunocompromised host by any means to explain the heteromorphism .
Conclusion:
In such immunosuppressive individual, such as **scaling tip teeth cleaning** may lead aspiration of oral pathogen .This Illustrated necessity furtherly investigation about intrapulmonary pathology for focal pulmonary nodule.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC45

肺部毛玻璃病病變起因為黴菌感染或巧合

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GGO caused by pulmonary fungal infection or just a coincidence

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Introduction: GGO lesion of lung is now frequently encountered clinical puzzle while the widespread application of CT for lung screening and for routine necessary imaging study. It seemed to be impossible to discriminate malignant from benign GGO just on CT result subjectively, because some benign lesions mimic malignancy.
Materials and methods: Brief description of the case
This 67 y/o house married wife with normal psychosocial status with no specific past history was admitted to our ward because a 1.2cm GGO was noted on HRCT account of hemoptysis. According to the patient, she was a heavy smoker (1ppd >15 years). She irregular followed up at OPD for chronic cough with sputum was noted. There was no fever, headache, nausea, vomiting, chest pain, chest tightness, short of breath, body weight loss, diarrhea or constipation. At ward, PE found clear breathing sound, regular heart beat without audible heart murmur and soft abdomen without tenderness. Under the tentative diagnosis of Lung nodule, suspected malignancy, she was admitted to our ward for further evaluation.
Result: BAL over RUL fungus culture revealed Aspergillus and candida. Others included cytology results all were negative. After 6 weeks anti-fungal antibiotics treatment, her RUL GGO seemed smaller from repeated HRCT 22 weeks later.
Discussion: The initial stage of aspergillosis might present as GGO. Most of such infections in immunocompetent host are self-limited, but some patients would develop pneumonitis or chronic lung infection in immunocompetent hosts, Imaging in immunocompetent or immunocompromised individuals were variable. Examination of BAL may identify fungus at least colonization. Lung aspergillosis presented as GGO mimicking malignancy on CT scan in elderly with underlying disease. The GGO sometime were inflammatory. Response to antibiotics is a simple method to exclude patients from further lengthy work-up, Following CT and appropriate interventional disposal about GGO when clearly be suspicious.
Conclusion: Protocol directed management included antibiotics, blood marker follow-up with CT , bronchoscope even biopsy via any methods without delaying appropriate treatment, significantly CT findings and pathological result still needed to be explored.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC46

開洞性節結性肺患者鳥型結核分枝桿菌感染復發分析

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Mycobacterium avium relapse in patient with nodular cavity lung

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Introduction:

Pulmonary NTM .TB remains similar as clinical and image presentations of the two are so similar and a definite diagnosis need specific lab method and time.

While NTM was cultured and identified in respiratory specimen, diagnosis of NTM infection required exclusion from contamination was quite tricky issue for the physician.

Materials and Methods: case brief description

The 52-year-old mainland spouse recovered after suffering from pulmonary TB 17 years ago, regularly tracking at Clinic. She denied any family history and allergy. General physical examination looks normal. She coughed up blood suddenly about 3 months ago.

Results: HRCT on Jan 2019 depicted LLL cavity and these abnormal physical conditions were diagnosed by computer tomography and endoscopy as M.avium infection (LLL cavity lesion). From then on, she took medicine as for M.avium for about 18 months and sputum culture persistent positive for M,avium.

Conclusion:

Combination drugs therapy require individuals to remain lengthy period of time. Affected individual should be monitored to detect disease response or medication side effect. Treatment should be lasting for 12 months until negative AFS sputum culture.

Discussion:

Some assumption that particular patients require longer courses of treatment or exploring their medical compliance were necessarily discussed in cavity lung disease infected with NTM.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC47

麴菌與膿瘍分枝桿菌合併感染於開洞肺病變案例

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Co-mixed infection with Mycobacterium abscess and Aspergillus in old female patient with small cavity lung

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Introduction: W*henever and wherever Mycobacterium* and *Aspergillus* are concomitantly cultured from BAL constitute clinical puzzle. In individuals with chronic lung diseases or bronchiectasis facilitate co-mixed infected and strengthened interactions of both pathogens. Unfortunate result is worsening of the underlying lung disease even fatal. Thus, as possible, all available tools to diagnosis and follow-up of potentially mixed infected patients in chronic lung diseases which demand immediate attention.

Materials and methods: Brief description of the case

This 76 y/o Hakka woman with past history of asthma .HTN and hyperlipidemia peritonitis and ATH, adhesion s/p exp. lap. with regular follow-up in our OPD. According to the patient statement, she suffered from short of breath, hemoptysis for 3 days intermittently, She was regular chest OPD F/U. There was no fever, chillness, chest tightness, abdomen pain, poor appetite, dysuria or BW loss. In chest clinics, under the impression of suspect LUL nodular cavit y lesion.with LUL peribronchial lesion, she arranged serial measures for further evaluation and treatment.

Result: HRCT depicted LUL one small cavity lesion, BAL: aspergillus + M. abscessus been treated with antifungal and anti-mycobacterium regimen then s/s improved

Discussion: Association and identification of both pathogens were not easy challenge. Image, interventional technology microbiological date were should be integrated. Serology result were often underestimated. Thus, this case demonstration underlines the importance of performing standard image and bronchoscope intervention to obtain tissue sample or BAL.

Conclusion: Therefore, patients infected by NTM and Aspergillus with chronic lung illness may require aggressively work out on early stage then follow guideline to cure them.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC48

貓奴咳血原因竟是人畜共患病

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Zoonoses occurred in Cat lady presentation as hemoptysis

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Introduction: Pasteurellosis is an infectious disease as typical zoonosis P. multocida existed in dogs and cats. The microorganism are transmitted to humans through scratches or bite wounds from dogs and cats and through airway infection Pasteurellosis is diagnosed by isolation culture from specimens.

Materials and Methods: case brief description

This 48 y/o woman.is a school nurse Smoking: denied Occupation Contact: denied Cluster: denied Psychosocial status : normal , had allergic rhinitis with post nasal drip and skin rash since childhood. This time she suffered from cough with yellowish sputum production for long time. She kept two cats for 3 years. Occasionally, she had deep brownish color sputum production. She denied nasal bleeding, chest pain, dyspnea, fever, abdomen pain or diarrhea. She had follow up in our CM OPD and was arranged bronchoscope for evaluation

Result: .HRCT depicted RLL lesion, Bronchoscope: RLL bloody stickily secretion. The BAL culture isolates: Pasteurella multocida.

Discussion: Clinically, respiratory infection by P. multocida has no special features, and varied from URI to dyspnea, bronchitis, pneumonia even lung abscess, and acute pneumonitis was most frequently encountered. Most patients were susceptible in middle-aged to elderly with underlying chronic illness.

About treatment, Penicillin is the first choice then doxycycline, ampicillin or sulfamethoxazole-trimethoprim.

Conclusion: Pasteurella is easily overlooked a potential airway pathogen in keep cats as pet in family life. Zoonosis is a disease that can be transmitted to humans from animals comes into contact with humans. Transmission occurs when animal infected with bacteria, viruses, if humans contact with animals in many ways.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC49

纖維化性開洞肺病變患者鳥型結核分枝桿菌感染復發

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Mycobacterium avium relapse in Lt destroyed fibro-cavity lung patient

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Introduction: NTM increased in chronic lung disease population worldwide .For those cavity lung disease individuals with fibro- cavities lungs if untreated, will aggravate more cavitation and fibrosis. Ultimately disease progression resulted in lung volume loss even lung failure .Relapse of NTM lung disease after treatment completion is very curious.

Materials and methods: Brief description of the case

The 67-year-old man had past history of old pulmonary tuberculosis s/p complete treatment, GU,, bronchiectasis . Aspergillus related lung. He sudden onset hemoptysis with fever for one day .He also got hoarseness and general malaise. Exported sputum showed AFS : 3+ x 2;AFS culture: positive ;ID:NTM . Therefore, he was admitted to our ward for further evaluation and management and suspected bronchiectasis with hemoptysis. A not well- nourished but well developed male ,with ill-looking, clear consciousness .Body weight : 41kg, Height : 170cm*Vital signs : B.P.111/76mmHg , P.R. 90/min , R.R. 18/min , B.T.36℃ chest Percussion : dullness between 2nd to 5th ICS. He was ever diagnosed M, avium via BAL and completed 18 month combination regimen course · Afterward 8 months later, he suffered hemoptysis again. We followed his CXR to find LUL fibro-cavity lung illustrating more opacity. Serial AFS sputum were followed.

Results:

CXR following depicted LLL exacerbation, AFS of 3 set serial sputum were followed and culture then molecular method confirmed his M. avium relapsed

Discussion:

Recurrence after successful treatment is frequent encountered in individuals with M. avium lung disease, especially those who had fibro-cavity lung

Conclusion:

Patients completely treated for M. avium lung disease should be regularly followed. Molecular assay may help to distinguish between relapse and reinfection. The truth is still unclear

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC50

麴菌與鳥型結核分枝桿菌感染接力感染於陳舊性肺結核案例

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Mycobacterium avium lung infection in patient just recovered from aspergillus invasion

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Introduction:
many old TB patients with airway sequelae may develop variable respiratory disease such as bronchiectasis, COPD even pneumonia .NTM and fungus .Colonization and infection with NTM and Aspergillus fumigatus are common in individuals with pre-existing lung destruction. Recurrence or reinfection in patient with TB sequelae should be noticed. Clinicians must keep in mind the possibility of NTM, Aspergillus infection even s/s were subtle.

Materials and Methods: case brief description:
This 53 y/o woman had past history of Old TB. Someday, the patient suffered from hemoptysis. The patient ever visited CM OPD regularly followed but the symptoms sustained. She was followed HRCT to find segmental atelectasis with infectious bronchiolitis in the right upper, right middle, and left lower lobes lesion needed to be excluded underlying malignancy. Due to above condition, then came to our OPD. At OPD, conscious Alert, vital sign showed BT:36.2 ℃, HR:71, RR:17/min ,BP:131/79 mmHg, PE disclosed clear bronchial sound, regular heart beat and soft abdomen no tenderness or distention. Under the impression of .Lt Lower lung mass arranged CT-guided biopsy, the patient was admitted for further management. Previous CXR depicted LLL lesion with BAL to find aspergillus fumigatus and had been completely treated half year ago.

Results: BAL over LLL with AFS culture as M. avium

Discussion:
Correlation about NTM and Aspergillus lung disease were important for diagnosis such disease in clinical practice. Patients infected with NTM may have coexisting lung disease as bronchiectasis or COPD that frequently interfered clinical judgment and treatment. Patients with chronic lung disease are also prone to Aspergillus, NTM colonization and infection

Conclusion:
Clinician regularly exam sputum of individuals for testing AFS ,screening for Aspergillus, and CXR to be helpful when assessing patient s with old TB presenting with non-specific infection, or other sequelae in early stage.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC51

水通道蛋白經由調控粒線體活性影響巨噬細胞極化

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Aquaporin Regulates Macrophage Polarization Through Mitochondrial Activity

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Abstract:
The acute respiratory distress syndrome (ARDS) is one of the devastating clinical syndrome that often occurred in the ICU. Studies have shown that macrophage may plays a crucial role in the initiation stage of ARDS development. The over activated macrophage triggers the massive infiltration of circulatory immune cells into the alveoli, thus eventually leads to the respiratory failure. Studies have shown that induction of M1 macrophage in mice exaggerated lung inflammation and injury; whereas promoting M2 polarization mitigate pulmonary and systematic inflammation. Aquaporin (AQP) is widely expressed water transporter, beside its channel nature, recent studies have shown that AQP plays a critical role in regulating macrophage activity, including migration, phagocytosis and inflammation response. However, the contribution of AQP to macrophage polarization is still unclear. In this study we aim to investigate the relationship and regulation mechanism between AQP and macrophage polarization.

Results:
Bone-marrow-derived macrophage (BMDM) were isolated and differentiated from bone marrow monocyte. Bone marrow were isolated from tibia and femur of C57BL/6 mice. Twenty ng/ml M-CSF were used to differentiate bone marrow monocyte to macrophage. Our results shown that AQPs inhibition reduces M1 (1 μg/ml LPS) and M2 (20 ng/ml IL-4) polarization of BMDM in both gene and protein level. Extracellular flux assay and MitoSOX assay revealed that mitochondria function in M1 polarization is restored by AQP inhibition, while further suppressed in M2 polarization. The general autophagy is upregulated with AQP inhibition in both M1 and M2 stimulation.

Discussion:
AQPs modulates BMDM polarization by regulating the mitochondria response to polarization stimuli. AQPs on mitochondria inner membrane may directly affect the functional activity of mitochondria. On the other hand, AQPs may affect the mitochondria net activity by regulating autophagy to interacts with mitochondrial dynamics. Further investigation would be focus on identify the certain AQPs and their contribution to the polarization event.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC52

以六分鐘走路測試之距離—血氧乘積來預測非囊性纖維化支氣管擴張症病患之死亡率

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Predicting mortality in non-cystic fibrosis bronchiectasis patients using distance-saturation product

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Background

The bronchiectasis severity index (BSI) and FACED score are currently used in predicting outcomes of non-cystic fibrosis (non-CF) bronchiectasis. Distance-saturation product (DSP), the product of distance walked, and lowest oxygen saturation during the 6-min walk test showed strong predictive power of mortality in non-CF bronchiectasis patients. This study aimed to compare the efficacy of these scores and DSP in predicting mortality.

Methods and Patient

Our retrospective study included non-CF bronchiectasis patients from January 2004 to December 2017. We recorded the basic data, pulmonary function, radiologic studies, sputum culture results, acute exacerbations (AE), emergency department (ED) visits, hospitalisation, and mortality.

Results

A total 130 non-CF bronchiectasis patients were analysed. The mean BSI score, FACED score, and DSP were 8.8±4.9, 3.4±1.7, and 413.1±101.5 m%, respectively. BSI and FACED scores had comparable predictive power for AE (p=0.011; p=0.010, respectively). The BSI score demonstrated a significant correlation with ED visits (p=0.0003). There were 12 deaths. Patients were stratified using a DSP cut-off value of 345 m% according to the best area under receiver operator characteristic curve (AUC) value in mortality. DSP was not correlated with AE and ED visits. BSI, FACED scores, and DSP demonstrated statistically significant correlations with hospitalisation (p<0.0001; p<0.0001; p=0.0007, respectively). The AUC for overall mortality was similar for BSI, FACED score, and DSP (0.80 versus 0.85, p=0.491; 0.85 versus 0.83, p=0.831).

Conclusion

DSP had comparable predictive power for mortality as the well-validated BSI and FACED scores and is relatively easy to use in clinical practice.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC53

Cefoperazone-sulbactam 與 piperacillin-tazobactam 在治療嚴重社區型肺炎的效果比較:回溯性多中心研究

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Efficacy of Cefoperazone-sulbactam versus piperacillin-tazobactam in treatment of severe community-acquired pneumonia: a retrospective, multicenter study.

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Purpose: To compare the clinical efficacy of cefoperazone-sulbactam with piperacillin-tazobactam in the treatment of severe community-acquired pneumonia (SCAP)

Materials and Methods: This study was a retrospective analysis, which extracted the baseline demographic data and clinical response data from a clinical study – the efficacy and safety of Brosym® (BATTLE study). BATTLE was a multicenter study, which conducted in nine hospitals including eight medical center and one regional hospital in Taiwan from March 1, 2018 to May 30, 2019. We compared the clinical outcome of patients receiving cefoperazone-sulbactam or piperacillin-tazobactam for more than 5 days in the treatment of SCAP.

Results: A total of 815 SCAP patients were enrolled. Among them, 343 and 472 patients received cefoperazone-sulbactam and piperacillin-tazobactam, respectively. Compared with the demographic characteristics of patients receiving piperacillin-tazobactam, patients received cefoperazone-sulbactam had higher Charlson score. In contrast, no significant difference in terms of age, gender, PSI score and CURB-65 score was observed between the patients receiving cefoperazone-sulbactam and piperacillin-tazobactam. The clinical cure rate of patients receiving cefoperazone-sulbactam and piperacillin-tazobactam was 84.2% and 80.3% respectively (p = 0.367). Regarding secondary outcome, cefoperazone-sulbactam group had clinical effective rate of 85.4%, which was comparable to piperacillin-tazobactam group (83.3%, p = 0.258). In addition, the overall mortality of cefoperazone-sulbactam group was 16% (n = 55), which was similar to piperacillin-tazobactam group (17.8%, n=84, p = 0.721). The similarity between cefoperazone-sulbactam and piperacillin-tazobactam regarding clinical outcomes remained unchanged after adjust disease severity and comorbidity status.

Conclusions: The clinical efficacy of cefoperazone-sulbactam in the treatment of adult patients with SCAP is comparable to piperacillin-tazobactam.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC54

產後隱球菌肺炎

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Postpartum cryptococcal pneumonia

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Pregnancy is considered a relatively immunosuppressed period to prevent fetal rejection that peaks during the third trimester and the immune response will return to the baseline by three to five months postpartum. A paradoxical change from immunosuppression to proinflammatory immune response at postpartum, results in quiescent infection to manifest as a symptomatic disease, a phenomenon recapitulate immune reconstitution inflammatory syndrome as commonly described in HIV patients initiating antiretroviral therapy. Pulmonary cryptococcosis usually develops in immunosuppressed patients. Cryptococcal pneumonia in immunocompetent patients during postpartum period has been rarely described. Understanding the postpartum immune status, could assist in early diagnosis and treatment of possible opportunistic infection. We report a case of postpartum cryptococcal pneumonia in a non-HIV 40 year-old woman who presented to the hospital with a two weeks history of fever and productive cough after a normal delivery.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC55

異體造血幹細胞移植後巨細胞病毒肺炎的發生率-單一醫院經驗

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The incidence of cytomegalovirus pneumonia after allogeneic hematopoietic stem cell transplantation: asingle institute experience

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Purpose

Cytomegalovirus (CMV) infection is one of the leading causes of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). It results from either reactivation of CMV in seropositive recipients or primary infection from seropositive donors to seronegative recipients. CMV infection is associated with multiorgan diseases such as pneumonia, hepatitis, gastroenteritis, retinitis, and encephalitis. Among them, CMV pneumonia is the most serious manifestation of CMV in HSCT recipients with a mortality of more than 50% from previous studies. The clinical presentation of pneumonia caused by CMV pneumonia is similar to that of Pneumocystis carinii, with fever, cough, hypoxemia, and diffuse radiographic opacities. Here, we retrospectively review and characterize CMV pneumonia among allo-HSCT recipients in Kaohsiung Medical University Hospital.

Materials and Methods

This is a retrospective study. We reviewed chart records from 2007 to 2019. Patients were included if they were aged 20 years or older and received allogeneic peripheral blood HSCT.To evaluate the efficacy outcome, we analyzed the incidence of CMV pneumonia. All statistical analyses were usingSPSS 20.0 software.

Results:

180 adults with hematological disease received an allo-HSCT. The median age was 39years(± 11.76), ninety percent of these patient were seropositive, the frequency of CMV pneumonia was significantly hight among patient who were seropositive than among patient who were seronegative (1.8% vs 0%,p＝0.862).

Conclusions:

Infection control and management is an important topic when caring patient underwent allo-HSCT. Typically, CMV infection appears within the first 100 days after allo-HSCT and affects mainly the lungs and the gastrointestinal tract. In addition to the direct impact of CMV end-organ disease, CMV is also associated with increased incidence of opportunistic infections, graft-versus-host disease (GVHD) in allo-HSCT recipients. Combined with the fact that high CMV seroprevalence in Asia, the importance of CMV infection in allo-HSCT population in Taiwan is profound. In our cohort, the incidence of CMV pneumonia was very low.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC56

社區性肺炎併呼吸衰竭之致病菌流行病學

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Pathogens for Community-acquired Pneumonia with Acute Respiratory Failure

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Introduction: Community-acquired pneumonia (CAP) with acute respiratory failure results in substantial mortality and a lot of antibiotics were empirically used. Identifying a viral cause in such instances might facilitate antibiotic stewardship.
Materials and Methods: Adult patients who newly received invasive mechanical ventilation for suspected CAP were prospectively screened at ICU. The exclusion criteria were witnessed aspiration pneumonia or patients in bedridden status. This study was conducted between May 01, 2019 and May 31, 2020 at the National Taiwan University Hospital. Other than routine pathogen survey, the respiratory aspirates were additionally used the FDA-approved mPCR FilmArray Respiratory panel and Pneumonia panel (BioFire Diagnostics, Inc.) which identifies adenovirus, coronavirus (strains HKU1, NL63, 229E, OC43); human metapneumovirus, rhinovirus/enterovirus; influenza (strains A, A/H1, A/H3, A/H1-2009, B); parainfluenza virus (strains 1,2,3,4) and RSV as well as the bacterial respiratory pathogens.
Results: A total of 30 patients were included. The ICU and hospital mortality were 13.3% and 20% respectively. The most common detected pathogen was influenza A (20%). It followed with *S. pneumoniae* (13.3%), parainfluenza virus 3 (6.7%), *S. aureus* (6.7%), *K. pneumoniae* (6.7%), *M. catarrhalis* (6.7%). There were still 30% patients without detected pathogen. Nine patients were tested with both Respiratory and Pneumonia panel. The concordance rate for virus detection was perfect. *K. pneumoniae* and *S. pneumoniae* were further detected by Pneumonia panel in two patients.
Conclusions: Viruses represent a major cause of CAP in critically ill patients requiring mechanical ventilator. Timely identifying such subjects presents an opportunity for discontinuing antibiotics.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC57

血液中結核菌之游離去氧核醣核酸在肺結核患者的臨床價值

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The clinical value of *Mycobacterium tuberculosis*–derived circulating cell free DNA in patients with pulmonary tuberculosis

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Purpose: Pulmonary tuberculosis (PTB) is a contagious disease and its early diagnosis remains a challenge. Although *Mycobacterium tuberculosis* (MTB)-derived cell-free DNA (cfDNA) in human plasma has been detected, the clinical significance and immunologic determinants of MTB-cfDNA positivity in patients with PTB are unclear. .

Materials and Methods: This prospective study enrolled PTB cases, patients with *Mycobacterium avium* complex lung disease (MAC-LD), and tuberculosis contacts. We conducted cfDNA extraction from plasma, quantitative PCR (qPCR), and droplet digital PCR (ddPCR) targeting the IS6110 gene fragment of MTB. We assessed the performance of MTB-cfDNA for PTB diagnosis and analyzed factors associated with MTB-cfDNA positivity.

Results: We enrolled 46 subjects in 1 year: 24 PTB, 7 MAC-LD, and 12 tuberculosis contacts. The sensitivity and specificity of IS6110-qPCR and IS6110-ddPCR to identify PTB cases were 50.0% (12/24) and 90.9% (20/22), respectively. For 18 smear-negative patients (13 PTB and 5 MAC-LD), the sensitivity and specificity were 46.2% (6/13) and 100% (5/5), respectively. MTB-specific interferon-γ levels were higher in MTB-cfDNA-positive PTB cases than in negative ones (7.24±2.80 vs 3.53±3.85 IU/mL, p=0.014). MTB-specific interferon-γ response was independently associated with MTB-cfDNA positivity (adjusted OR 1.710, 95% CI 1.070-2.733, p=0.025). Among PTB cases, the MTB-cfDNA levels declined after 2 months of anti-tuberculosis therapy (median cycle threshold value for IS6110-qPCR: 38.20 at baseline versus 45 at 2 months, p<0.001).

Conclusions: MTB-cfDNA was detected in nearly half of the smear-negative PTB cases and MTB-cfDNA positivity was associated with interferon-γ response, suggesting the potential of MTB-cfDNA for PTB diagnosis, treatment monitoring, and its association with MTB-specific immune responses.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC58

周邊血液嗜酸性白血球增多症在慢性阻塞性肺病急性發作的角色

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Role of peripheral eosinophilia in acute exacerbation of chronic obstructive pulmonary disease

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Purpose: Nucleic acid amplification tests (NAAT) have been used as a diagnostic tool for pulmonary tuberculosis (PTB) in Taiwan for many years. In accordance with Taiwanese legislation, health care personnel are required to notify the Centers for Disease Control and Prevention (CDC) in case of suspected PTB. This study aimed to investigate the impact of NAAT(Gen-Probe) on the notification system for PTB and anti-tuberculosis treatments in Taiwan.

Materials and Methods: A retrospective study on the impact of NAAT (Enhanced Amplified Mycobacterium tuberculosis Direct Test [E-MTD], Gen-Probe, San Diego, CA, USA) [NAAT(Gen-Probe)] was carried out at Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation from March 2011 to December 2017. During the study period, microscopic acid-fast-bacilli smears and mycobacterial cultures were available for PTB diagnosis. NAAT(Gen-Probe) was first introduced at the hospital in January 2014 for use as a diagnostic method for PTB. Positive sputum culture was considered as the gold standard for PTB diagnosis. We excluded clinically-diagnosed PTB cases.

Results: When NAAT(Gen-Probe) was applied, the rate of error notification to CDC decreased from 64.3 to 7.0% ($P<0.001$), and unnecessary anti-TB treatments administered to suspected cases decreased from 14.9 to 6.5% ($P = 0.005$). In the non-PTB group, the mean duration of unnecessary anti-TB treatments changed from 38.9 ± 38.3 days to 37.0 ± 37.9 days ($P = 0.874$). In the PTB group, the mean time from notifying CDC to initiating treatment decreased from 3.05 ± 6.95 days to 1.48 ± 1.99 days ($P = 0.004$). The sensitivity, specificity, positive predictive value, and negative predictive value of NAAT(Gen-Probe) were 99.0, 92.3, 99.0, and 92.3%, respectively.

Conclusions: Use of NAAT(Gen-Probe) led to decrease in the rate of error notification of suspected PTB cases to the CDC, avoidance of unnecessary use of anti-TB treatments, and accelerated initiation of appropriate treatments.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC59

一結核淋巴病變病例合併高血清 CA125 及 paradoxical reaction 表現

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A case of TB neck LAP with high serum CA125 and post-treatment paradoxical reaction

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We reported a 66-year-old man of seronegative HIV test presents with a 1-month history of a progressively growing mass on his right lower neck. The neck mass was soft, elevated, non-tender and measured 5.5cm at its widest diameter. A CT scan of the neck and chest revealed multiple, enlarged lymph nodes with peripheral enhancement extending from the right lower neck region to the mediastinum; there was a small pleural effusion and ascites on the right side. Besides, serum cancer antigen 125 level was high (477.3 U/ml) too. A series of examinations were made and no malignancy was found. A culture of the aspirate grew Mycobacterium tuberculosis 5 weeks later. A diagnosis of mycobacterial cervial lymphadenitis was made.

Full-course of anti-TB therapy was performed. The neck mass manifested a paradoxical reaction in the first 3 months of treatment, which resolved gradually by the 5th month. The serum CA 125 level returned to normal range after treatment 5 months later (18.9 U/ml).

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC60

醫療工作人員潛伏結核感染盛行率與臨床因子分析-多中心前瞻性觀察性研究

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Prevalence and Factors Associated with Latent TB Infection in Health Care Workers in Taiwan- A Multi-center Prospective Observational Study

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Purpose: Diagnosis and treatment of latent tuberculous infection (LTBI) are pivotal steps to eliminate TB in Taiwan. However, prevalence of LTBI in health care workers remains uncertain in Taiwan. A multi-center based study is required to elucidate the issue.
Materials and Methods: This multi-center, prospective, observational study was carried out in four medical centers in Taiwan. Health care workers that worked in hospitals for more than one year were eligible for enrollment. The status of LTBI was determined by QuantiFERON-TB Gold Plus. Clinical factors associated with LTBI in health care workers were investigated. We also surveyed the willing of receiving LTBI treatment before and after LTBI testing, and reasons of LTBI treatment refusal.
Results: A total of 215 health care workers, including 23 physicians, 161 nurses, 20 health professionals, and 11 administration staffs, were included for analysis. Their mean age was 36.0 ± years old and the prevalence of LTBI was 10.2% (22/215). Individuals with LTBI were older, had higher BMI, more likely to work in ICU, and were more likely to be health professionals and administrative staffs. In multivariate analysis, independent factors associated with LTBI in health care workers included older age (aHR 1.10, 95% CI 1.03-1.17), health professionals and administrative staffs (aHR 5.76, 95% CI 1.48-22.35), and working in ICU (aHR 18.05, 95% CI 3.12-104.39). More than 30% of health care workers refused LTBI treatment, especially physicians and health professionals. The most common reasons of LTBI treatment refusal were concern of adverse drug reactions (46.5%).
Conclusions: LTBI is not common in health care workers in Taiwan. Older age, health professionals, administrative staffs, and working in ICU were significant factors associated with LTBI. Concern of adverse reactions were most common barrier of LTBI treatment in health care workers.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC61

少見的溶骨性骨破壞-骨結核的臨床表現：病例報告及文獻回顧。

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Unusual Osteolytic Bone Destruction- A Presentation of Tuberculosis Osteomyelitis: A Case Report and Literature Review.

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Introduction

Tuberculosis infection is a common disease in Taiwan. Pulmonary TB accounts for 90% of TB infection. Extrapulmonary TB includes miliary TB, TB pleurisy, TB osteomyelitis, etc. Here we present a case of pulmonary TB with TB pleurisy and unusual bone destruction. After biopsy, TB osteomyelitis was impressed.

Case Report

The 84 year-old gentleman has past history of ESRD, DM, CAD and CHF. He suffered from fever and was admitted to our ICU under the impression of pneumonia and respiratory failure s/p ETT and MV. Due to persistent pleural effusion, we performed pleural biopsy, which showed granulomatous inflammation. We arranged chest CT, which showed bilateral upper lobe bronchiolitis, and suspect infectious process over left sterno-clavicular area, and 1st rib-sternal area. We performed chest wall debridement and pathology showed caseous granulomas and osteomyelitis, bone and soft tissue. TB osteomyelitis was impressed. Finally, his sputum TB culture also showed Mycobacterium tuberculosis complex. We started anti-TB therapy and he was discharged under stable condition.

Discussion

The patient has a protruding mass over left sternoclavicular joint for half an year and it became enlarged in recent 3 weeks. Chest CT showed osteolytic, sclerotic margin and mild soft tissue infiltration. It is difficult to differentiate abscess from malignancy. Biopsy is needed for him, which showed caseous granulomas and osteomyelitis. After anti-TB treatment, the bone mass regressed.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC62

從正常腎功能跟透析病人，探討潛伏性肺結核免疫抑制點的表現狀況

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The status of Immune checkpoints expression in latent tuberculosis infection: from normal renal function to dialysis patients

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Introduction: The incidence of active tuberculosis (TB) is 10-20 times in hemodialysis patients compared with general population and often has been delayed diagnosed and correlates with significant mortality. To prevent TB development, latent TB infection (LTBI) is a great issue in dialysis patients. However, beyond the screening and treatment, the status of immune status is not clear. In particular, T-cells and monocytes, playing important roles to defend Mycobacterium tuberculosis (M.tb) infection, are found to be exhausted in TB. The impact of immune exhaustion is scarcely reported in LTBI, especially for hemodialysis before.

Methods: We prospectively enrolled dialysis patients and TB contacts with normal renal function for LTBI intervention from two medical centers and one regional hospital in Taiwan. LTBI was diagnosed using Quatiferon TB GOLD-in-Tube (QFT) test. The participants with normal renal function and negative QFT were classified as the health control (HC) group. LTBI participants were divided to two groups including LTBI-nonCKD (normal renal function) and LTBI-HD (hemodialysis). The expression of T cell immunoglobulin mucin (Tim) 3, programmed cell death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) on CD4, CD8 T cells and PD-1 ligand 1 and CD14 over monocytes were examined at baseline and after treatment in LTBI groups.

Results: In the study, we enrolled 27 HC, 24 LTBI-nonCKD and 43 LTBI-HD participants. The age and sex were not significantly different between HC and LTBI subgroups. The neutrophil to lymphocyte ration was higher in LTBI whereas monocyte to lymphocyte ratio was lower than the HC group. Immune checkpoints (Tim-3, PD-1 and CTLA-4) on CD4, CD8 and PD-L1 on monocytes were significantly higher in LTBI-nonCKD than that in the HC group. Tim3 on CD4 cells (CD4Tim-3) (5.8±4.0 vs. 10.9±5.4, p <0.001), CD4CTLA-4 (10.0±5.4 vs. 18.2±7.3, p<0.001), and CD8CTLA-4 (19.2±9.2 vs 29.0±10.5, p=0.001) were further significantly higher in LTBI-HD than LTBI-nonCKD. The expression of CD4Tim3, CD4CTLA-4, and CD8CTLA-4 significantly reduced after LTBI treatment.

Conclusion: Immune exhaustion of CD4, CD8 T cells and monocytes were noted in general contacts with LTBI, possibly indicting the pathogenesis. The dialysis status might correlate more increasing Tim3, and CTLA4 expression than the subjects with normal renal function. Further study on immune exhaustion in M. tuberculosis infection since even latent status and its prevention might be reasonable.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC63

分枝桿菌肺病是潛伏結核感染的相關風險因子?-一個醫學中心的前瞻性研究

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Is Nontuberculous Mycobacterial Lung Disease A Risk Factor of Latent Tuberculous Infection? - A Prospective Study in A Medical Center

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Purpose: Nontuberculous mycobacterial lung disease (NTM-LD) is apt to occur in patients with parenchymal lung destruction and compromised immune system. These patients have been reported to have a higher risk of latent tuberculous infection (LTBI). However, it is still not clear whether the higher risk of LTBI is due to NTM-LD or their host status. In this study, we compared the prevalence of LTBI in patients with NTM-LD and NTM lung colonization (LC) to discriminate the effect of NTM infection.

Materials and Methods: We prospectively enrolled patients with sputum positive for NTM from December 2011 to June 2019 in National Taiwan University Hospital. All patients were classified to NTM-LD and NTM-LC groups by ATS guideline. Patients with prior tuberculosis (TB) or human immunodeficiency virus infection were excluded. We also recruited healthy population as the control group. We examined their QuantiFERON TB Gold In-tube tests and defined as LTBI if they have a positive result. We compared the prevalence of LTBI in the control, NTM-LD and NTM-LC groups and analyzed the risk for LTBI by logistic regression tests.

Results: A total of 417 participants were enrolled. Among these patients, 82 in the healthy control group, 181 in the NTM-LD group and 154 in the NTM-LC group, respectively. The mean age was significantly younger in the healthy control group than NTM-LD and NTM-LC group (58.42 vs 61.92 vs 66.11 years old, p<0.001). Body mass index (BMI) was lower in the NTM-LD group (control 23.46, NTM-LD 20.98, NTM-LC 22.61, p<0.001). LTBI prevalence was significantly higher in NTM-LD and NTM-LC groups (control 6%, NTM-LD 23%, and NTM-LC group 20%, p=0.009). In multivariate logistic regression test with age, sex, BMI, diabetes mellitus, cancer and NTM status, we found that NTM-LD (adjusted odds ratio [aOR] 5.785, 95% C.I. 2.110-15.862, p=0.001) and NTM-LC (aOR 4.070, 95% C.I. 1.482-11.179, p=0.006) were both independent factors for LTBI.

Conclusions: Compared to the healthy control group, LTBI was significantly higher in both NTM-LD and NTM-LC groups. The results implied not only NTM-LD, but also the clinical conditions prone to NTM airway isolation are predisposing factors of LTBI. Further validation and the investigation for the detailed risk factors of LTBI in NTM-LC population is required.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC64

支氣管鏡合併經支氣管鏡肺活檢縮短了肺結核的治療延遲

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Bronchoscopy with Transbronchial Lung Biopsy Shortens the Treatment delay of Pulmonary Tuberculosis

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Purpose: Pulmonary tuberculosis (TB) still bears a high global burden and carries intermediate to high incident rates in Asia. In this retrospective study, we investigate the role of transbronchial lung biopsy (TBLB) in facilitating timely diagnosis of pulmonary TB and early start of anti-tuberculous (anti-TB) treatment.

Materials and Methods: We retrospectively identified all patients who received anti-TB treatment for pulmonary TB after bronchoscopy from August 2018 to July 2019. We excluded those who already had a diagnosis of active TB before the bronchoscopy, those who had a positive test result of TB-PCR of sputum, and those who started anti-TB treatment without microbiological evidence. We used Fisher's exact test and used Wilcoxon rank-sum test to find out factors that shorten the time interval between the bronchoscopy to start the anti-TB treatment.

Results: A total of 44 patients were identified according to the inclusion and exclusion criteria for further analysis. 26 patients had received bronchoscopy with TBLB (with TBLB group), while 18 patients had received bronchoscopy without TBLB (without TBLB group). There were no significant differences between groups regarding to sex, age, the major characteristics in chest CT, and EBUS finding. The patients in the "with TBLB" group had a significantly shorter time interval from the bronchoscopy to the start of anti-TB treatment compared to those in "without TBLB" group (median [IQR]: 6.0 [4.0 – 10.3] vs. 14.5 [5.0 – 23.3] days, $p = 0.030$). In 17 patients with TB-PCR negative BW samples of the whole enrolled 44 patients, 3 patients with positive findings on pathology examination of the TBLB specimens had a significantly shorter time interval from the bronchoscopy to the start of anti-TB treatment compared to the other 14 patients (median [IQR]: 8.0 [6.0 – 17.0] vs. 21.5 [19.8 – 25.0] days, $p = 0.011$).

Conclusions: Our study demonstrated that TBLB shortens the anti-TB treatment delay for the patient without TB-PCR positive sputum samples. The TBLB histopathology examination is an important role in shortening the anti-TB treatment delay, especially for patients with TB-PCR negative bronchial washing samples.

A. □原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC65

瀰漫性非結核分枝桿菌感染之小細胞肺癌患者案例報告

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Disseminated NTM Infection in a Small Cell Lung Cancer Patient

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Introduction: Nontuberculous mycobacterium (NTM), a group of bacteria with acid-resistant staining characteristics, are widely dispersed in the natural environment. NTMs can cause infections in a wide variety of body sites, most commonly in the lungs; other areas include localized lymph nodes (most commonly in children), skin, soft tissue (typically following surgery, trauma, injection of medications or other substances), and device associated infections (e.g., central line associated bloodstream infection, exit site infections, pacemaker pocket site infections, etc.). NTMs most commonly affect immunocompromised patients. According to the classification of Runyon, NTMs are divided into four categories based on its pigment production and growth rate after light exposure. In southern Taiwan, the most common bacterial species are *Mycobacterium abscessus*, a rapidly growing nontuberculous mycobacteria (RGMs), which is cultivated within a week. Few studies have examined risk factors for NTM bloodstream infections (BSI) involving indwelling vascular catheters (IDVC). We present a case with small cell carcinoma with IDVC who was suffered from NTM BSI.

Case Presentation: The 58-year-old man with stage IV small cell carcinoma with liver metastasis received second line chemotherapy with Topotecan since 2020/6/18 due to disease progression. Intermittent lower grade fever and local heat were noted 2 months later. Chills after injection from the venous port was noted. Because of venous port infection, we removed it and collected the tip and blood culture. The culture report revealed *Mycobacterium abscessus* in the bloodstream. Chest Computed Tomography showed localized fluid accumulation with the wall thickening in the right medial upper arm. Needle aspiration for the fluid was performed, and strong positive of acid fast stain was noted. TEE (transesophageal echocardiography) showed vegetations over aortic valve and mitral valve, suspect infective endocarditis. Then we started NTM treatment with Amikacin, Imipenem/Cilastatin, and Macrolide. Clinical condition stabilized after NTM Treatment.

Discussion: RGMs, including *M. abscssus,* are emerging pathogens whose diagnosis warrants consideration in bacteremia patients with long-term intravascular catheters. Because the fast-growing characteristics of RGMs are similar to bacteria, drug administration must rely on antibiotic drug sensitivity tests. RGM is resistant to standard antituberculous agents but susceptible to other antimycobacterial agents, including imipenem, amikacin, azithromycin, etc. Bacteremia was resolved in all patients after catheter removal and appropriate antibiotics.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC66

潛伏結核感染者使用 3HP 處方之不良反應危險因子分析：從臨床因子、基因型到群體藥動學模型

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Analyzing adverse events among persons receiving 3HP regimen for treatment of latent tuberculosis infection: from clinical features, genetic polymorphism to population pharmacokinetic model

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Purpose: We aim to identify risk factors of significant adverse events (grade 2 or higher toxicity) in persons receiving 3HP regimen for treatment of latent tuberculosis infection (LTBI).
Materials and Methods: Clinical features, renal and hepatic function, genetic polymorphism of metabolic enzymes and transporters of 35 persons with LTBI were identified. Adverse events (AE) during treatment were prospectively recorded and graded by the Cancer Therapy Evaluation Program common toxicity criteria. Plasma concentrations of isoniazid (INH) and rifapentine (RPT) were drawn at 3, 6, 24 and 48 hours after dose administration and analyzed by liquid chromatography with tandem mass spectrometry. Maximum concentration (C_{max}) and area under the plasma concentration-time curve (AUC) of INH and RPT were predicted using nonlinear mixed effects modeling (Monolix) for further evaluated the relationship between the parameters and AE ≥ grade 2. The optimal cut-off point was estimated by Youden index and receiver operating characteristic (ROC) curve.
Results: Among 35 persons who at least received 1 dose of INH and RPT, 25 developed ≥ grade 2 AE: 10/35(28.6%) with grade 2 and 5/35 (14.3%) with grade 3 AE. AE occurred after a median of 15 days (the 3rd dose) and resolved in a median of 3 days. *NAT2* phenotype and renal function strongly affected individual INH AUC_{24}, which could be calculated as INH AUC_{24} (mg*h/L) = 60.5 + 59.4 (slow NAT2 acetylator) − 0.65(eGFR). In multivariate logistic regression analysis, INH AUC_{24} (adjusted odds ratio [aOR] 1.03; 95% confidence interval [CI], 1.00, 1.05) was the only factor independently associated with AE ≥ grade 2 after adjusting age, sex, *CYP2E1* and *OATP1B3* genetic polymorphism. Persons with INH AUC_{24} ≥ 30 μg/mL were statistically significantly more likely to experience ≥ grade 2 AE (OR 7.4; 95%CI, 1.6, 35.5).
Conclusions: We identified the positive association between INH AUC_{24} and significant AE in LTBI population who received 3HP regimen. Persons with INH AUC_{24} ≥ 30 μg/mL were at increased risk for significant AE. Clinical monitoring of INH AUC_{24} for people who were slow acetylator and renal dysfunction might be warranted.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC67

利用人工智能來分辨分枝桿菌肺部疾病之胸部 X 光影像

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Deep learning-based algorithms for chest X-ray interpretation and diagnosis in presumptive mycobacterial lung disease patients

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Purpose: Mycobacterial lung diseases including pulmonary tuberculosis (TB) and nontuberculous mycobacteria lung disease (NTM-LD) can cause significant morbidity and mortality. However, distinguishing pulmonary TB from NTM-LD remains very challenging due to considerable overlap in the clinical and radiographic findings. We aim to evaluate the clinical utility of artificial intelligence to facilitate the differentiation between the two radiographically similar lung diseases.
Materials and Methods: Patients with pulmonary TB and NTM-LD diagnosed between September 2008 to June 2019 were identified from the clinical databases of National Taiwan University Hospital (NTUH). From them, 300 and 300 chest radiographs were collected, respectively (TB and NTM groups). We also randomly selected 300 suspects of mycobacterial lung disease whose sputum cultures were negative for mycobacteria from November 2014 to March 2018 in NTUH and obtained their chest radiographs (NG group). The final enrolled datasets were split into training (n=660, 73.3%), validation (n=120, 13.3%), and test cohort (n=120, 13.3%). We developed a deep learning–based algorithm for chest radiograph interpretation and diagnosis. The model performance was measured using area under the receiver operating characteristic curves among test cohort. Besides, the diagnosis accuracy for test cohort was compared with 12 chest physicians including 6 senior and 6 junior physicians.
Results: The deep learning–based algorithm demonstrated classification performance with area under curve of 0.88 for pulmonary TB, 0.77 for NTM-LD and 0.72 for NG. For diagnosis accuracy, the deep learning–based algorithm showed a significantly higher performance in classification accuracy (63%) compared to senior and junior chest physicians (51% and 48%, $p < 0.001$).
Conclusions: In our study, deep learning–based algorithm demonstrated an acceptable discrimination among pulmonary TB, NTM-LD and NG patients. The diagnosis accuracy may also outperform chest physicians and thus could be helpful for the differential diagnosis of mycobacterial lung disease in clinical setting. Further external validation is needed to evaluate the model generalizability.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC68

接受免疫檢查點抑制劑治療後發生開洞性鳥型分枝桿菌肺病 – 病例報告

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Development of Cavitary *Mycobacterium avium* complex Lung Disease in a Patient receiving Immune Checkpoint Inhibitors – A Case Report

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Purpose: Immune checkpoint inhibitors (ICIs) have significantly improved outcomes in patients with cancer. Notably, some reports showed cases of development of nontuberculous mycobacteria lung disease (NTM-LD) after ICIs treatment. Although one case report described improvement of NTM-LD in cancer patients receiving ICIs. The effects of ICIs on NTM-LD still remained unknown. Here, we report a case of *Mycobacterium avium* complex (MAC)-LD after ICIs therapy.

Case Report: A 58-year-old man has been diagnosed with renal cell carcinoma, with multiple lung, liver, bone metastases, and inferior vena cava invasion, as well as pulmonary tumor embolism. Three months after diagnosis, he started anti-PD-1 inhibitor (Pembrolizumab) and target therapy (Axitinib). The chest X-ray and computed tomography (CT) revealed bilateral lower lung nodular lesions but no cavitary lesion. However, 6 months after treatment initiation, chest X-ray showed multiple newly developed cavitary lesions. Chest CT revealed multiple cavitary lesions in RUL, RLL, and LUL, and several irregular nodular lesions in RLL and LLL. His sputum-smear was positive for acid-fast bacilli, which was negative in Gene-Xpert. The sputum was culture-positive for NTM, which was identified as MAC species by genotyping method. Under the suspicion of metastatic lung lesion or MAC infection, the patient received thoracoscopic RLL wedge resection. In one RLL nodule, the pathology revealed lung parenchyma with coagulative necrosis, which was compatible with pulmonary infarct. Notably, in a wedge-shaped lung tissue, measuring 6 x 3.5 x 1 cm, the pathology demonstrated acute and chronic inflammation with necrosis and presence of mycobacterial infection. Thus, a diagnosis of mycobacterial lung disease, caused by MAC infection, with tissue invasion was made at the time of 8th cycle of Pembrolizumab. He discontinued treatment for 6 months after operation and restarted 6 months later due to disease progression. The patient received anti-MAC treatment for only 5 months due to intolerance of side effect. He had persistent sputum-positive for MAC but there was no new lung cavity formation. Finally, the patient passed away due to hemoptysis resulted from cancer progression with pulmonary embolism.

Discussions: Immunotherapy with ICIs improved outcomes of patients with various cancers. A case report described improvement of NTM-LD in cancer patients receiving ICIs. However, it may have adverse effect on mycobacterial infection. Because cases of NTM lung disease after ICIs have been reported recently, physicians should be aware of NTM-LD in ICIs-treated patients.

Conclusions: This case report may remind us that physicians should carefully consider the risk of NTM-LD in cancer patients receiving ICIs treatment.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC69

剪力彈性超音波於淋巴結核治療反應之預測應用

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Application of ultrasound shear-wave elastography in prediction of paradoxical upgrading reaction in tuberculosis lymphadenopathy treatment course

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***Purpose**:* Patients of tuberculosis lymphadenopathy (TB-LAP) may experience an unanticipated worsening of symptoms during appropriate anti-tuberculosis therapy, including swelling, rupture, or new lesions. Little research has focused on the development of an objective tool to predict such deterioration. The aim of the present study was to investigate the diagnostic performance of ultrasound shear wave elastography (SWE) in predicting treatment response of peripheral TB-LAP.

Materials and methods: This prospective observational study was conducted at a tertiary hospital in northern Taiwan. Diagnosis of TB-LAP was made based on histology, microbiology or nucleic acid amplification. The paradoxical upgrading reaction (PUR) was defined as worsening of TB-LAP related symptoms, including swelling, pus formation, pain or new lesions, within one month after ultrasound examination. All participants were examined by using the Aplio 500 Platinum Ultrasound System (Toshiba). Each target lymph node was investigated with conventional gray-scale, color Doppler, and two dimensional shear wave elastography (2D-SWE). Maximum elasticity value (Emax) was acquired for 2D-SWE. Generalized estimating equations were used to analyze the association between PUR and Emax.

Results: A total of 207 patients with neck lymphadenopathies received 2D-SWE ultrasonography between Dec. 2017 and Aug. 2020. Twenty TB-LAP patients with an average of 5.4 times of 2D-SWE examinations were included for analyses. The mean age of the enrollees was 49.6 ± 22.7 years, with female predominant (n=15, 75%). Among them, 8 has pulmonary TB (40%). The most common comorbidity was diabetes (n=6, 30%). Sonographic features at initial diagnosis included hilum loss sign, short to long axis > 0.5, and heterogeneous in echogenicity. In prediction of next-month PUR by using 2D-SWE examination, the area under receiver operating characteristic curve (AUROC) was 0.899. The cut-off value of Emax 85 kPa attained the highest accuracy of 84.5% (95% CI: 76.9 －92.0) with a sensitivity of 81.1% and a specificity of 87.9%. Multivariable analysis indicated that **Emax>85** (OR: 14.23 [1.92－105.69], p=0.009), **Emax increment per month >2** (OR: 40.45 [6.29 － 260.16], p<0.001), **heterogeneous echogenicity** (OR: 5.73 [1.39 － 23.59], p=0.016) were independent determinants of PUR in the coming month.

Conclusions: This study showed a high Emax without adequate decrease in elasticity level during treatment and heterogeneous echogenicity were associated with PUR within the following month. 2D-SWE appears to be a feasible tool to predict paradoxical treatment response of TB-LAP.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC70

活動性肺結核患者中 miR-431-3p 的低表現會經由其標的基因 BCL2/MDR1/RIPOR2 信號傳導來促成 ESAT6 對單核細胞凋亡的抑制作用

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miR-431-3p under-expression in active pulmonary TB patients contributes to ESAT6-suppressed apoptosis of monocyte through targeting BCL2/MDR1/RIPOR2 signaling

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Purpose: The aim of this study is to explore the role of microRNAs (miR)-431-3p/500a-5p/ 1258-5p targeting cell apoptosis pathway in host immune responses in active pulmonary tuberculosis (TB) disease and latent TB infection (LTBI).

Method: Gene expression levels of the three miRs, and the predicted target genes of peripheral blood mononuclear cells were measured in 36 patients with sputum culture (+) active pulmonary TB disease, 13 subjects with LTBI (IGRA+), and 13 non-infected healthy subjects (NIHS; IGRA-) by quantitative RT-PCR method. Human monocytic cell lines were transfected with specific miR-mimics or Si-RNA under stimuli with Mycobacterium TB-specific antigen.

Results: Both miR-431-3p and miR-500a-5p gene expressions were decreased in active TB patients versus either LTBI or NIHS group, while miR-1258-5p gene expression was increased in both active TB and LTBI groups versus NIHS group (all p values <0.05). Multidrug Resistance Protein 1 (MDR1; an efflux pump excluding medical drugs from cells) gene expression was increased in active TB patients versus either LTBI or NIHS group (both p values<0.05). In vitro stimuli with ESAT-6 resulted in down-regulations of both miR-431-3p and miR-500a-5p genes, and up-regulation of miR-1258-5p. Transfection with miR-431-3p mimic partly reversed ESAT6-induced cell apoptosis along with reversions of its predicted target gene expressions, including MDR1, BCL2, RIPOR2, MEFV, HSF1, and MMP16.

Conclusions: MiR-431-3p was down-regulated both in active pulmonary TB patients and in response to Mycobacterium TB-specific antigen stimuli. MiR-431-3p augmented cell apoptosis of monocyte and regulated immune function via targeting BCL2 and MDR1. Over-expression of the miR-431-3p may be a new host-directed immunotherapy for active TB disease.

A. ■原著論文 (Original Paper) □病例報告論文 (Case Report)
B. □口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC71

肺結核感染對上吸呼消化道癌症病人的存活影響:一個觀察九年的全國性人口世代研究

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Prognostic effect of pulmonary tuberculosis on patients with upper aerodigestive cancers: A 9-year observational study in a nationwide cohort

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Purpose: The proportion of TB infection among cancer patients is rising in Taiwan, which is opposite to the decline of annual TB incidence in Taiwanese population. Our study aimed to clarify the risk subgroups and subsequent prognostic impact of TB infection toward patients with upper aerodigestive cancers.

Materials and Methods: We conducted a retrospective, nationwide cohort study from 1 January, 2009 to 31 December, 2014, based on Taiwanese National Health Insurance (NHI) reimbursement datasets, Taiwan Cancer Registry (TCR), catastrophic illness and cause of death data for Taiwan population and followed up all participants till the end of 2016. Patients newly diagnosed as oral cancers, nasopharyngeal cancer, laryngeal cancer and esophageal cancer using International Classification of Diseases for Oncology, third edition (ICD-O-3) from TCR were defined as our aerodigestive cancers cohort. Active TB infection was identified as a time-dependent variable in analyzing the risk subgroups and prognostic impact on our study cohort.

Results: Total 57,543 aerodigestive cancer patients were enrolled as our cohort. 890 patients (1.55%) were diagnosed as active pulmonary TB during the period of follow-up and the incidence of pulmonary TB was 502 per 100,000 person-years. The TB incidence was highest in patients with esophageal cancer (1443 per 100,000 person-years) and lowest in patients with nasopharyngeal cancer (236 per 100, 000 person-years). Risk factors for TB were age above 65 years (HR 1.94, 95% CI 1.62-2.33), male gender (HR 2.00, 95% CI 1.48-2.72), advanced cancer stages (stage III: HR: 1.79, 95% CI: 1.37-2.33, and stage IV: HR: 2.09, 95% CI: 1.63-2.68), COPD (HR: 1.35, 95% CI: 1.10-1.65) and old TB (HR: 3.29, 95% CI: 2.06-5.25). Further survival analysis demonstrated that those cancers patients with TB infection have a shorten survival than those without TB infection (HR: 1.86, 95% CI: 1.70-2.04), after matching cancer types, cancer stage and the calendar year of cancer diagnosis in both groups.

Conclusions: Aerodigestive cancers rank within the top ten mortality rate in Taiwanese population and the TB incidence of those cancer patients is much higher than general population. Our study showed that pulmonary TB infection act as a poor prognostic factor in those patients. Identifying the risk subgroups for TB is quite important not only in infectious disease control but also for outcome evaluation in those patients with aerodigestive cancers.

A. ☐原著論文 (Original Paper) ■病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC72

大葉性肺炎合併複雜性胸水摻雜結核肋膜炎於塵肺症個案

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Lobar pneumonia combined TB pleurisy in pneumoconiosis patient with complicated parapneumonic effusion

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Introduction:
For analysis with pleural LDH and ADA leucocyte differential count ratio in diagnosing TB pleruisy and parapneumonic effusion even malignancy were utmost points to work up. Sometime when these diseases co-occur, a complicated and prolonged course will occur in diagnosis and treatment.
Materials and Methods: case summary
A 47 year- old sloopy man suffered from cough with whitish and yellowish sputum for half month then dyspnea on exertion for 3-4months and exacerbation for 3-4 days. He had also suffered from rhinorrhea for 1 -2 months as history of allergic rhinitis accompany symptoms with more purulent nasal discharged than before, He denied fever, sore throat, dizziness, headache, nausea, vomiting, diarrhea or abdominal pain. His occupation was wall-digger worker for 10 years. He denied travel history or contact history. Due to mention above, he came to CM OPD for help. At OPD, BT was 36.9C. PE showed faint wheezing over both lungs and left lower lobe breathing sound, abdomen soft without tenderness or fullness, no pitting edema. Chest X-ray disclosed RLL infiltration increase, micronodules over BUL, left pleural effusion and cardiomegaly. At ordinary ward, fever was noted. Panadol 1# ST was noted. One touch was 86. Under the impression of pneumoconiosis, BUL with perilymphatic distribution, fever, suspect pneumonia related and left pleural effusion, he was admitted for further management. So empirical antibiotic treatment and pulmonary surveying were underwent.
Result:
Ultrasound guide aspiration was done on left pleural effusion, the mount: 440 ml, pleural effusion - glucose:89, LDH:968, total protein:5.3, Pleural fluid analysis-ppearanceYellow/Cloudy:RBC:360, WBC:5400, Neutrophil:2%, Lymphocyte:96% and 10/01 pleural effusion ADA:41, Intermittent fever during empirical antibiotics for 3 weeks, We added anti-TB drug AK35# QD +PZA 4# QD 5 after anti-TB regimen as HERZ fever and CXR improved though fever once as gout attacked, lung field became more clear . Under his relative stable condition and negative HIV test, he was discharged and OPD followed up. CT of chest depicted lobar pneumonia, pneumoconiosis and pleural effusion.
Discussion:
Whenever clinician encountered lymphocytic pleural effusion individuals in epidemic regions, TB pleurisy and malignancy should be first listed in priority of diagnosis though acute or chronic lung diseases coexist in the same case.
Conclusion
ADA of pleural fluid demonstrated precise sensitivity and specificity for the differential diagnosis about TB pleurisy and bacterial parapneuomic effusion. Pleural LDH played as biomarker to differentiate complicated or uncomplicated pleura effusion especially for empyema. The emphasis is on lymphocytic pleurisy especially with chronic lung disease such as COPD , occupational lung disease etc.

A. ■原著論文 (Original Paper) ☐病例報告論文 (Case Report)
B. ☐口頭報告 (Oral Presentation) ■海報競賽 (Post)

PC73

免疫檢查點蛋白與非結核分枝桿菌肺病：游離型 T 細胞免疫球蛋白黏液分子 3 之角色

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Immune checkpoint proteins in patients with pulmonary nontuberculous mycobacterial isolates: the role of soluble T-cell immunoglobulin mucin domain-3 (sTIM-3)

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Purpose: The incidence of nontuberculous mycobacteria lung disease (NTM-LD) is increasing worldwide. Even though the ATS criteria for NTM-LD diagnosis is available, it is challenging to differentiate pulmonary NTM colonization from NTM-LD. Recently, reports showed that immune checkpoint proteins including programmed cell death protein-1 (PD-1) and T-cell immunoglobulin mucin domain-3 (TIM-3) are correlated with prognosis of certain infectious disease. However, the values of soluble PD-1 and TIM-3 on differentiating NTM-LD from colonization remains unclear.

Materials and Methods: This is a prospective study conducted during 2016-2019 at Taipei Veterans General Hospital. We enrolled adult patients with respiratory samples culture-positive for NTM and recruited healthy controls. According to ATS diagnostic criteria, we classified patients into NTM-LD group and NTM colonized group. All patient received blood drawing to test soluble TIM-3 and soluble PD-1 by enzyme-linked immunosorbent assays (ELISA). We assessed factors associated with NTM-LD by multivariate logistical regression.

Results: We total enrolled 101 patients, including 22 controls and 79 patients with respiratory NTM isolates (49 NTM-LD, 30 colonization). We found that soluble TIM-3 was significant higher in NTM colonization group than in NTM-LD and control groups (856.3±518.7 versus 595.3±352.6 437.0±267.4 pg/ml). But, the level of soluble PD-1 was not significantly different between groups. Of NTM-positive patients, sTim-3 was associated with NTM-LD (per 100-pg/ml increment, OR 0.865 [95% CI 0.768-0.974], p=0.016). In multivariate analysis for factors associated with NTM-LD, soluble TIM-3 (per 100-pg/ml, OR 0.658 [0.502-0.864], p=0.003) and extensive lung involvement (radiographic score ≥5) (OR 11.304 [1.612-79.253], p=0.015) are strongly associated with NTM-LD after adjustment for age, sex, body mass index, smear-positivity and NTM species.

Conclusions: Among patient with respiratory sample culture-positive for NTM, soluble TIM-3 was significantly higher in the colonized groups than in the ATS-meeting NTM-LD group and it was an independent factor to discriminate NTM colonization from NTM-LD. Our findings suggest that TIM-3 may have a role in the pathogenesis of NTM-LD. Further validated study is warranted to explore the prognostic values of TIM-3 and other immune-checkpoint proteins in NTM-LD.

台灣胸腔暨重症加護醫學會

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