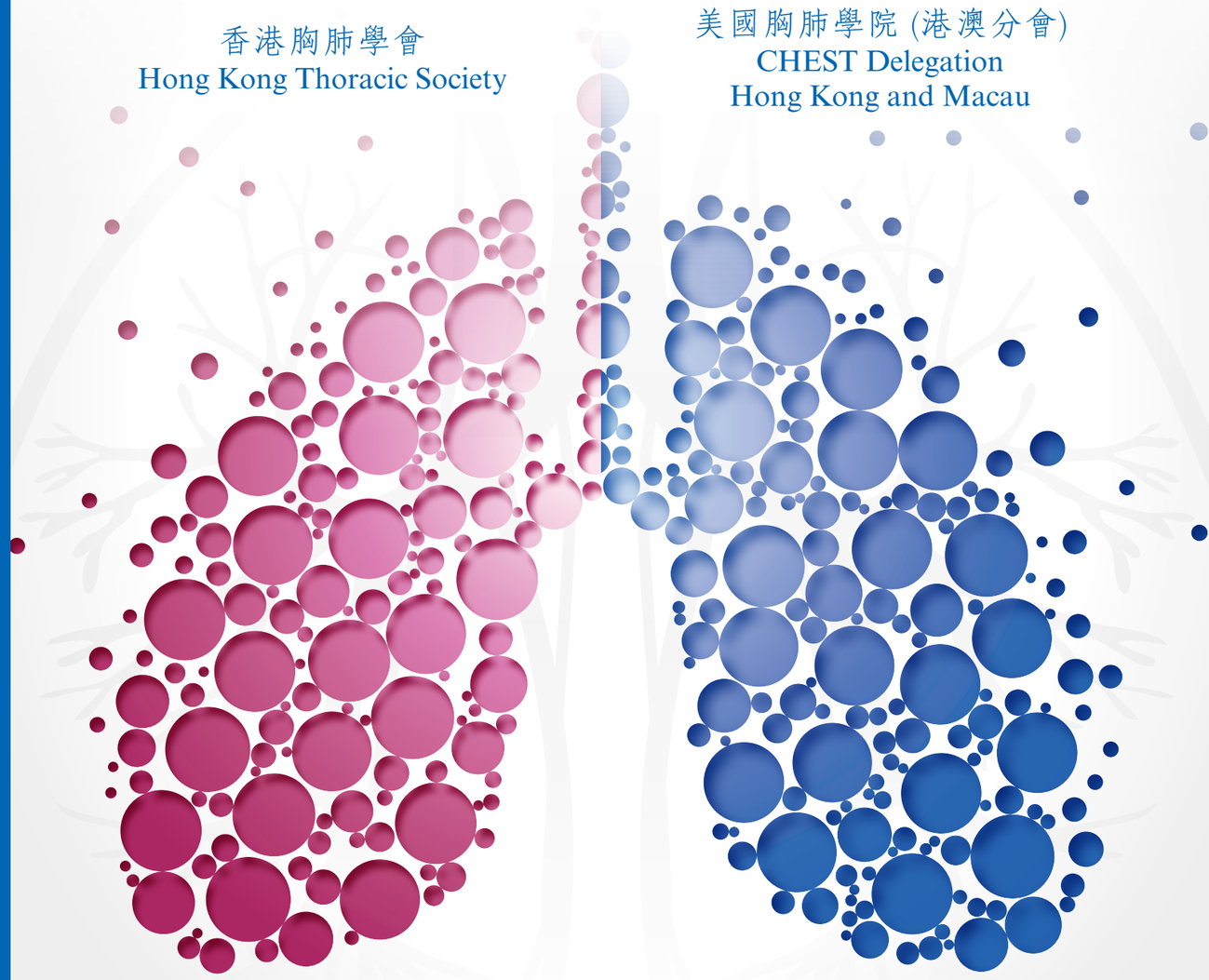
Volume 28 Number 2 • Jul 2018

聯合會員通訊
Newsletter

香港胸肺基金會
Hong Kong Lung Foundation

香港胸肺學會
Hong Kong Thoracic Society

美國胸肺學院 (港澳分會)
CHEST Delegation
Hong Kong and Macau



Hong Kong Thoracic Society

Hong Kong Lung Foundation

CHEST®
Delegation Hong Kong and Macau

A Trimonthly joint communiqué of Hong Kong Lung Foundatioin, Hong Kong Thoracic Society
& CHEST Delegation Hong Kong and Macau

2017/2019

HKTS
香港胸肺學會

Council of the
Hong Kong Thoracic Society

President
Dr. YEE Kwok Sang Wilson

Vice-President
Dr. LAM Chi Leung David

Honorary Secretary
Dr. LAM Sin Man Grace

Honorary Treasurer
Dr. NGAI Chun Li Jenny

Chief Editor: Newsletter & Website
Dr. LUI Mei Sze Macy

Address for Correspondence
Dr. LAM Sin Man Grace
Intensive Care Unit,
Pamela Youde Nethersole Eastern Hospital
3 Lok Man Road, Chai Wan, Hong Kong

Council Members
Dr. SO Kit Ying Loletta
(Immediate Past President)

Dr. CHAN Wai Ming
Dr. CHEUNG Chun Fong Jane
Dr. HO Chung Man James
Prof. HUI Shu Cheong David
Dr. KO Wai San Fanny
Dr. KWOK Yuk Lung
Dr. LAW Wai Lam
Dr. LO Ho Yin Angus
Dr. LO Yi Tat
Dr. MA Chan Chung
Dr. TSANG Wah Tak Kenneth
Dr. TSE Hoi Nam
Dr. TSE Pak Yiu
Dr. WONG Kam Cheung

CHEST Delegation Hong Kong and Macau
美國胸肺學院 (港澳分會)

Executive Committee of the
CHEST Delegation
Hong Kong and Macau

President
Dr. NG Chun Kong

Vice-President
Dr. LAM Wai Kei

Honorary Secretary/Treasurer
Dr. LEE Man Po

Global Governor
Dr. CHAN Chun Kwong Jane

Address for Correspondence
Dr. LEE Man Po
Department of Medicine
Queen Elizabeth Hospital
30 Gascoigne Road, Kowloon
Hong Kong

Executive Committee Members
Dr. LAM Chi Leung David
(Immediate Past President)

Dr. CHAN Wai Man Johnny
Dr. CHANG Kwok Chiu
Dr. CHOO Kah Lin
Dr. CHU Chung Ming
Dr. CHEUNG Pik Shan Alice
Dr. HO Sheng Sheng Alice
Dr. LAM Chung Mei Jamie
Dr. LAU Chun Wing
Dr. LAU Kam Shing
Dr. NG So Shan Susanna
Dr. WONG Chi Fong
Dr. WONG King Ying
Dr. WONG Mo Lin Maureen
Dr. WONG Wei Yin Ida
Dr. YEUNG Yiu Cheong

HKLF
香港胸肺基金會

Executive Board of
Hong Kong Lung Foundation

Chairman
Dr. WONG Mo Lin Maureen

Vice-chairman
Dr. CHAN Wai Man Johnny

Honorary Secretary
Dr. HO Chung Man James

Honorary Treasurer
Dr. TSE Pak Yiu

Address for Correspondence
Dr. HO Chung Man James
Department of Medicine
Queen Mary Hospital
102 Pokfulam Road,
Hong Kong

Executive Board Members
Dr. TAM Cheuk Yin
(Immediate Past Chairman)

Dr. CHAN Chun Kwong Jane
Dr. CHAN Hok Sum
Dr. CHAN Kin Sang
Prof. CHAN Mo Wah Moira
Dr. CHAN Shiu-lun
Dr. CHAN Wai Ming
Dr. CHOO Kah Lin
Dr. CHU Chung Ming
Dr. HO Sheng Sheng
Prof. HUI Shu Cheong, David
Prof. IP Sau Man, Mary
Dr. KO Wai San Fanny
Dr. LAI Kei Wai Christopher
Dr. LAM Chi Leung, David
Prof. LAM Wah Kit
Dr. LAU Chun Wing Arthur
Dr. MOK Yun Wing Thomas
Dr. NG Chun Kong
Dr. PANG Che Kong Joseph
Dr. SO Kit Ying Loletta
Dr. SO Shun Yang
Dr. TSANG Wah Tak, Kenneth
Dr. WONG Kam Cheung
Dr. YAM Yin Chun Loretta
Dr. YEE Kwok Sang, Wilson

2017/2019

HKTS/
CHEST Delegation HK and Macau
Conjoint Website

http://www.hkresp.com

FROM THE EDITOR

Topics are all hot in this issue of newsletter, in this meltingly hot summer.

Liquid biopsy is an important advent in lung cancer diagnostic that eases the pressure on tissue requirement for molecular profiling of lung cancer. Dr. Anthony Yau, Kowloon Hospital, has summarized the current state of art on the use of liquid biopsy. Dr. Fiona Lim, clinical oncologist of Princess Margaret Hospital, has kindly shared the knowledge and experience on Stereotactic Body Radiotherapy (SBRT) for early stage lung cancer. The availability of SBRT has brought hopes for a superior local control with good safety profile, in medically inoperable patients with lung cancer.

We are also grateful to have Mr. SW Ng, Ms. Maggie Lit and nursing coworkers from five HA hospitals, who shared with us a clinical audit on the NIV care program. Mr. William Ko, occupational therapist of Kowloon Hospital, shared the experience in pulmonary rehabilitation program for chronic respiratory diseases other than COPD. In addition to the clinical meeting summaries from Dr. Pauline Yeung (AICU, QMH) and Dr. CK Lo (CTSU, QEH), we have the chance to know about the three young fellows who are successful in the recent exit examination. The newsletter draws to a close by Dr. Ryan Ko, TMH, with his pen full of fatherly love.

Macy Lui

Department of Medicine
Queen Mary Hospital
102 Pokfulam Road
Hong Kong
Email: drmslui@hku.hk

Instructions to Contributors

Contributions from invited guests and all members are welcomed. Articles should be prepared with suitable software such as MS Word. Attachments such as tables should be saved in the same file. The content of the articles should avoid inclusion of details identifiable of the subjects. The file should be sent via e-mail to the Editor. While the accuracy of the materials published is the responsibility of the contributors, they must ensure that the materials submitted do not infringe copyright. Contributors should be aware that submitted materials would also be posted to our website unless they specifically indicated otherwise.

Disclaimer

CONTENT

1–2 SEPTEMBER 2018
HONG KONG

SYMPOSIUM ON ASTHMA AND COPD: NOW AND FUTURE

Organizers:

Hong Kong Thoracic Society

CHEST®
Delegation Hong Kong and Macau

Sponsor:

Hong Kong Lung Foundation

Please refer to *www.hkresp.com* for event details and registration

SPOTLIGHT TOPICS

Liquid biopsy

Dr Anthony PY Yau
Respiratory Medical Department
Kowloon Hospital

The development of targeted therapy in the treatment of non-small cell lung carcinoma (NSCLC) has emerged as a new hope for patients who are either physically not fit for operation or having late stage diseases. In-particularly, the identification of oncological activation of certain tyrosine kinases, namely epidermal growth factor receptor (*EGFR*), rearrangements of the anaplastic lymphoma kinase (ALK) gene, ROS1 and BRAF mutations helps to identify potential targets for treatment. For those who develop EGFR tyrosine kinase inhibitor (EGFR-TKI) resistance during targeted therapy, the identification of T790M mutation guides the next step of management (e.g. the use of third generation EGFR-TKI Osimertinib).

Traditionally, the identification of these oncological mutations relies on tissue samples. The advancement in interventional pulmonology techniques, such as Endobronchial Ultrasonography (EBUS), Electromagnetic Navigation Bronchoscopy (ENB) and Pleuroscopy, can improve diagnostic yield. However, tissue sampling may fail in some occasions. Around 30-40% of NSCLCs are not testable, while 10% to 20% of all NSCLC biopsies are inadequate for molecular analysis because of a lack of either sufficient tumor cells or amplifiable DNA. Up to 25% of patients are too weak for invasive procedure. False negative results also occur, due to intra and inter-tumoural heterogenicity.

The identification of circulating tumour cells (CTC) and cell free tumour DNA (ctDNA) in peripheral blood provides an alternative way to identify the genotype in a less invasive manner. CTCs were thought to detach from the primary tumour through the epithelial-mesenchymal transition (EMT) process, which allowing tumour cells to gain motility before penetration into the blood stream. Although CTCs were first identified in 1869 in a case of breast cancer during autopsy, its clinical application is limited by the need for complex cellular isolation platforms.

Cell free tumour DNA (ctDNA) was first identified in 1948. It was thought to be derived from tumour deposits and CTCs. Identification of ctDNA by PCR based platforms have the advantage of short turnaround time of as short as one day. But it can only cover a short range of mutations e.g. EGFR mutations. The United States Food and Drug Administration (FDA) approved platform, Cobas v2, is an example that utilizes allele specific real time PCR techniques to detect EGFR mutations (table 1). Next generation Sequencing (NGS)-based plasma genotyping platforms can give a much broader picture, at the expense of longer turnaround time. Generally speaking, these new investigation modalities are highly specific, but it may also detect allelic alterations that are present at a low frequency or of unknown clinical significance.

Nonetheless, ctDNA assays are not perfect. Due to the variable amount of tumour DNA being spilled over to the circulation, false negative results occur. The sensitivity of liquid biopsies ranges from 60% to 80%. Also, liquid biopsies do not give information for the programmed death-ligand 1 (PD-L1) tumour proportion score.

The International Association for the Study of Lung Cancer (IASLC) recommended the use of liquid biopsy to identify EGFR mutations if tissue is limited and/or insufficient for molecular testing. Based on expert consensus, physicians may also use liquid biopsies to identify EGFR T790M mutations in lung adenocarcinoma patients with progression or secondary clinical resistance to EGFR-TKI. However, there is insufficiency evidence to support the use of liquid biopsies for the diagnosis of primary lung adenocarcinoma for the time being.

Table 1. Mutations detected by cobas v2

G719X mutations (G719S, G719A, G719C) in exon 18
Deletions and complex mutations (29 types) in exon 19
T790M and S768I mutation in exon 20
Common insertions (5 types) in exon 20
L858R (2 types) and L861Q mutation in exon 21

Reference

1. Journal of Thoracic Oncology Vol. 11 No. 10: 1690-1700
2. Cancer Discov. 2014;4(6):650. Epub 2014 May 6.
3. A case of cancer in which cells similar to

those in the tumors were seen in the blood after death. Aust Med J. 1869;14:146–9.

4. Les acides nucleiques du plasma sanguin chez l'homme. C R Seances Soc Biol Fil. 1948;142:241–3
5. Association Between Plasma Genotyping and Outcomes of Treatment With Osimertinib (AZD9291) in Advanced Non-Small-Cell Lung Cancer. J Clin Oncol. 2016;34(28):3375. Epub 2016 Jun 27.
6. Prospective Validation of Rapid Plasma Genotyping for the Detection of EGFR and KRAS Mutations in Advanced Lung Cancer. JAMA Oncol. 2016 Aug;2(8):1014-22.
7. EGFR mutation detection in circulating cell-free DNA of lung adenocarcinoma patients: analysis of LUX-Lung 3 and 6. Br J Cancer. 2017;116(2):175. Epub 2016 Dec 22.
8. Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. Journal of Thoracic Oncology Vol. 13 No. 3: 323-358

Stereotactic body radiotherapy for early stage non-small cell lung cancer

Dr Fiona Lim
Department of Oncology
Princess Margaret Hospital

Introduction

Lung cancer is the second most common cancer in Hong Kong 2015. (1) About 85% are non-small cell lung cancer (NSCLC) and among them 15-20% are early stage I-II diseases. Radical surgery was the standard care for early stage diseases with reported 5-year overall survival of around 60%. (2) For those who refused surgery or considered medically inoperable due to advanced age or co-morbidities, conventional radiotherapy of 60 to 66 Grays (Gy) given in 30 to 33 daily treatments over 6 to 6.5 weeks were the alternative. However, the reported 5-year overall survival is much lower and ranged from 20-30%.(3-4) Local recurrence was the most common reason of failure with a median rate of 40%. (3) Although a radiation dose-response relationship had been demonstrated for NSCLC, a high radiation dose given by conventional radiotherapy technique was limited by the associated toxicities to normal tissues especially esophagitis and pneumonitis. (5-6)

Stereotactic body radiotherapy (SBRT) originates from the use of stereotactic radiosurgery to intra-cranial tumors. It is a unique form of external radiotherapy which allows delivery of a high radiation dose precisely to the tumor over one to few (usually less than 5) treatment fractions while minimizing radiation to adjacent normal tissues. The rationale and specific techniques of SBRT for early stage NSCLC will be reviewed in this article.

Rationale of SBRT compared with conventional radiotherapy

The ionizing effects from radiation to tumor and normal tissues depend on the 5 R's of radiobiological principles, namely radiosensitivity, repair, repopulation, redistribution and reoxygenation of cells. Linear-Quadratic model (LQ) (7) is the most commonly used tool to quantify radiation-induced cell kill, in what the linear cell kill was due to unrepairable lethal damage from a single hit and quadratic cell kill was by the cumulative repairable cell damage from multiple hits. To compare the biological effects various radiation dose and fractionation schedules on tumors and normal tissues,

biological effective dose (BED) calculation could be used which take into account the dose per fraction (d), number of treatments (n), total dose (nd) and radiosensitivity of tissue (α/β, usually 3 for normal tissue and 10 for tumor) :

$$BED = nd\left(1 + \frac{d}{\alpha/\beta}\right)$$

Table 1 showed the BED to tumor of commonly used SBRT regimes compared with the conventional radiotherapy schedule. In general, SBRT delivers a much higher BED frequently over 100Gy. This together with other proposed mechanisms including vascular damage and immune-modulation underlie the potential benefits of SBRT in better local tumor control. (8)

Table 1. Biological effective dose (BED) of common SBRT regimes and conventional radiotherapy

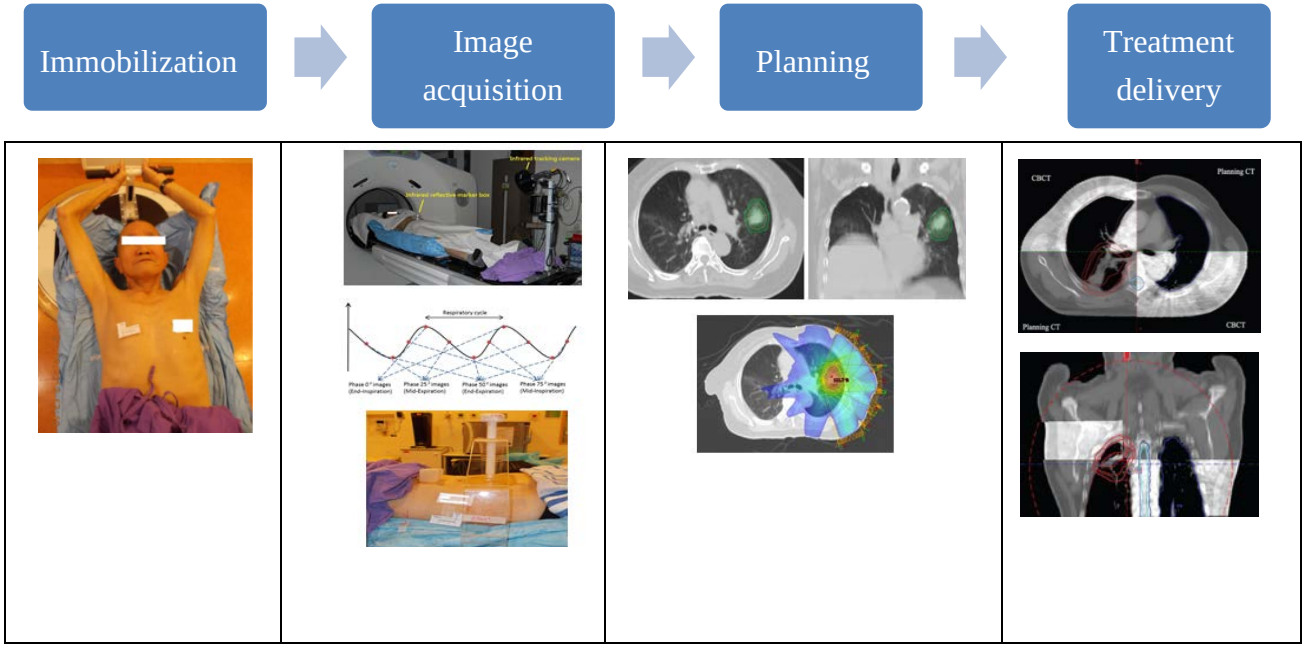
No of fractions	Dose per fraction (Gy)	BED (Gy)
Conventional radiotherapy		
30-33	2	72-79.2
SBRT regimes		
3	15	112.5
3	18	151.2
5	10	100
5	12	132
8	7.5	105

SBRT technique

The success of SBRT lies in the ability to deliver a high radiation dose precisely and accurately to tumor while minimizing radiation to surrounding normal tissue in order to optimize the therapeutic ratio. This requires integration of advanced techniques during the whole radiotherapy planning procedure as

highlighted in Figure 2 to ensure accurate repositioning from simulation to treatment and organ motions management during treatment. To start with, patient should be immobilized in a reproducible and comfortable position to minimize intra-treatment motion. Usual position is supine with arms above head to facilitate beam entry from various angles, and immobilized using commercially available devices like body frames or vacuum cushions. The next step is acquisition of images during treatment position. Tumor motion should be evaluated during this stage to decide on the margin for treatment field. Four-dimensional (4D) computed tomography which records multiple images during the respiratory phases is most commonly used. Additional tumor motion control should be employed when there is large motion amplitude (usually ≥0.5-1cm), including abdominal compression, synchronization of radiation with a particular phase of respirator cycle (gating) and real-time movement of radiation beam following tumor motion (tracking). During planning phase, both tumor and surrounding normal tissues (e.g. lung, spinal cord, tracheal, bronchial system, heart) should be contoured with appropriate dose constrains given. Multiple radiation beams (usually 7-12) or arc rotations should be used to ensure conformal radiation dose to tumor and rapid decrease of dose levels outside it (dose fall-off). Lastly, sophisticated real-time image guidance (e.g. on-board cone beam computer tomography when on treatment couch) should be used to allow visualization of tumor, verification and correction of treatment position to same as simulation before radiation delivery.

Figure 2. Steps and key features in radiotherapy planning for SBRT in lung cancers



• Accurate and reproducible • Patient comfort	• Tumor motion assessment and management - 4D computer tomography - Abdominal compression - Respiratory gating - Tumor tracking	• Accurate target delineation (tumor and normal tissue) • Multiple beams • Conformal and sharp fall-off of dose outside target	• Image-guided radiation delivery

Evidences of SBRT for early stage NSCLC

Use of SBRT in medically inoperable stage I NSCLC with tumor diameter less than 5cm had been well accepted based on its proven efficacy, safety and superior outcomes when compared with conventional radiotherapy in numerous studies. Earliest evidence came from studies in Japan and the Indiana University in early 20's. Uematsu et al published their results in 2001 which showed a high local tumor control of 94% and 3-year overall survival of 66% after a median follow-up of 36 months in 50 patients (medically inoperable or refused surgery) with T1-2N0M0 NSCLC treated with SBRT (50-60Gy in 5-10 fractions over 1-2 weeks) (9). Thereafter, several prospective trials demonstrated the promising efficacy of SBRT in this group of patients with 3-year local control rate over 80-90% and 3-year overall survival of 50-70% (Table 1). (10-16) The optimal radiation dose and fractionation scheme remained unclear. Dose-response relationship was first demonstrated by the phase I dose escalation study from the Indiana University using a starting dose of 8Gy per fraction for total 3 fractions delivered over 2 weeks and an increment of 2Gy per fraction to the maximum tolerated dose (MTD). In this study, MTD was not reached for T1 tumors, 60-66Gy in 3 fractions for T2 tumors of 2-5cm and 72Gy in 3 fractions for T2 tumors larger than 5cm. (17) Another multi-institutional study in Japan suggested a significantly better local control (91.6% versus 57.1%, $p<0.001$) and improved 5-year overall survival (70.8% versus 30.2%) with a minimum threshold BED of 100Gy. (18). However, too high BED may be of concern due to the more frequent grade 3-5 adverse events observed with high BED >146Gy in a meta-analysis of 34 observational studies containing a total of 2587 patients. Thus the authors proposed a medium (83.2-106Gy) or medium-to-high (106-146Gy) BED may be more beneficial. (19). Another challenge is

about the use of SBRT for “centrally located” tumors, which is defined as tumors within 2cm of proximal bronchial tress (carina, left and right main bronchi, left and right upper lobe bronchi, intermedius bronchus, right middle lobe bronchus, lingular bronchus, left and right lower lobe bronchi). Some studies also included tumors touching or within 1-2cm of other mediastinal structures including heart, great vessels, esophagus and spinal cord. An early phase II prospective trial by Timmerman et al (20) reported a 6 % treatment deaths and an 11-fold increased risk of developing grade 3 or above toxicities after using SBRT 60-66Gy in 3 fractions in this group compared with those with peripherally located tumors. Subsequent studies therefore adopt a risk-adaptive approach with more fractionated scheme and showed promising results. One of them was the retrospective review of 63 patients treated with 60Gy in 8 fractions over 2.5 weeks in Vrije Universiteit (VU) University Medical Center of Amsterdam which showed a 3-year local control and overall survival of 90% and 60% respectively. Only 6.3% of patients experienced grade 3 toxicities and none had grade 4 or 5 toxicities (21). Another recently completed RTOG 0813 prospective trial also showed a safe dose escalation to 60Gy in 5 fractions with low grade 3 or above toxicities (18%) (22). Even with such approach, special precautions should be made when treating “ultra-central” lesions that are directly touching the proximal bronchus as mortalities as high as 21% had been reported after SBRT using 60Gy in 5 fractions. (23)

Table 1. Prospective studies of SBRT in medically inoperable NSCLC

	No of patients	Dose	Outcomes		≥ Grade 3 toxicity
			3-year local control	3-year overall survival	
Fakiris et al 2009 [10]	70 (48 peripheral tumors ; 22 central tumors)	T1: 3 x 20Gy T2: 3 x 22Gy	88%	43%	16% (10.4% for peripheral tumors ; 27.3% for central tumors)
Baumann et al 2009 [11]	57	3 x 15 Gy	92%	60%	28%
Timmerman et al	70	3 x 20Gy	95%	55%	11%

2006 [12]		3 x 22Gy			
Koto et al 2007 [13]	31	3 x 15Gy 8 x 7.5Gy	78%	72%	3.2% *
Ricardi et al 2010 [14]	62	3 x 15Gy	88%	57%	3.4% *
Timmerman et al 2010 (RTOG 0236) [15]	55	3 x 18Gy	98%	56%	16%
JCOG 0403 [16]	100	4 x 12Gy	88%	60%	11%

* Only rate of pneumonitis was evaluated

Outcomes of SBRT versus conventional radiotherapy had been directly compared in three randomized controlled trials. The first one was from the Sweden Scandinavian SPACE trial (Stereotactic Precision And Conventional radiotherapy Evaluation) which enrolled 102 patients with stage I medically inoperable NSCLC to either receive SBRT of 66Gy in 3 fractions or conformal radiotherapy to 70Gy in 35 fractions. After a median follow-up of 37 months, there was no significant difference in progression free survival (Hazard ratio 0.85, 95% CI 0.52-1.36) and overall survival (HR 0.75, 95% CI 0.43-1.30) although SBRT arm had more T2 tumors (47% vs 25%). However, patients after SBRT had better health-related quality of life and less toxicities in terms of pneumonitis (19% vs 34%) and esophagitis (8% vs 30%) (24). Unlike the first one, the Australia Trans-Tasman "CHISEL" study showed a longer time to local failure (HR 0.29, p=0.002) and improved overall survival (HR 0.51, p=0.020) after SBRT (54Gy in 3 fractions) than conventional radiotherapy (60-66Gy in 30-33 fractions). Again, SBRT was well tolerated with only one grade 4 toxicity of cough. (25). The last one is the Canadian "LUSTRE" trial which is still under recruitment and results are eagerly awaited. (26).

On the other hand, far fewer studies assessed the use of SBRT in operable early stage NSCLC. The JCOG 0403 and RTOG 0618 were the two most well-known prospective phase II studies. In JCOG 0403 trial using 48Gy in 4 fractions, the 3-year local control and overall survival were 88% and 75% respectively. In the RTOG 0618 trial using 54Gy in 3 fractions, the 2-year local control and overall survival were 92.3% and 84.4% respectively. Both data were similar

to those reported in inoperable disease. When compared with surgery, there was concern about the risk of regional nodal recurrence after SBRT due to no systemic mediastinal lymph node dissection was done. Several propensity score-matching analyses showed similar overall survival and cancer specific survival after SBRT or sub-lobar resection in patients with high surgical risk. (27-31) Three phase III randomized studies had been initiated to compare SBRT with standard lobectomy however all were closed prematurely due to slow accrual. A pooled analysis of two of them including 58 patients showed similar 3-year local control rate and overall survival but slightly more regional nodal recurrence after SBRT than surgery (96% vs 100% ; 95% vs 79%; 13% vs 3.7% respectively). (32) Treatment was better tolerated with SBRT than surgery (grade 3 toxicities 10% vs 37%; mortalities 0% vs 4%). However, interpretation of results should be made with cautions due to the small sample size, not truly randomized nature of trials and relatively short follow-up period of median 40.2 months. Before the availability of more solid evidence, lobectomy remained the preferred treatment for patients with standard operative risk while SBRT serve as an alternative to patients with high operative risk as supported by the recommendations from international guidelines including National Comprehensive Cancer Network (NCCN) (33) and American Society of Clinical Oncology (ASCO). (34)

Our experience

In our hospital, SBRT had been used since mid 2011 for early stage I-II NSCLC with maximum tumor diameter of less than 5cm. All of them had good performance status of Eastern Cooperative Oncology Group (ECOG) 0-2 and were not surgical candidates either due to medical co-morbidities or patient refusal. Advanced age and impaired lung function were not absolute contraindication for SBRT. But patients who failed to have regular breathing cycle and cooperation during treatments were excluded. All patients had diagnostic computer tomography of thorax and upper abdomen with intravenous contrast for staging. Positron emission tomography (PET) is optional to exclude any occult regional lymph node involvement that precludes the use of SBRT. Histological diagnosis of lung cancer is preferred but clinical diagnosis is accepted if there is high radiological suspicion of primary lung cancer and histological confirmation is technically difficult.

All patients were immobilized with customized vacuum bag in supine position and with arms above head. Tumor motions with respiratory cycles were assessed by four-dimensional computer tomography (CT) using Varian Real-time Position Management System with

infrared tracking camera. Additional breathing control measures (e.g. abdominal compression, breath-hold, gating) were used if tumor motion amplitude were over 5mm. The target volume to be treated (i.e. planning target volume PTV) included the gross tumor seen on CT lung window and a 5mm margin to account for any set-up uncertainty. Radiation dose of 60Gy in 5 fractions over 2 weeks was given (50Gy in 5 fractions if centrally located tumors within 2cm from proximal bronchial tree). Cone beam CT on treatment couch was done before each treatment to allow online position verification and correction. After treatment, patients will be followed-up at one month, then every 3 months for 2 years, half yearly till 5 years and then yearly afterwards. Imaging with CT will be done at 3 months, 6 months then yearly interval.

From July 2011 till September 2016, a total of 39 patients were treated (male=24, 62%; female=15, 38%). Median age was 75 years (range: 51-85). Around one fourth (26%) had underlying chronic obstructive pulmonary disease, 18% had history of pulmonary tuberculosis and 15% had history of prior lung surgery (n=6, four had lobectomy and one had wedge resection for past history of lung cancer, one had wedge resection for benign pulmonary nodule). Half of them (49%, n=19) had T2aN0 and the other half (51%, n=20) had T1N0 diseases. Two third of them (62%) had baseline PET scan as initial workup. Median gross tumor volume and planning target volume were 17.7cm^3 (range: 2.8-56.8cm^3) and 48.3cm^3 (range: 12.50-120.60cm^3) respectively. All patients did not receive any concomitant systemic therapies.

After a median follow-up of 25 months (range: 3-75 months), twenty patients died (14 due to lung cancer, 6 due to non-cancer causes). The 1-year, 3-year and 5-year overall survival and cancer-specific survival were 89.7% and 100%, 46.1% and 55%, 33.6% and 40.1% respectively. Median overall survival was 35 months (range 3.5-74.6 months). Nineteen patients (48.7%) had disease progressions (Figure 3) but local progression was not common (n=9, 23%; and only 4 had local recurrence alone, 10%). The 1-year, 3-year and 5-year local control rate were 89.3%, 65.3% and 65.3% respectively. The 1-year and 5-year progression free survival were 71.8% and 35.5% respectively. Treatment was well tolerated. Fourteen patients (36%) had acute toxicities as defined by the Common Toxicity Criteria of Adverse Events (CTCAE). All were grade one (Table 2) except one grade three dyspnea and pneumonia required hospitalization which resolved afterwards. Three patients (8%) reported chronic toxicity of grade one chest wall pain.

Figure 3. Pattern of recurrence after SBRT

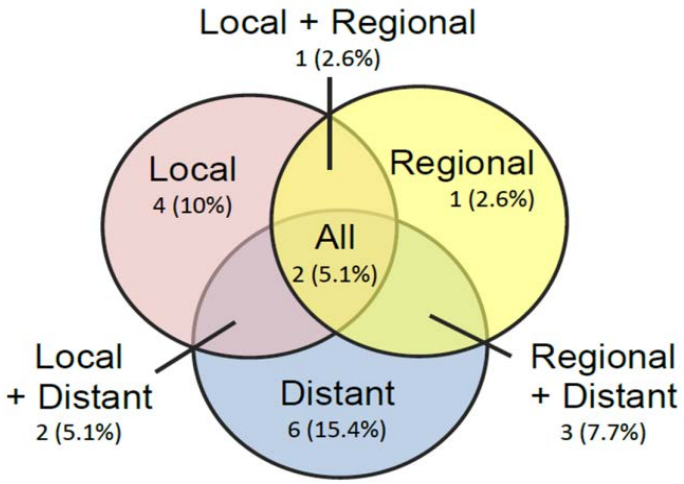


Table 2. Acute toxicities of SBRT

Grade 1	n (%)
Malaise	4 (10%)
Cough	3 (8%)
Nausea	2 (5%)
Chest wall pain	2 (5%)
Dyspnea	1 (3%)
Dizziness	1 (3%)
Chills	1 (3%)

Conclusion

For early stage I-II NSCLC who is not surgical candidate, SBRT achieves high local control rate, overall survival and cancer-specific survival comparable to radical surgery. Comparing to conventional radical chest radiotherapy, SBRT is better tolerated and should be the preferred treatment when radical surgery is not to be considered. Care should be taken when treating centrally located tumors with SBRT, preferably using less hyprofractionated regimes over 5-10 fractions to avoid excessive toxicities. Sophisticated techniques including reproducible and accurate positioning, tumor motions assessment and control, and image-guided radiation delivery should be employed to optimize the therapeutic ratio of SBRT. Use of SBRT in operable early stage NSCLC still debatable due to lack of phase III data, but it remained an option after multidisciplinary review.

Reference:

1. Hong Kong Cancer Registry. http://www3.ha.org.hk/cancereg/pdf/overview/Summary%20of%20CanStat%202015.pdf
2. Goldstraw P, Crowley J, Chansky K et al. On behalf of the International Association for the study of lung cancer international staging committee and participating institutions. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007 ; 2 : 706-714
3. Goldstraw P, Crowley J, Chansky K et al. On behalf of the International Association for the study of lung cancer international staging committee and participating institutions. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. J Thorac Oncol 2007 ; 2 : 706-714
4. Juan P. Wisnivesky, Marcelo Bonomi, Claudia Henschke et al. Radiation therapy for the treatment of unresected stage I-II Non-small cell lung cancer. Chest 2005 ; 128(3) : 1461-1467
5. Kupelian PA, Komaki R, Allen P. Prognostic factors in the treatment of node-negative non-small cell lung carcinoma with radiotherapy alone. IJROBP 1996 ; 36 : 607-613
6. Rosenzweig KE, Fox JL, Yorke E et al. Results of a phase I dose-escalation study using three-dimensional conformal radiotherapy in the treatment of inoperable nonsmall cell lung carcinoma. Cancer 2005 ; 103(10) : 2118-2127
7. Fowler JF. The linear-quadratic formula and progress in fractionated radiotherapy. Br J Radiol. 1989; 62: 679-694
8. Chi Q, Liao Z, Nguyen NP et al. Systemic review of the patterns of failure following stereotactic body tadiation therapy in early-stage non-small-cell lung cancer: clinical implications. Radiother Oncol 2010; 94(1): 1-11
9. Uematsu M, Shioda A, Suda A et al. Computed tomography-guided frameless stereotactic radiotherapy for stage I non-small cell lung cancer: a 5 year experience. Int J Radiat Oncol Biol Phys 2001; 51(3): 666-670
10. Fakiris AJ, McGarry RC, Yiannoutsos CT et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. Int J Radiat Oncol Biol Phys 2009; 75(3): 677-682
11. Baumann P, Nyman J, Hoyer M et al. Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic

body radiotherapy. JCO 2009; 27(20): 3290-3296

12. Timmerman R, McGarry R, Yiannoutsos C et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. JCO 2006; 24(30): 4833-4839
13. Koto M, Takai Y, Ogawa Y et al. A phase II study on stereotactic body radiotherapy for stage I non-small cell lung cancer. Radiother Oncol 2007; 85(3): 429-434
14. Ricardi U, Filippi AR, Guarneri A et al. Stereotactic body radiation therapy for early stage non-small cell lung cancer: results of a prospective trial. Lung Cancer 2010; 68_1): 72-77
15. Timmerman R, Raulus R, Galvin J et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010; 303(11): 1070-1076
16. Nagata Y, Hiraoka M, Shibata T et al. Prospective Trial of Stereotactic Body Radiation Therapy for Both Operable and Inoperable T1N0M0 Non-small Cell Lung Cancer: Japan Clinical Oncology Group Study JCOG0403. Int J Radiat Oncol Biol Phys 2015;93:989-996
17. Timmerman R, Papiez L, McGarry R et al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer. Chest 2003; 124: 1946-1955
18. Onishi H, Shirato H, Nagata Y et al. Hypofractionated stereotactic radiotherapy (HypoFXSRT) for stage I non-small cell lung cancer: updated results of 257 patients in a Japanese multi-institutional study. J Thorac Oncol 2007; 2: S94-100
19. Zhang J, Yang F, Li B et al. Which is the optimal biologically effective dose of stereotactic body radiotherapy for stage I non-small-cell lung cancer? A meta-analysis. Int J Radiat Oncol Biol Phys 2011;31: e305-316
20. Timmerman R, McGarry R, Yiannooutsos C et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. JCO 2006;24(30):4833-4839
21. Haasbeek JA, Lagerwaard FJ, Slotman BJ et al. Outcomes of stereotactic ablative radiotherapy for centrally located early-stage lung cancer. J Thorac Oncol 2011;6:2036-2043
22. Bezjak A, Paulus R, Gaspar LE et al. Efficacy and Toxicity Analysis of NRG Oncology/RTOG 0813 trial of stereotactic body radiation therapy (SBRT) for centrally located non-small cell lung cancer (NSCLC). IJROBP 2016;96(2):s8
23. Tekatli H, Haasbeek N, Dahele M et al. Outcomes of hypofractionated high-dose radiotherapy in poor-risk patients with “ultracentral” non-small cell lung cancer. J

Thorac Oncol 2016; 11(7): 1081-1089

24. Nyman J, Hallqvist A, Lund JA et al. SPACE-A randomized study of SBRT vs conventional fractionated radiotherapy in medically inoperable stage I NSCLC. Radiotherapy and Oncology 2016; 121: 1-8
25. Ball D, Mai T, Vinod S et al. CHISEL: A randomized phase III trial of SABR vs conventional radiotherapy for inoperable stage I non-small cell lung cancer. TROG 09.02, ALTG 09.05. WCLC 2017
26. Swaminath A, Wierzbicki M, Parpia S et al. Canadian Phase III Randomized trial of Stereotactic Body Radiotherapy versus Conventionally Hypofrationated Radiotherapy for Stage I, Medically inoperable Non-small-cell lung cancer-Rationale and protocol design for the Ontario Clinical Oncology Group (OCOG)-LUSTRE Trial. Clin Lung Cancer 2017; 18(2): 250-254
27. Palma D, Visser O, Lagerwaard FJ et al. Treatment of stage I NSCLC in elderly patients: a population-based matched-pair comparison of stereotactic radiotherapy versus surgery. Radiother Oncol 2011; 101:240-244
28. Varlotto J, Fakiris A, Flickinger J et al. Matched-pair and propensity score comparisons of outcomes of patients with clinical stage I non-small cell lung cancer treated with resection or stereotactic radiosurgery. Cancer 2013; 119: 2683-2691
29. Matsuo Y, Chen F, Hamaju M et al. Comparison of long-term survival outcomes between stereotactic body radiotherapy and sublobar resection for stage I non-small-cell lung cancer in patients at high risk for lobectomy: a propensity score matching analysis. Eur J Cancer 2014; 50: 2932-2938
30. Port JL, Parashar B, Osakwe N et al. A propensity-matched analysis of wedge resection and stereotactic body radiation therapy for early stage lung cancer. Ann Thorac SUrg 2014; 98: 1152-1159
31. Wang P, Zang D, Guo XD et al. A propensity-matched analysis of surgery and stereotactic body radiotherapy for early stage non-small cell lung cancer in the elderly. Medicine 2016; 95: e5723
32. Chang JY, Senan S, Paul MA et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomized trials. Lancel Oncol 2015; 16: 630-637
33. https://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf
34. Bryan JS, Megan ED, Erin BK et al. Stereotactic body radiotherapy for early-stage non-small-cell lung cancer: American Society of Clinical Oncology Endorsement of the American Society for Radiation Oncology Evidence-based guideline. JCO 2018; 26(7): 710-719

CLINICAL MEETING SUMMARIES ON 10TH MAY 2018

Iatrogenic chest injury from thoracocentesis

Drs CK Lo & Stephen KW Yam

Department of Cardiothoracic Surgery
Queen Elizabeth Hospital

Introduction

Bedside pleural intervention is one of the most commonly performed procedures in clinical practice nowadays. It aims at evacuating air and/or fluid from the thoracic cavity and obtaining biopsy from pleura, whether in emergency or elective, life-saving or palliative settings [1]. These include pleural tapping, pleural biopsy, and chest drain insertion.

Common indications for above procedures include pneumothorax, pleural effusion, haemothorax (iatrogenic or traumatic), blunt or penetrating traumatic injury, chylothorax, etc [2]. The average complication rate is quoted from 5% to 10% [1, 3]. Complications are usually classified into early/acute presentation (within the first 24-48 hours), and late/delayed presentation (beyond this initial period) [4]. Cumulative rates of 'early' and 'late' complications are 3–5% and 8–10%, respectively [1]. The commonest complications are pneumothorax, procedure failure, pain and haemorrhage [5]. In a meta-analysis including 24 studies and 6605 thoracocenteses, the incidence of post-procedural pneumothorax is found to be around 6% [6]. The risk of haemothorax is lower with an overall estimated incidence of 1% to 2% [7,8].

In subsequent sections of this article, we review cases which underwent surgical interventions for iatrogenic haemothorax after pleural procedures including pleural tapping, pleural biopsy and chest tube insertion. We also look into guidelines and advices for safer procedure in order to reduce the incidence of potential complications.

Method

This is a single-center retrospective cohort study, from year 1999 to 2018, in which we aimed to review patients who underwent surgical interventions for iatrogenic haemothorax following pleural procedures. Case records with operative diagnosis of 'haemothorax' were identified and retrieved from operative record listing function in Clinical Management System. Causes for haemothorax in identified cases were further studied, and those with iatrogenic haemothorax following pleural procedures were included in the study; while those with any other causes such as traumatic haemothorax or spontaneous haemopneumothorax were excluded. Data such as demographic information, indications and modalities of pleural procedures, modes and symptoms of presentation, drain output, intraoperative blood loss and outcome, etc. were also collected and studied.

Results

From 1999 to 2018, there were a total of 22 patients identified who underwent surgical

interventions for iatrogenic haemothorax following pleural procedures. Pleural procedures included pleural tapping in 5 patients, pleural tapping and biopsy in 9 patients, pigtail/small-bore catheter insertion in 2 patients, and chest drain insertion in 6 patients. Indications for pleural procedures included pleural effusion/empyema in 19 patients (86.3%) and pneumothorax in 3 patients (13.7%). Among these 22 patients, 14 of them are male (63.6%) and 8 are female (36.4%). Age ranged from 50 to 89 years old.

Their mode of presentation could be classified into early presentation (within 24 to 48 hours) in 13 patients (59.1%) and late presentation (beyond this initial period) in 9 patients (40.9%). Presenting signs and symptoms included shortness of breath, hypotension and even cardiac arrest in acute setting.

The mean output from pigtail or chest drain before surgical intervention was 1846ml (ranged from 900 to 2200ml). Intraoperative mean blood loss was 4500ml (ranged from 900 to 11500ml). 6 patients (27.3%) had bleeding source identified from lacerated intercostal artery, 1 (4.5%) from great vessel, 2 (9.1%) from diaphragmatic laceration, 2 (9.1%) from lung parenchymal laceration and 5 (22.7%) from chest wall muscles. Generalized diffuse oozing without specific single bleeding site was found in 6 patients (27.3%) who were already in condition of diffuse intravascular coagulopathy.

Predisposing factors for potential post-pleural procedural haemothorax were identified in 15 patients (68.2%), including coagulopathy (thrombocytopenia or INR more than 2) in 3 patients (6.8%), antiplatelet therapy in 6 patients (27.3%), end stage renal failure in 2 patients (9.1%), mechanical ventilation in 3 patients (13.7%), and previous pulmonary surgery in 1 patient (4.5%).

In-hospital mortality rate of entire cohort was 50%. Causes of death were acute renal failure, pneumonia, myocardial infarction and other complications secondary to massive blood transfusion. Mortality rate among early presentation group was 61.5% (8 out of 13 patients), and was 33.3% (3 out of 9 patients) among late presentation group.

Discussion

Pleural interventions from simple pleural tapping to chest drain insertion are commonly performed in clinical practice by practitioners from different specialties. Possible complications, haemothorax and visceral injury for example, could be potentially fatal and should be made aware of. Close monitoring with vital parameters and chest X-ray are mandatory after the procedures. Although post-procedural haemothorax is rare, suspicion should be raised especially there is clinical deterioration or radiological evidence of increasing effusion.

Safety techniques and advices to reduce the incidence of complications are described in the *British Thoracic Society guideline 2010* and *Society of Interventional Radiology and Cardiovascular & Interventional Radiological Society of Europe* [5, 11]. Non urgent procedures should be avoided in anticoagulated patients until INR <1.5, and those with anti-platelet drugs. Use of thoracic ultrasound guidance for marking the site of procedure is strongly recommended especially when pathology is loculated or is away from triangle of safety. With the use of ultrasound, the incidence of post-procedural pneumothorax could be significantly reduced, by as high as six-fold [6, 9]. In a review of 19,339 thoracocenteses performed in 414 hospitals, there was a 38.7% reduction in incidence of haemorrhage, with ultrasound guidance [10].

The preferred site for insertion of the needle should be inside the *triangle of safety* except loculated pathology outside the triangle. The triangle is bordered anteriorly by the lateral edge of pectoralis major, laterally by the lateral edge of latissimus dorsi, inferiorly by the fifth intercostal space and superiorly by the base of axilla [5]. The advantages are less muscular dissection, far away from diaphragm and invariable position of intercostal artery within the groove. The needle should be inserted just above a rib so as to avoid damaging the neurovascular bundle which runs in a groove in the inferior aspect [5]. The patient may take a semi-reclined position with arm raised and hand behind head, or may sit up and lean over a table with padding support the arms [5]. Measures to secure and manage the drainage system and to monitor the patient are also explained in the guideline.

However there were several limitations in this study. Firstly this was a single-center retrospective study. Secondly patients who had self-limited post-procedural haemothorax without surgical intervention or succumbed before surgical intervention were excluded. In addition details of procedures were absent including technique, site of intervention and experience of operating staff. To overcome above limitations, a multi-center prospective cohort study is necessary.

With better knowledge and greater awareness of the potential complications, preventive strategies and safety techniques, we hope that bedside pleural intervention could serve its purpose at its best and unnecessary iatrogenic injuries could be avoided.

Reference:

1. Mao M, Hughes R, Papadimos TJ, Stawicki SP. Complications of chest tubes: a focused clinical synopsis. Curr Opin Pulm Med. 2015;21:376–386.
2. Kwiatt M, Tarbox A, Seamon MJ, et al. Thoracostomy tubes: a comprehensive review of complications and related topics. Int J Crit Illn Inj Sci 2014; 4:143–155.
3. Bailey RC. Complications of tube thoracostomy in trauma. J Accid Emerg Med 2000; 17:111–114.
4. Collop NA, Kim S, Sahn SA. Analysis of tube thoracostomy performed by pulmonologists at a teaching hospital. Chest 1997; 112:709–713.
5. Havelock T, Teoh R, Laws D,Gleeson F; Group BTSPDG. Pleural procedures and thoracic ultrasound: British Thoracic Society Pleural Disease Guideline 2010. Thorax 2010; 65 (Suppl 2):ii61–ii76.
6. Gordon CE, Feller-Kopman D, Balk EM, Smetana GW. Pneumothorax following thoracentesis: a systematic review and meta-analysis. Arch Intern Med 2010; 170:332–339.
7. Mahmood K, Wahidi MM. Straightening out chest tubes: what size, what type, and when. Clin Chest Med 2013; 34:63–71.
8. Chan JWM, Ko FWS, Ng CK, Yeung AWT, Yee WKS, So LKY, Lam B, Wong MML, Choo KL, Ho ASS, Tse PY, Fung SL, Lo CK, Yu WC. Management of patients admitted with pneumothorax: A multi-centre study of the practice and outcomes in Hong Kong. Hong Kong medical journal, 15(6): 427-33
9. Duncan DR, Morgenthaler TI, Ryu JH, Daniels CE. Reducing iatrogenic risk in thoracentesis: establishing best practice via experiential training in a zero-risk environment. Chest 2009; 135:1315–1320.
10. Patel PA, Ernst FR, Gunnarsson CL. Ultrasonography guidance reduces complications and costs associated with thoracentesis procedures. J Clin Ultrasound 2012; 40:135–141.
11. Patel IJ, Davidson JC, Nikolic B, Salazar GM, Schwartzberg MS, Walker TG, Saad

Wa. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radio 2012; 23: 727-36

Overseas training at Massachusetts General Hospital

Drs Pauline Yeung and WM Chan

Adult Intensive Care Unit

Queen Mary Hospital

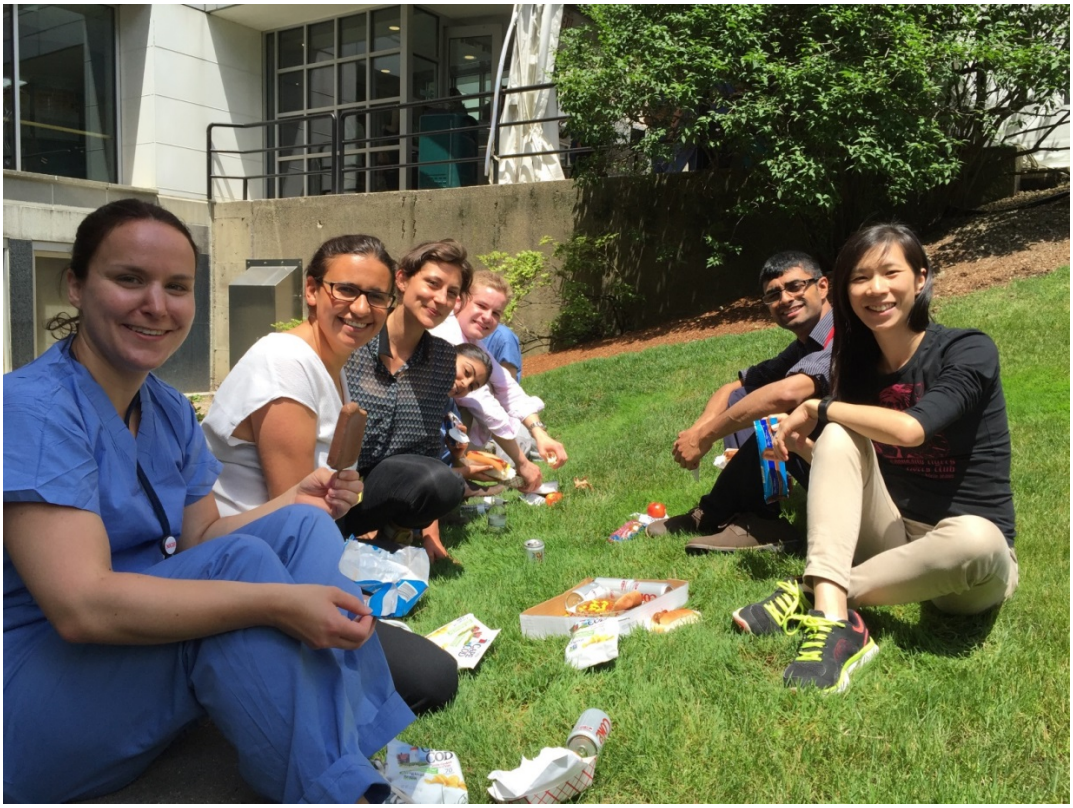
The six months spent as a Research Fellow at MGH was as an immersive, intellectual, and inspirational experience. I had hardly warmed up to the environment in the Eikermann Lab in the second week of reporting when I was entrusted the task of finalizing the manuscript for a multicenter, randomized, placebo controlled trial.[1] It was a foretaste of what was to follow in six months of challenging research work.

Despite working in a university-affiliated hospital and having personal research interests, the busy clinical schedules in Hong Kong precluded room to explore in depth the world of research. At MGH, researchers seize the opportunities of working in a world-class institution and devoted incredible amounts of time and energy into their research efforts. I soon found myself surrounded by highly-focused individuals and was motivated to be the same. Working with the goal of finishing a project in six months, my work mainly involved outcomes research. It required data acquisition and organizational skills in handling a dataset of more than 180,000 cases, hypothesizing and feasibility testing, knowledge in statistical software and analytical methods, but above all, a collaborative spirit where we all benefited from the synergism of different researchers. During my time in the lab, we submitted more than five scientific abstracts to the upcoming Anesthesiology 2017 meeting, and were awarded four oral presentations. The preparation for full manuscripts is underway.[2]

My main project was to examine the association between having a diagnosis of patent foramen ovale (PFO) and the outcome of perioperative ischemic stroke within 30 days of surgery. The hypothesis was that the perioperative period is one that posed excess risks of thrombi formation and paradoxical embolism, due to intraoperative hemodynamic changes that increase right-to-left shunting, and postoperative factors such as immobilization. In a cohort of more than 150,000 cases, we found that having a PFO was associated with a substantially increased risk of perioperative stroke (adjusted odds ratio 2.66), and that this PFO-attributable risk was in fact more increased in individuals otherwise considered at low risk for stroke. We also found evidence to support the biological mechanism of paradoxical embolism in PFO-related strokes. To date, the American Heart Association / American Stroke Association and the NICE-accredited guidelines do not address the management of patients with PFO undergoing surgery.[3,4] We believe our work has important implications for this patient subgroup, providing data to suggest that these patients may benefit from intensifying stroke preventive measures in the perioperative period. The manuscript is

currently under review in a reputable peer-reviewed journal.

Nothing will negate the lasting impact this fellowship has on my medical career and personal growth. I return to a position I already passionately love with a rekindled sense of curiosity and purpose. It is the cumulation of unreserved support from my mentor Dr Wai-Ming Chan, the unsuspecting generosity of Dr Eikermann to take on a complete stranger, the selflessness of my colleagues in the AICU to bear with my absence, and the sponsorship of the Hong Kong Lung Foundation that paved the way for this unforgettable journey.



References

1. Anstey MH, Wibrow B, Thevathasan T, Roberts B, Chhangani K, Ng PY, Levine A, DiBiasio A, Sarge T, Eikermann M. Midodrine as adjunctive support for treatment of refractory hypotension in the intensive care unit: a multicenter, randomized, placebo controlled trial (the MIDAS trial). BMC Anesthesiol. 2017 Mar 21;17(1):47.

2. Bagchi A, Ruldolph MI, Ng PY, Timm FP, Long DR, Shaefi S, Ladha K, Melo MFV, Eikermann M. The association of postoperative respiratory complications in 109,360 patients with pressure-controlled or volume-controlled ventilation. Accepted at Anaesthesia.

3. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, Fang MC, Fisher M, Furie KL, Heck DV, Johnston SC, Kasner SE, Kittner SJ, Mitchell PH, Rich MW, Richardson D, Schwamm LH, Wilson JA; American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2014;45:2160-236.

4. National clinical guideline for stroke. 2016. https://www.strokeaudit.org/SupportFiles/Documents/Guidelines/2016-National-Clinical-Guideline-for-Stroke-5t-(1).aspx (accessed June 15, 2017.)

THORACIC IMAGING CORNER

A mimicry of pulmonary embolism

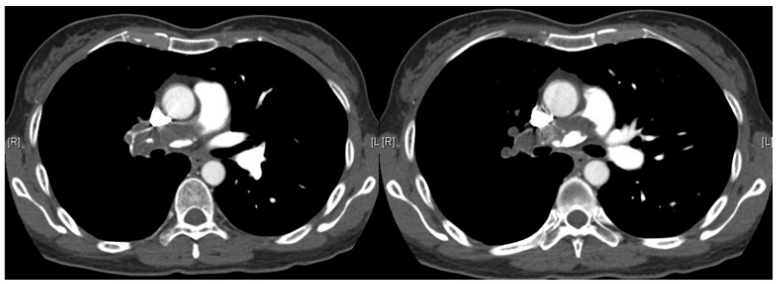
Drs Sonia Lam[1] & Macy Lui[2]

[1]Department of Diagnostic Radiology, University of Hong Kong

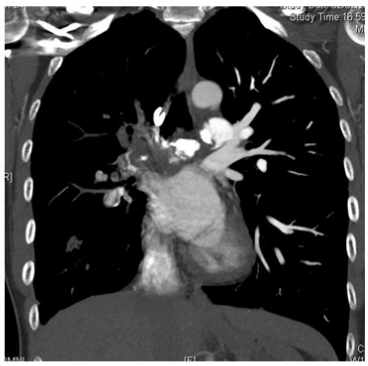
[2]Department of Medicine, Queen Mary Hospital

A lady in her forties presented to persistent chest tightness and dyspnea over a few weeks. She did not have any cough, sputum, wheezing nor fever. There was no ankle swelling, palpitation or orthopnea. She had unremarkable past health and was not on any medications or contraceptive pills. She was a non-smoker and was working as a private investment banker. She did have any record of long travel in the prior year.

She had undertaken investigations in the private sector. CXR and blood tests including D-dimer were unremarkable. CT pulmonary angiogram (CTPA) showed large filing defects with central calcification at right main pulmonary artery with extension into the lobar arteries supplying right upper lob, right middle lobe and right lower lobe down to segmental pulmonary arteries. She was treated as pulmonary embolism and started on low molecular weight heparin and warfarin. Her ECG showed sinus rhythm of 70/min, and echocardiogram did not reveal any evidence of pulmonary hypertension or right ventricular strain. Doppler ultrasound of lower limb veins and ultrasound abdomen and pelvis were both normal. She did not have any family history of thromboembolic diseases.



A B

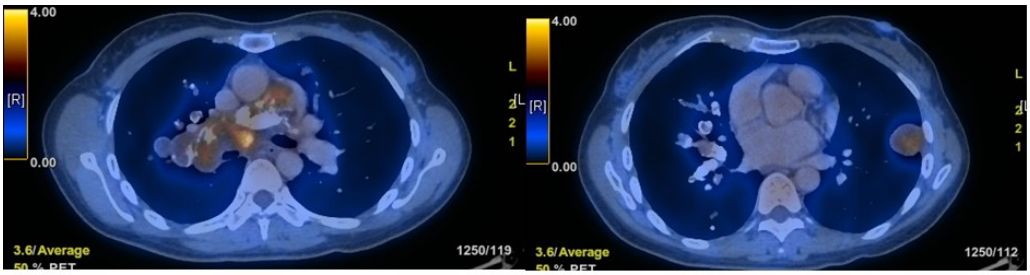


C

Figure A,B: axial images of CT pulmonary angiogram, at the level of right main pulmonary artery. Eccentric filing defect obliterated the lumen of right main pulmonary artery with extension to the branches. Figure C: coronal image of CTPA, showing the area of central calcification within the filing defect, and the relative reduction in arterial supply (oligemia) over right lung.

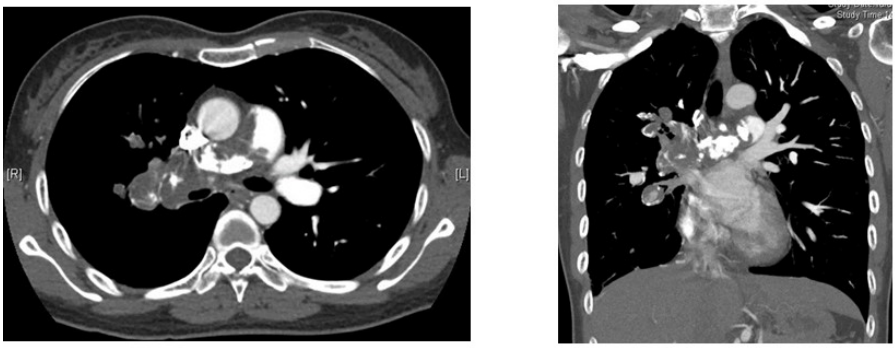
In view of the extensive involvement, she was assessed by cardiologist and cardiothoracic surgeon for thrombectomy. However, she was reluctant for invasive procedures including right heart catheterization as a pre-operative assessment.

She was followed up and was noted to have a new nodule over left lower zone on CXR a few months after the diagnosis of pulmonary embolism. A PET-CT scan was performed which found areas of metabolic activity (SUV 4) within the occluded pulmonary arteries. The left lower lobe lesion abutting the pleura was solid and avid (SUV 3). CT guided trucut biopsy of the lung lesion showed features compatible with spindle cell neoplasm. A repeated CTPA, in comparison with the prior CT, demonstrated the expansile features and invasion into the arterial wall and mediastinum. After multi-disciplinary review, the clinical impression was metastatic initimal sarcoma. She was reluctant for surgical biopsy and systemic chemotherapy. She was on palliative care.



FDG update within the right pulmonary artery involving the mediastinum.

The solid and avid left lung lesion



The 'calcified filing defect' was expansile and invaded the arterial wall and mediastinum, with loss of tissue planes.

Pulmonary intimal sarcoma is extremely rare tumor.(1) It usually manifests radiologically as a low-attenuation filling defect in pulmonary arteries on CT, often resembling pulmonary thromboemoblism. A few case reports had highlighted the more subacute and indolent presentation of intimal sarcoma in comparison to massive pulmonary embolism, given the often alarming extent of arterial involvement on CTPA. D-dimer has also been reported to be normal in cases of initimal sarcoma, which is considered atypical in thromboembolic disease. The absence of overt pulmonary hypertension on echocardiogram is not typical of chronic thromboembolic pulmonary hypertension (CTEPH), which can occasionally give rise to calcification within thrombi. Presence of low-attenuation lesion occupying the entire lumen of proximal and main pulmonary arteries, expansion of involved arteries and extraluminal

tumour extension, as observed in our patient, are features more in favour of pulmonary artery sarcoma and could help to distinguish from pulmonary embolic disease. Central calcification associated with the lesion as noted in our patient is also a feature less typical of pulmonary embolic disease where eccentric calcification would be expected instead. MRI could be specific in recognising pulmonary artery sarcoma since the tumour enhances with gadolinium contrast. These tumours are metabolically active and would show FDG positivity on PET-CT scans which could also allow differentiation from thrombi as in our patient.

DISSERTATION ABSTRACTS AND YOUNG FELLOWS' CORNER

Blood eosinophil and risk of exacerbation in chronic obstructive pulmonary disease patients: a retrospective cohort analysis

Dr Dave MC Chan
Department of Medicine & Geriatrics,
Princess Margaret Hospital

Dissertation Abstract

Background

Blood eosinophil is an easily available biomarker to reflect the eosinophilic inflammation in COPD patients, yet its association with exacerbation was inconclusive. It was uncertain which measurement, eosinophil percentage or absolute eosinophil count, should be used and what was the optimal cutoff.

Methods

247 COPD patients followed up in Princess Margaret Hospital were included. Blood eosinophil during stable disease state, baseline demographics and exacerbation data in 12 months before and 12 months after the index complete blood count (CBC) were recorded.

Results

Patients with blood eosinophil ≥ 2% was associated with more frequent exacerbations than patients with eosinophil < 2% in the 12 months before the index CBC (Mean exacerbation 1.12 in the high eosinophil group *vs* 0.68 in the low eosinophil group, p = 0.026) and in the 12 months after the index CBC (Mean exacerbation 1.07 in the high eosinophil group *vs* 0.34 in the low eosinophil group, p < 0.001). Adjusted odds ratio for exacerbation in 12 months after the index CBC for blood eosinophil ≥ 2% was 2.98. Comparing blood eosinophil percentage with absolute eosinophil count for exacerbation prediction using receiver operating characteristics curve, the area under the curve of eosinophil percentage was significantly higher than that of absolute eosinophil count (0.678 *vs* 0.640, p = 0.010). The optimal blood eosinophil cutoff for exacerbation prediction was 2.8%.

Conclusion

Blood eosinophilia was associated with higher exacerbation risk in COPD patients. Further studies are required to determine the optimal treatment strategy to reduce exacerbations in

eosinophilic COPD patients.

New Fellow's sharing

It is my honor to become fellow in the respiratory medicine. There are many exciting developments in our specialty, and I am interested in intervention pulmonology. I hope I can have further training in this field and contribute to the HKTS/ CHEST Delegation HK & Macau in the future.

Hobbies

I like playing sports, which is a good way to relieve the stress from work. I enjoy playing badminton because of the speed of the shuttle and fast pace of the game. I am also fond of hiking and jogging and had previously joined the Trailwalker and marathon.

Prognosis of malignant pleural effusion in lung cancer: a longitudinal study

Dr Fifian KY Chiang
Department of Medicine, Queen Mary Hospital

Dissertation Abstract

Background:

Malignant pleural effusion (MPE) due to lung cancer is an important condition in Hong Kong. Data informing its prognosis and outcomes is lacking. This study aims to identify factors predicting survival and the need of repeated thoracocentesis in patients with MPE related to lung cancer.

Methodology:

A longitudinal cohort study on adult subjects diagnosed with MPE and lung cancer at Queen Mary Hospital from 2011 onward was performed. Prognostic factors of survival were analyzed with Cox regression model. Predictors of the need of repeated thoracocentesis were identified by logistic regression analysis.

Results:

509 medical records were screened and 233 subjects were eligible for inclusion. 93% of MPE was adenocarcinoma. Better performance status ($p<0.001$), lower morbidities burden ($p=0.04$), absence of distant metastasis ($p=0.001$), higher blood albumin level ($p<0.001$) and use of anti-cancer treatment ($p<0.001$) were associated with better survival in patients with lung cancer and MPE. 36 (50.7%) subjects in the subgroup receiving best supportive care, 54 (42.5%) subjects on oral targeted therapies and 12 (34.3%) subjects on systemic anti-cancer therapy required repeated thoracocentesis at later course of the disease ($p= 0.25$). Higher blood albumin ($p=0.039$) and definitive MPE control measure upon diagnosis ($p<0.001$) including pleurodesis or indwelling pleural catheter insertion, were associated with reduced likelihood of subsequent pleural intervention.

Conclusion:

Survival of patients with MPE and lung cancer was prolonged with anti-cancer treatments, though the lifetime need of repeated thoracocentesis was not significantly reduced. Early definitive MPE control measures were required to reduce the need of repeated pleural drainage.

Career Aspiration

There have been vigorous research and development on pleural medicine in recent years and that have significantly affected our usual management practice. With the increasing number of patients and demand, further understanding on pleural medicine is warranted to provide an optimal management for our patients. I treasure different training activities on pleural medicine and hope to provide a better service to our patients. I am also interested to join activities organized by HKTS/CHEST Delegation HK & Macau.

Hobbies

I enjoy trail-walking as I can get close to nature and rest my soul. Travelling and exploring different cultures are also my favourite activities, do let me know in case you are looking for a hiking or travelling buddy!

Prevalence and risk factors of osteoporosis in COPD patients in a government hospital in Hong Kong

Dr Steven Tseng

Department of Medicine & Geriatrics, Kwong Wah Hospital

Dissertation Abstract

Introduction

It is well recognized that patients with COPD often suffer from extra-pulmonary conditions that affects their quality of life and survival. Osteoporosis is a well-known co-morbidity in COPD patients, and it poses a significant fracture risk. This is of particular importance as vertebral fractures can impair lung function and COPD patients are already at increased operative risks. Despite increasing interest on the topic, prevalence of osteoporosis in COPD patients in Hong Kong remains unknown. It is likely under-detected and thus under-treated. As a chronic illness, there are effective treatment modalities available for osteoporosis. Early detection, as well as early intervention may significantly affect management and outcome in COPD patients.

Aim

To determine the prevalence of osteoporosis in COPD patients at a local hospital and identify risk factors for osteoporosis in COPD patients

Methods

This cross-sectional study evaluated 111 COPD patients from a local hospital with dual-energy X-ray absorptiometry(DEXA) scans for bone mineral density(BMD) of the hip and lumbar spine.

Results

A total of 14(*12.6%*) COPD patients were osteoporotic, 64 patients (*57.7%*) had osteopenia, while 33(*29.7%*) had normal BMD. Compared with non-osteoporotic COPD patients, COPD patients with osteoporosis were characterized by a lower BMI(*19.72 ± 3.62 vs 22.94 ± 4.7, p = 0.016*), less years quitted smoking(*7.88 ± 4.73 vs 12.19 ± 8.86, p = 0.014*), more commonly on a proton-pump inhibitor([PPi], *42.8% Vs 13.4%, p = 0.018*), lower FEV_1/FVC%(*43.36 ± 7.98 vs 48.94 ± 12.33, p = 0.034*), FEV_1 actual in liters(*0.89 ± 0.44 vs 1.25 ± 0.56, p = 0.026*), FVC actual in liters(*2.03 ± 0.76 vs 2.50 ± 0.78, p = 0.039*) and higher CAT score (*16.07 ± 6.51 vs 12.09 ± 6.06, p = 0.025*). In a multivariate regression, only the use of a PPi (*odds ratio[OR] 4.781, 95% confidence interval [95% CI] 1.135 –*

20.129; p = 0.033) and BMI (*OR 0.760, 95% CI 0.614 – 0.939; p = 0.011*) were significantly associated with risk of osteoporosis in COPD.

Conclusion

The prevalence of osteoporosis in COPD patients is 12.6% in a local hospital in Hong Kong, which is higher than some of the reported prevalence in the local general population. Meanwhile, majority of patients were osteopenic (57.7%). The use of PPi and BMI were identified as independent risk factors for osteoporosis in COPD patients.

Career Aspiration & Hobbies

Over the years of training, it has been an eye-opening experience to witness the advances in respiratory medicine that shifted as rapidly as the landscape of Antarctica. I am most grateful for the ample learning opportunities provided by the Hong Kong Thoracic Society, from the regular clinical meetings, brilliant newsletters, to an abundance of workshops and seminars by world-class leaders which enables a budding physician to optimize care for patients. Given the right opportunity, I am eager to contribute to the society, sharing my experience with colleagues and the general public.

Of particular interest, the evolving and appealing efficacy of metastatic lung cancer treatment has been promising, and obtaining adequate tissue for diagnosis as well as molecular testing appears to be of increasing importance. In the future, I would like to further pursue and improve my skills in interventional pulmonology to facilitate appropriate treatment.

As a father of two toddlers, I thoroughly enjoy different modalities and aspects of sleep. However, travelling around the globe and learning about different culture has been very inspiring and rewarding too, as it is fully compatible with my favorite Chinese proverbs, "reading ten thousand books is not as useful as travelling ten thousand miles".

NURSING CORNER

An assisted ventilation program: "D.E.S.E.R.V.E."

Mr SW Ng[1], Ms SFW Wai[2], Ruth Lau[3], PS Kwan[4] & Maggie Lit[5]

[1]Department of Medicine & Geriatrics, United Christian Hospital,

[2]Department of Medicine, North District Hospital,

[3]Department of Medicine & Geriatrics, Princess Margaret Hospital,

[4]Department of Medicine, Pok Oi Hospital, [5]Department of Medicine, Queen Elizabeth Hospital

Non-invasive ventilation (NIV) has been shown to reduce intubation and in-hospital mortality in patients with acute exacerbation of COPD complicated by acute respiratory failure[1,2]. It has been shown that patients requiring NIV would have less complications[3,4] and better clinical outcomes if they were located at specialty areas[5,6,7,8] and cared by trained healthcare personnel[9,10,11,12,13]. Patients requiring non-invasive ventilation support are often cared in non-respiratory wards. High care burden and variations in quality of care are the challenges in managing patients requiring NIV support outside specialty areas.

According to an audit of Hospital Authority (HA) in Hong Kong, there were 3484 patients requiring NIV in the Department of Medicine of five acute hospitals in 2015[14]. In order to enhance the standard of care for patients requiring ventilation support, 38 designated ventilator beds have been funded in total 13 pilot hospitals in 7 clusters under HA since 2013.

Objectives

1. To establish a NIV program
2. To enhance care of patients requiring NIV treatment with minimal discomfort and complications
3. To evaluate the effectiveness of nursing care of the program

Methodology

DEsignated beds

Designated beds were equipped with enhanced respiratory equipment and monitoring capabilities in the Department of Medicine & Geriatrics of the pilot hospitals.

Standard of care (Appendix 1)

A standard of care[15] and a guideline[16] for patients with non-invasive ventilation had been established by HA in 2015 and 2014 respectively.

Enhancement of Competency

Training on advanced nursing care had been conducted respectively before the commencement of the program in the pilot hospitals and via the enhanced curriculum of corporate training.

Review and monitoring of **V**entilator utilization

The utilization rate and trend of NIV machines are being reviewed and monitored regularly for reporting and healthcare planning.

Evaluation

The compliance of enhanced nursing care and quality indicators had been audited in 2013, 2015 and 2017 respectively.

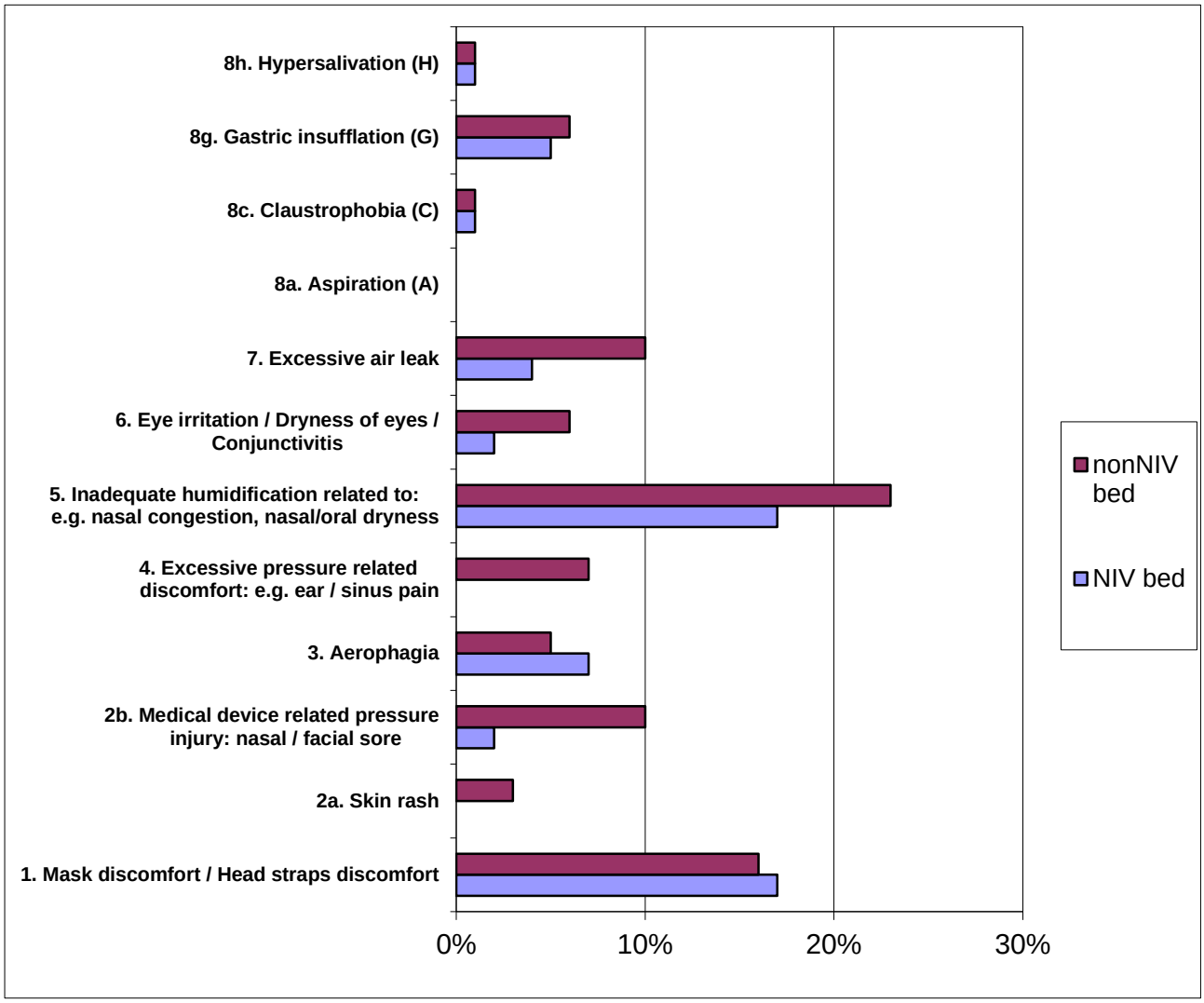
Results (Table 1 & Figure 1)

Three audits had been conducted for a total 569 cases (279 designated NIV beds and 290 general beds) for the audits in 2013, 2015 and 2017 respectively in the pilot hospitals. There was better compliance rate of nursing care of 98%-99% VS. 85%-95%, less medical device (mask) related pressure injury of 2%-5.6% VS. 8-10%, less incident rate of adverse effects of 7%-8% VS. 10.79%-12% between designated NIV beds and general beds. The mask leak was less as 20.93-23.1L/minute VS. 24.7-33.7L/minute in NIV VS. general beds.

Table 1. Three audit results in the year of 2013, 2015 and 2017 on Care of adult patients with non-invasive ventilation

Designated NIV VS. General beds, (n= sample size, 279VS.290)	2013 (n= 108 VS. 97)	2015 (n= 90 VS. 88)	2017 (n= 81 VS. 105)
Compliance of standard of care, % (range of all item compliance)	99% (85-100%) VS. 85% (55-100%)	98% (93-100%) VS. 92% (68-100%)	99% (93-100%) VS. 95% (84-100%)
Average air leak, Liter/minute	20.93L/min. (13.7-30.2L/min.) VS. 33.7L/min. (21.2-50.2L/min.)	21.1L/min. (9.7-46.3L/min.) VS. 24.7L/min. (7.8-47.0L/min.)	23.1L/min. (1-60L/min.) VS. 29.2 (0-70 L/min.)
Incident rate of medical device (mask) related pressure injury, %	2.5% VS. 8.95%	5.6% VS. 8%	2% VS. 10%
Incident rate of adverse effects, %	7.42% VS. 10.79%	8 % VS. 12%	7% VS. 11%

Figure 1. Incident rate of adverse effects of patients receiving NIV



Conclusion

Patients suffering from acute hypercapnic respiratory failure requiring non-invasive ventilation would have better nursing care, less complications and minimized discomfort during the NIV treatment if they were cared for in designated NIV beds with trained healthcare workers and enhanced monitoring capabilities. The associations between the better nursing care and other clinical outcomes should be further studies such as mask air leak and mortality rate.

References

1. Garpestad, E., Brennan, J. & Hill, N.S. (2007). Noninvasive Ventilation for Critical Care. *Chest*, *132*(2), 711-720.
2. Global Initiative of Chronic Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease (Revised 2017). Retrieved on 16th December, 2017 form http://goldcopd.org/download/326/

3. Fauroux, B., Lavis, J.F., Nicot, F., Picard, A., Boelle, P.Y., et al (2005). Facial side effects during noninvasive positive pressure ventilation in children. *Intensive care Med*. 31:965-969.
4. Gay, P.C. (2009). Complications of Noninvasive Ventilation in Acute Care. *Respiratory care*;54(2):246-257.
5. Ambrosino, M. and Vagheggini, G. (2008). Noninvasive positive pressure ventilation in the acute care setting: where are we? *European Respiratory Journal*; 31: 874-886.
6. British Thoracic Society (2016). The BTS/ICS Guideline for the ventilatory management of acute hypercapnic respiratory failure. Retrieved on 16th December, 2017 form https://www.brit-thoracic.org.uk/document-library/clinical-information/acute-hypercapnic-respiratory-failure/bts-guidelines-for-ventilatory-management-of-ahrf/
7. Crimi, C., Noto, A., Princi, P., Esquinas, A. and Nava, S. (2010). A European survey of noninvasive ventilation practices. *European Respiratory Journal*; 36: 362-369.
8. Nicholas, S.H. (2009). Where should Noninvasive Ventilation be delivered?. *Respiratory Care*;49(1): 72-87.
9. Carlucci, A., Delmastro, M., Rubini, F., Claudio, F., Nava, S. (2003). Changes in the practice of non-invasive ventilation in treating COPD patients over 8 years. *Intensive Care Med* 29:419-425.
10. Davies, D.J., Gentile, M.A. (2009). What does it take to have a successful Noninvasive ventilation program?. *Respiratory Care*; 54(1):53-59.
11. Hess, D.R., Pang, J.M. and Camargo, A.C. (2009). A survey of the use of Noninvasive Ventilation in academic emergency departments in the United States. *Respiratory Care*;54(10):1306-1312.
12. Hill, N.S. 2009. Where should Noninvasive Ventilation be delivered? *Respiratory Care* 2009;54(1):62-69.
13. Nava, S. and Ceriana, P. (2003). Causes of failure of Noninvasive Mechanical Ventilation. Respiratory Care; 49(3): 295-303.
14. Hospital Authority of Hong Kong (2015). HA Central Committee on Chronic Obstructive Pulmonary Diseases. Audit on Care of Patients with Non-Invasive Ventilation.
15. Hospital Authority of Hong Kong (2015). *Guidelines for specialty Nursing Services*: Respiratory Care. Standard no.2 Care of patient with Non-Invasive Ventilation(NIV).
16. Hospital Authority of Hong Kong (2013). *Respiratory working group*. NIV guidelines for acute exacerbation of COPD with acute hypercapnic respiratory failure.

Appendix 1

CARE OF ADULT PATIENTS WITH NON-INVASIVE VENTILATION (NIV)

STANDARD STATEMENT

Patient requiring non-invasive ventilation has oxygenation and ventilation status improved and the work of breathing reduced with minimal discomfort.

STRUCTURE / PROCESS STANDARD

1. Assess patient's level of consciousness, vital signs, respiratory status and oxygenation saturation (SpO_2).
2. Reassure and explain the reasons, procedures and potential complications to patient/ significant other.
3. Apply infection control measures according to hospital policy if indicated.
4. Take safety precautions for electric hazards and/or oxygen.
5. Set up and verify the NIV machine according to prescribed settings.
6. Set up appropriate alarm limits and examine all alarms accordingly.
7. Select and apply appropriate size and type of interface and accessories.
8. Minimize air leak but small leak is acceptable.
9. Facilitate patient to acclimatize to the NIV.
10. Minimize and managing facial skin problems related to interface.
11. Optimize oxygenation status
12. Observe and monitor patient's tolerance to NIV, work of breathing, patient-ventilator synchrony and physiological parameters reflecting respiratory status.
13. Maintain adequate hydration to prevent drying and thickening of oral secretions.
14. Identify complications and abnormalities and take appropriate action accordingly.
15. Ensure that necessary instruments and equipment are ready for emergency intubation.
16. Document the nursing observation and interventions.

OUTCOME STANDARD

1. Patient / significant others express understanding and satisfaction with the explanation and care given.
2. Patient's ventilation and oxygenation status are improved.
3. Patient's work of breathing has reduced to normal.
4. Patient experiences minimal untoward complications when using NIV.
5. Accurate records are maintained.

OCCUPATIONAL THERAPY CORNER

Pulmonary rehabilitation program for patients with chronic respiratory diseases other than COPD

Mr William Ko
Occupational Therapist II
Occupational Therapy Department, Kowloon Hospital

Introduction

Pulmonary rehabilitation program (PRP) is a non-pharmacological treatment approach for people with chronic respiratory diseases. Traditionally, majority of the PRP participants recruited were patients with chronic obstructive pulmonary disease (COPD). However, the ATS/ERS statement and the BTS guideline for PRP elaborated that pulmonary rehabilitation should not be limited to COPD patients, but also people with other chronic lung diseases (CLD), such as lung fibrosis, bronchiectasis, chronic asthma, and pre/post lung transplant. Although with different disease pathology and disease progression, these patients experience a range of daily symptoms, such as activity limitation, dyspnoea, impaired mood, and, lowered quality of life which are similar to those with COPD. On the other hand, research interest in pulmonary rehabilitation offered to people with other CLD has been increasing. For example, Cochrane review on pulmonary rehabilitation for people with interstitial lung diseases stated that pulmonary rehabilitation may bring improvements in functional exercise capacity; dyspnoea and quality of life to these patients. Studies on PRP for bronchiectasis patients also suggested that supervised pulmonary rehabilitation may help improve short term exercise capacity and health related quality of life.

Situation in Kowloon Hospital

In Kowloon Hospital, there has been an increasing trend of patients with other CLD being recruited to PRP (figure 1). Majority of the participants recruited suffered from pulmonary fibrosis, while the second and third most frequently recruited disease groups were bronchiectasis and asthma respectively (figure 2). In our hospital, patients with other CLD attended PRP together with COPD patients, such that patients with various respiratory conditions attended group sessions together.

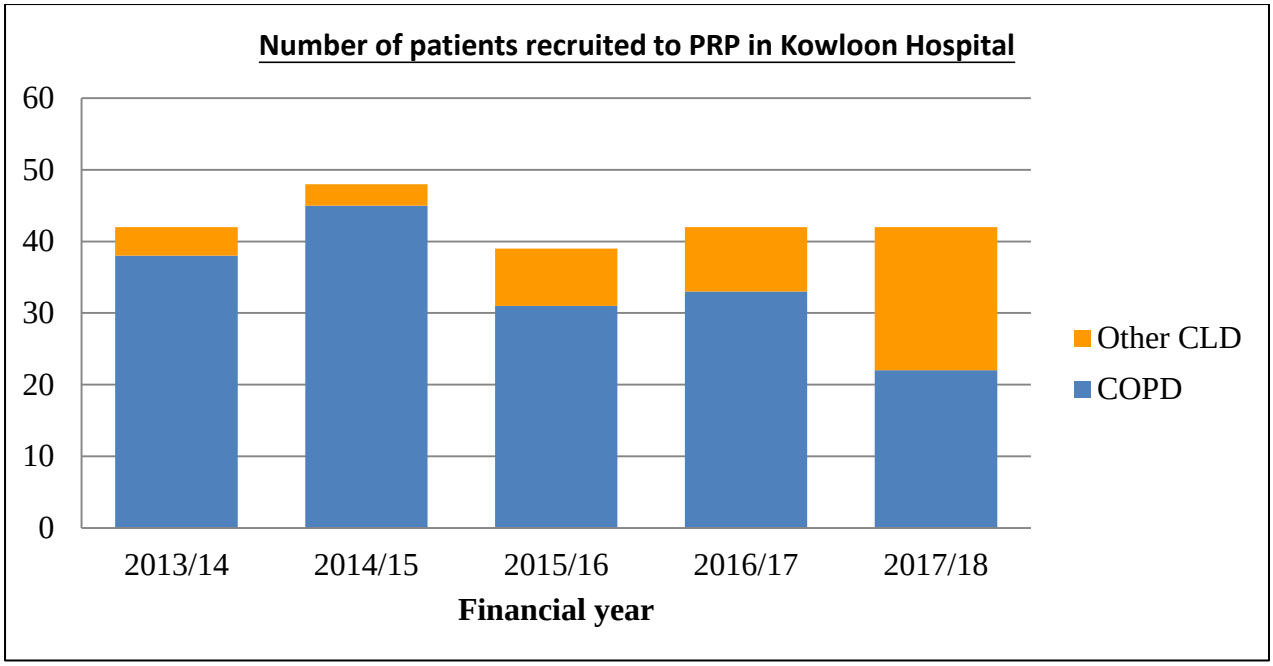


Figure 1 Distribution of PRP participants with diagnosis as COPD and other CLD

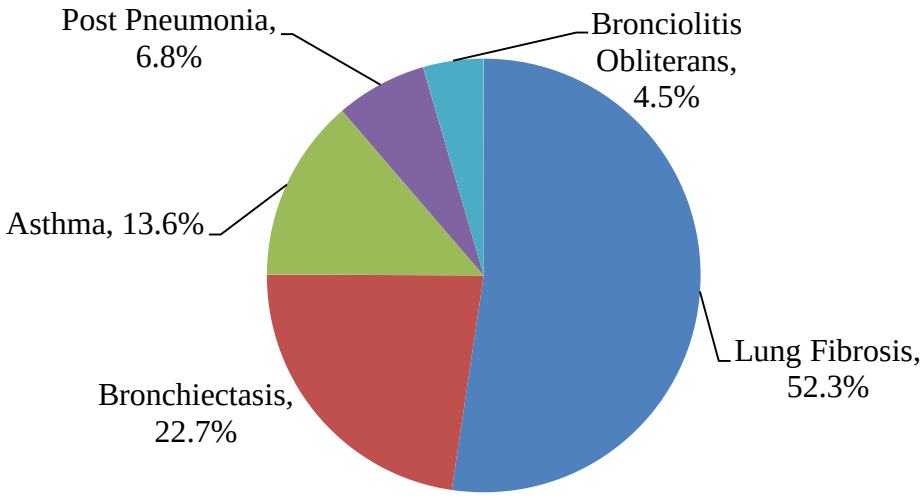


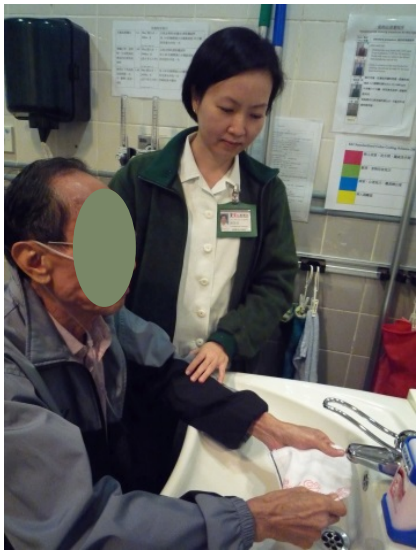
Figure 2 Distribution of diagnosis for PRP participants with other CLD

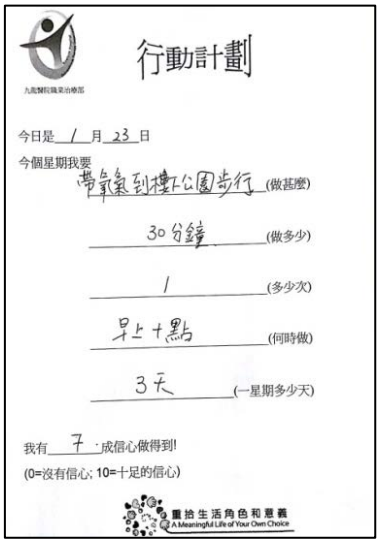
Self-management in PRP

In Occupational Therapy Department, other than improving exercise capacity, the focus of Occupational Therapists is to help patients cope with their symptoms in their daily lives and engage in a healthy lifestyle, so that they could enjoy a better quality of life. To achieve such rehabilitation goal, the department adopted the self-management approach to guide rehabilitation for both COPD and non COPD patients.

The self-management approach is different from traditional rehabilitation which focused only on exercise and knowledge education. Instead, Occupational Therapists collaborate

with patients and empower them to manage their own disease. Under this approach, Occupational Therapists conducted comprehensive assessments to understand patients' needs and developed individualised rehabilitation goals with patients. In training sessions, therapists encouraged skill practice in real life to enhance patients' self-efficacy in managing their symptoms. Individual counselling was also provided to help patients develop their own action plans for a healthy lifestyle (figures 3-6). Throughout the rehabilitation journey, Occupational Therapists formed partnership with patients and made use of motivational interviewing strategies to facilitate specific behavioural changes.





Figures 3-6 Upper left, education of self-management; Lower left & middle, practice of disease self-management skills; Right, setting up action plan for home practice.

Special considerations in PRP

While the ATS/ERS statement and the BTS guideline for PRP stated that PRP could be offered to people with CLD, they also mentioned that special considerations should be made to cater clinical conditions of different disease groups. Therefore, the Occupational Therapy department made modifications in the training program to meet these patients' individual needs. For patients with pulmonary fibrosis, they may be subject to severe resting or exertional hypoxemia. These patients were assessed for a proper Oxygen regime for their Home Oxygen Therapy. Also, suitable portable oxygen devices (e.g. portable oxygen concentrators) and oxygen conserving devices were prescribed for indicated patients. For patients with chronic asthmatic condition, the Asthma Control Test would be used for symptom monitoring rather than the COPD Assessment Tool. Also, pre-exercise warm-up and bronchodilators were recommended to avoid exercise induced bronchoconstriction.

To meet the needs of the increasing trend of patients having other CLD being recruited to PRP, some future consideration could be made. First, use of specific assessment tools for outcome measurement could be considered because the tools designed for COPD patients may not be totally transferable to other disease

groups. For example, the Leicester Cough Questionnaire could be used to measure the impact of cough for bronchiectasis patients.

Second, other standardised program materials for some specific disease groups may be considered. For example, PRP providers can consider adopting the Living Well with Pulmonary Fibrosis program for people with pulmonary fibrosis related diseases. In this program, self-management approach is also used, but the educational materials (e.g. disease knowledge education, symptoms management) were modified to cater the clinical picture of people with fibrotic lung diseases.

Finally, although there has been increasing research in PRP for patients with other CLD, more high quality studies could be done locally to support the positive effects of PRP and self-management for different lung disease group. These culturally relevant data may help guide local respiratory healthcare providers to improve their PRP programs in future.

Conclusion

The target population of Pulmonary Rehabilitation has been extended from mainly COPD patients to also patients with other chronic respiratory conditions and there is increasing research interest in the benefits of PRP to these patients. While self-management approach may be a feasible rehabilitation modality, special consideration should be made to meet patients' individual needs. In the future, more specific assessment tools and treatment materials may give stronger evidence to support PRP and self-management for people with other CLD.

Reference

1. Spruit MA, Singh SJ, Garvey C, et al. An official American Thoracic Society/European Respiratory Society Statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med 2013*; 188: e13–e64.
2. Bolton CE, Bevan-Smith EF, Blakey JD, et al. British Thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax 2013;* 68: ii1–ii30
3. Holland AE, Wadell K, Spruit MA. How to adapt the pulmonary rehabilitation programme to patients with chronic respiratory disease other than COPD. *Eur Repir Rev 2013*; 22: 577-586.
4. Zwerink M, Brusse-Keizer M, van der Valk PD, et al. Self-mangement for patients with chrinuc obstructive pulmonary disease. *Cochrane Database Syst Rev 2014*; 3(3): CD002990
5. Dowman L, Hill CJ, Holland AE. Pulmonary rehabilitation for interstitial lung disease. *Cochrane Database of Systematic Reviews 2014;* 10: CD006322.
6. Carson KV, Chandratilleke MG, Picot J, Brinn MP, Esterman AJ, Smith BJ. Physical training for asthma. *Cochrane Database of Systematic Reviews 2013*, 9: CD001116.
7. Lee AL, Hill CJ, McDonald CF, Holland AE. Pulmonary Rehabilitation in Individuals with Non-Cystic Fibrosis Bronchiectasis: A Systematic Review. *Archives of Physical Medicine and Rehabilitation*. 98: 774-782.

RESPIRATORY UPDATE

Dr Terence CC Tam

Department of Medicine, Queen Mary Hospital

1. Only indexed international and local respiratory-related articles published between issues of Newsletter would be archived.
2. Notwithstanding the combined efforts of the Newsletter Board and various hospital representatives, this column does not guarantee a complete listing of all publications and the final archive is the choice and decision of the Board.
3. Submissions and suggestions are welcome and can be directed to: luims@ha.org.hk

From 05 Apr 2018 to 22 Jul 2018, 30 papers, all from local authors were chosen to be shared with readers.

Sleep Medicine

Ng SSS, To KW, Ngai J, Ko FWS, Hui DSC assessed the asthma control, airway responsiveness, daytime sleepiness and health status at baseline and 3 months after continuous positive airway pressure (CPAP) treatment among asthma patients with nocturnal symptoms and Obstructive Sleep Apnea Syndrome (OSAS). There was no significant difference in Asthma Control Test (ACT) score but the CPAP group had a greater improvement in Epworth Sleepiness Scale (ESS), Asthma Quality of Life Questionnaire and vitality domain in the SF-36 questionnaire after 3 months. [1]

Hui DS, Ng SS et al performed a prospective, controlled study in new referrals with suspected OSAS randomized into home-based (using Embletta sleep study) or hospital-based (using polysomnography) diagnostic approach, followed by CPAP for 3 months for those with AHI $\geq$ 15/hr. There was no difference in ESS but greater improvement in Sleep-Apnea-Quality-of-Life-(SA-QOL) Index at 3 months in the home-based group. The mean cost difference was HK$-13,769 per patient favoring home-based approach. In addition, the waiting time from the first clinic consultation to the diagnostic sleep test, auto-CPAP titration, and CPAP treatment was 189.6, 148.8 and 145.0 days shorter in home-based group respectively. [2]

Chronic Obstructive Pulmonary Disease (COPD) / Asthma

Chan HS, Ko FWS, Chan JWM, So LKY, Lam DCL, Chan VL, Tam CY, Yu WC performed a computerized, multicenter, retrospective review of the characteristics of patients discharged from 16 participating hospitals with the primary discharge diagnosis of COPD in the year 2012. In total, 9,776 subjects

(82.6% men, mean age = 78 years) were identified. Of the 1,918 subjects with lung function coding, 4.4%, 25.5%, 42.1%, and 28.0% subjects belong to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 1, 2, 3, and 4 classes, respectively. Patients with higher GOLD classes had higher number of hospital admissions, longer hospital stay, increased usage of noninvasive mechanical ventilation (NIV), combinations of long-acting bronchodilators, and higher mortality. Overall, 23.3% of subject received NIV, but invasive mechanical ventilation use was found only in 1.4%. 45.3% subjects had died by the end of 2014. The top causes of death were COPD, pneumonia, lung cancer, and other malignancies. [3]

Ko FWS & Hui DSC contributed to a study to identify COPD phenotypes, evaluate the distribution of these phenotypes and calculate the 1-year change in lung function and quality of life according to subgroup. Analysis revealed that body mass index (BMI), Charlson comorbidity index (CCI), St. George Respiratory Questionnaire (SGRQ) total score and FEV1 were the principal factors. Using these 4 factors, cluster analysis identified 3 distinct subgroups with differing disease severity and symptoms. Patients in subgroup 2 (severe disease and more symptoms) had the most frequent exacerbations, most rapid FEV1 decline and greatest decline in SGRQ total score. [4]

Ko FWS participated in an update review on COPD & Asthma for Respirology. For COPD, updates include (1) Aberrant DNA methylation may explain the role of cigarette smoke in COPD pathogenesis, (2) use of bronchodilators after extra-pulmonary surgery can prevent post-operative respiratory complications, (3) use of high-flow nasal oxygen during exacerbations can reduce CO2 levels, (4) exercise alone is effective for pulmonary rehabilitation in non-hospital settings, and (5) hypoxemia during exercise can predict pulmonary hypertension (PHT) in patients that are not hypoxemic at rest. As for asthma, updates include (1) fractional exhaled nitric oxide (FeNO) levels above 31 ppb can predict asthma exacerbations in children and young adults, (2) reduced lung function in infancy predicts asthma in young adults, (3) older asthmatic patients have high odds of irreversible airway obstruction and severe asthma phenotype, (4) in ovalbumin-sensitized and -challenged murine models, statins ameliorate airway hyper-responsiveness (AHR), and (5) probiotics seems to be a promising strategy for asthma prevention and treatment. [5]

Lam DCL was involved in a study on the satisfaction, preference and error occurrence of 3 dry powder inhalers (Breezhaler, Ellipta and Genuair) as assessed by a cohort naïve to inhaler operation. The satisfaction score of comfort for Breezhaler was significantly higher than that for Ellipta, while the satisfaction score on confidence of use and overall satisfaction score was highest for Genuair. After reading the instructions, the critical errors was commonest with Breezhaler, followed by Genuair and then Ellipta. Demonstration reduced the number of critical errors made by subjects for each DPI to one third or lower. [6]

Lung Cancer

Mok TS at al reported on the results of ARCHER 1050, a randomized, open-label, phase III study of dacomitinib versus gefitinib in treatment-naïve patients with advanced non-small cell lung cancer (NSCLC) and activating Epidermal growth factor receptor (EGFR) mutations. The hazard ratio (HR) for overall survival (OS) was 0.760 (P = 0.044) favoring dacomitinib, and the median OS was also longer (34.1 vs. 26.8 months) with gefitinib. [7]

Mok TS at al also reported on the final OS results in the PROFILE 1014 trial comparing crizotinib with chemotherapy as first-line treatment in patients with anaplastic lymphoma kinase (ALK) -positive advanced NSCLC. HR for OS was 0.760 (P = 0.0978). Median OS was not reached with crizotinib and was 47.5 months with chemotherapy. Survival probability at 4 years was also higher with crizotinib (56.6% vs. 49.1%). Even after crossover adjustment, there was still an improvement in OS that favored crizotinib (hazard ratio, 0.346). [8]

Along similar line, *Ho JCM & Mok TS* contributed to PROFILE 1029 trial, where eastern Asian ALK-positive lung cancer patients were randomized to receive crizotinib or Pemetrexed / Platinum doublet at the first-line setting. Crizotinib significantly prolonged progression-free survival (PFS) (HR = 0.402) and offer better objective response rate (ORR) (87.5% vs, 45.6%). [9]

Mok TS also contributed to a study that assessed the PD-L1 expression in 713 consecutive NSCLC patients by 4 commercially available PD-L1 immunohistochemical assays, namely, 22C3, 28-8, SP142 and SP263. High PD-L1 expression (≥50% as cutoff) was significantly associated with male sex, ever smoking history, squamous cell carcinoma, large cell carcinoma, lymphoepithelioma-like carcinoma (LELC), sarcomatoid carcinoma, mutant KRAS and wild-type EGFR. Elevated PD-L1 expression was also significantly associated with shorter survival in patients with adenocarcinoma. Among the four assays, 22C3, 28-8 and SP263 were highly concordant for tumor cell scoring, with an inter-rater agreement >97%. [10]

Ho JCM was involved in a study exploring the utility of T790M mutant copy number quantification in a plasma cell-free DNA (cf-DNA) assay for predicting clinical outcomes of osimertinib treatment, and found that high mutant copy number (≥ 105 per mL of plasma) was associated with shorter PFS (median: 5.5 months vs. not reached) and overall survival (median: 9.1 months vs. NR). [11]

On the other hand, *Mok TS* contributed to a study that aim to correlate of extent of ALK FISH positivity and crizotinib efficacy in three prospective studies of ALK-positive patients with NSCLC. ORR for patients with ≥20% ALK-positive cells was 56%, 55% for those with ≥15% ALK-positive cells, and 38% for those with 15-19% ALK-positive cells. [12]

Finally, *Mok TS et al* reported on the first real-world cohort of comprehensive genomic assessments of patients with NSCLC in a Chinese population. In the adenocarcinoma and NSCLC group 91% had variants identified, and 42% had ≥ 1 of the 7 National Comprehensive Cancer Network (NCCN)-recommended genomic targets; interestingly, Concurrent detection of driver and resistance mutations were identified in 6 of 13 patients with EGFR driver mutations and in 3 of 5 patients with EML4-ALK fusions. All patients with squamous cell carcinoma had multiple variants identified, including FGFR1, ERBB2 (HER2) and PIK3CA amplification. [13]

Pleural diseases

Lam DCL and the QMH group contributed to the multicenter AMPLE-2 trial that aims to identify whether daily (aggressive group) vs. symptom-guided drainage was the optimal regimen of drainage after indwelling pleural catheter insertion. The mean daily breathlessness scores did not differ significantly between the 2 groups, but more patients in the aggressive group developed spontaneous pleurodesis in the first 60 days (37.2 vs. 11.4%) and at 6 months (44.2 vs. 15.9%. Patient-reported quality-of-life measures were better in the aggressive group, whereas pain scores, total days spent in

hospital, and mortality did not differ significantly between groups. [14]

Yu WC, Yeung CY et al investigated the efficacy, safety, and factors associated with success of the use of endobronchial one-way valves for treatment for persistent air leak. Eight-nine percent of the 37 patients studied had secondary spontaneous pneumothorax, of which 19 underwent endobronchial valves implantation (number of valve per patient 1-6). The air leak ceased within 72 hours for only 8 patients (22% of the complete cohort). All successful cases had computed tomographic evidence of bilateral intact interlobar fissures. The median CCI index was 1 vs. 2 for the success group and failure group, respectively (P=0.029). Of note, all patients in the no-endobronchial valve group survived, whereas three patients in the endobronchial valve group died within 30 days of endobronchial valve implantation. [17]

Smoking-related

Lam TH et al investigated the effectiveness of quitting immediately vs. cutting down to quit in promoting smoking abstinence among smokers in an outpatient clinic. At the 6-month follow-up, the self-reported quit rate of subjects in the quit immediately group was significantly higher (18.0 vs. 4.0%); however, this difference was not significant at the 12-month follow-up (12.0% vs. 4.0%). [16]

Lam TH et al found that while adolescent smoking was associated with parental smoking, the association was attenuated or reversed in those who rejected parental smoking. [17]

In addition, *Lam TH* contributed to a study on the role of family relationship in adolescent use of emerging tobacco products. The odds of current use increased with worse perceived family relationship quality with adjusted odds ratio (aOR) of up to 2.92 for cigarettes, 7.28 for e-cigarettes, 5.04 for water pipe, 8.09 for smokeless tobacco and 5.25 for poly-tobacco products use. [18]

Infection

To KKW, Hung IFN & Yuen KY et al investigated the differential white blood cell (WBC) count and the levels of 29 plasma cytokines/chemokines between adult hospitalized patients with rhinovirus and influenza infection. Rhinovirus patients had significantly higher WBC (especially for eosinophil) and IL-5 level, while the levels of 9 other cytokines/chemokines were significantly lower. Notably, CXCL-10 had the highest area under the receiver operating characteristic curve (AUC) in differentiating rhinovirus from influenza patients (AUC, 0.918). [19]

To KKW, Yuen KY et al performed a prospective diagnostic validity study comparing the detection rate of respiratory viruses between saliva and nasopharyngeal aspirate (NPA) among adult hospitalized patients using Xpert® Xpress Flu/RSV, and found that the overall agreement were 93.3%. The overall sensitivity and specificity were 90.8% and 100% for saliva, and 96.1% and 98.5% for NPA. The time and cost associated with the collection of saliva were 2.26-fold and 2.59-fold lower, respectively, than those of NPA. [20]

Yuen KY, together with *Hung IFN and others*, evaluated the efficacy of a triple combination of zanamivir, clarithromycin and flufenamic acid (FFA) in the treatment of influenza virus A (H1N1) infection in mice. Triple combination led to a significantly better survival rate than those receiving zanamivir and clarithromycin (88 vs. 44%) or zanamivir monotherapy (88 vs. 26%). Mice in the triple combination group also exhibited significantly less body weight loss than those in the double combination group. [21]

Peiris JSM was involved in an experiment that demonstrated avian H7N9 virus can infect, transcribe, and replicate its viral genome, induce cytokine upregulation and cause cytopathic effects in human brain cells, which may potentially lead to profound central nervous system injury. [22]

Peiris JSM was also involved in another in-vitro study on human airway organoids and ex-vivo bronchus cultures in response to influenza virus, and found that H1N1 and avian H7N9 subtype viruses replicated to significantly higher titers than did the highly pathogenic avian influenza (HPAI) H5N1, whereas HPAI H5N6 replication was moderate. This provide an alternative physiologically relevant experimental model for investigating virus tropism and replication competence that could be used to assess the pandemic threat of animal influenza viruses. [23]

Tuberculosis

To KW, Ng S, Ngai J, Lee SS et al explored the clinical role of GeneXpert in managing pulmonary tuberculosis (TB) in an intermediate burden city. For TB diagnosis, the sensitivity, specificity, positive (PPV) & negative predictive value (NPV) was 80%, 98%, 92.3% & 95.1% respectively. [24]

Leung CC contributed to a review on the value of comprehensive phenotypic and/or genotypic drug susceptibility testing. Phenotypic drug resistance can now often, but with variable sensitivity, be predicted by molecular drug susceptibility testing based on whole genome sequencing, which in the future could become an affordable method for the guidance of treatment decisions. Ongoing clinical trials with novel and repurposed drugs will potentially further improve cure-rates, and may substantially decrease the duration of MDR-TB treatment necessary to achieve relapse-free cure. [25]

Chang KC, Leung CC et al also wrote a review article on new drugs and regimens for tuberculosis, with particular focus on (1) standardized versus individualized therapies as dictated by rapid drug susceptibility testing, (2) alternative regimens for managing drug-susceptible TB, (3) evidence for the World Health Organization (WHO)-recommended longer and shorter regimens for multidrug-resistant TB and (4) evidence for using repurposed and novel drugs. [26]

Yew WW contributed to a study that identified a new mutation (EthAW21R) in Mycobacterium bovis Bacillus Calmette-Guérin, which corresponds with co-resistance to both Ethionamide (ETA) and prothionamide (PRO). The findings suggest that mutation EthAW21R could be used as a marker site for testing PRO and ETA cross-resistance. [27]

Yew WW along with *Leung CC et al*, looked at the epidemiological, clinical and mechanistic perspectives of tuberculosis in older people. [28]

Yew WW, Chang KC, Chan DP addressed whether and how oxidative stress, and more broadly, disturbance in redox homeostasis alongside mitochondrial dysfunction, may contribute to the hepatotoxicity induced by first-line anti-TB drugs. [29]

Finally, *Yew WW & Leung CC et al* investigated on the dietary intake of antioxidant vitamins and carotenoids and the risk of developing TB. *Leung CC* looked at the role of repurposed metformin to prevent and treat TB. *Chang KC, Lam FM, Chau CH, Mok TY, Yew YWW & Leung CC et al* reported on the early local experience with delamanid-containing regimens in the treatment of complicated multidrug-resistant tuberculosis. *Yew WW* contributed to a study on the molecular targets related drug resistance mechanisms in MDR-, XDR-, and TDR-Mycobacterium tuberculosis strains. We will

share the details with the audience once the manuscript(s) are made available online.

Lung Transplantation

Hsin MKY, Wong CF, Yan SW et al review the history of lung transplantation in Hong Kong. As it turns out, the recipient pathology in our local cohort is very different from the International Society for Heart and Lung Transplantation (ISHLT) database, with complete absence of cystic fibrosis and alpha-1-antitrypsin deficiency, and a predominance of diseases of the pulmonary circulation. Lymphangioleiomyomatosis (LAM) has a much higher representation on the waiting list than the ISHLT. The survival of patients who received a lung transplant in Hong Kong compares favorably with international data. [30]

Reference

1. Ng SSS, Chan TO, To KW, Chan KKP, Ngai J, Yip WH, Lo RLP, Ko FWS, Hui DSC. Continuous positive airway pressure for obstructive sleep apnoea does not improve asthma control. Respirology. 2018 Jul 10. doi: 10.1111/resp.13363. [Epub ahead of print]

2. Hui DS, Ng SS, Tam WWS. Home-based Approach is Non-inferior to Hospital-based Approach in Managing Patients with Suspected Obstructive Sleep Apnoea Syndrome. Am J Respir Crit Care Med. 2018 May 1;197(9):1233-1234. doi: 10.1164/rccm.201711-2185LE.

3. Chan HS, Ko FWS, Chan JWM, So LKY, Lam DCL, Chan VL, Tam CY, Yu WC. Comorbidities, mortality, and management of chronic obstructive pulmonary disease patients who required admissions to public hospitals in Hong Kong - computerized data collection and analysis. Int J Chron Obstruct Pulmon Dis. 2018 Jun 13;13:1913-1925. doi: 10.2147/COPD.S163659. eCollection 2018.

4. Kim WJ, Gupta V, Nishimura M, Makita H, Idolor L, Roa C, Loh LC, Ong CK, Wang JS, Boonsawat W, Gunasekera KD, Madegedara D, Kuo HP, Wang CH, Wang C, Yang T, Lin YX, Ko FWS, Hui DSC, Lan LTT, Vu QTT, Bhome AB, Ng A, Seo JB, Lee BY, Lee JS, Oh YM, Lee SD. Identification of chronic obstructive pulmonary disease subgroups in 13 Asian cities. Int J Tuberc Lung Dis. 2018 Jul 1;22(7):820-826. doi: 10.5588/ijtld.17.0524.

5. Benton MJ, Lim TK, Ko FWS, Kan-O K, Mak JCW. Year in review 2017: Chronic obstructive pulmonary disease and asthma. Respirology. 2018 Mar 4. doi: 10.1111/resp.13285. [Epub ahead of print]

6. Man KNM, Tian Z, Lam DC, Wan JMF, Tan-Un KC. Satisfaction, preference and error occurrence of three dry powder inhalers as assessed by a cohort naïve to inhaler operation. Int J Chron Obstruct Pulmon Dis. 2018 Jun 15;13:1949-1963. doi: 10.2147/COPD.S152285. eCollection 2018.

7. Mok TS, Cheng Y, Zhou X, Lee KH, Nakagawa K, Niho S, Lee M, Linke R, Rosell R, Corral J, Migliorino MR, Pluzanski A, Sbar EI, Wang T, White JL, Wu YL. Improvement in Overall Survival in a Randomized Study That Compared Dacomitinib With Gefitinib in Patients With Advanced Non-Small-Cell Lung Cancer and EGFR-Activating Mutations J Clin Oncol. 2018 Jun 4:JCO2018787994. doi: 10.1200/JCO.2018.78.7994. [Epub ahead of print]

8. Solomon BJ, Kim DW, Wu YL, Nakagawa K, Mekhail T, Felip E, Cappuzzo F, Paolini J, Usari T, Tang Y, Wilner KD, Blackhall F, Mok TS. Final Overall Survival Analysis From a Study Comparing First-Line Crizotinib Versus Chemotherapy in ALK-Mutation-Positive Non-Small-Cell Lung Cancer. J Clin Oncol. 2018 May 16:JCO2017774794. doi:

10.1200/JCO.2017.77.4794. [Epub ahead of print]

9. Wu YL, Lu S, Lu Y, Zhou J, Shi YK, Sriuranpong V, Ho JCM, Ong CK, Tsai CM, Chung CH, Wilner KD, Tang Y, Masters ET, Selaru P, Mok TS. Results of PROFILE 1029, a Phase III Comparison of First-Line Crizotinib versus Chemotherapy in East Asian Patients with ALK-Positive Advanced Non-Small Cell Lung Cancer. J Thorac Oncol. 2018 Jun 29. pii: S1556-0864(18)30721-4. doi: 10.1016/j.jtho.2018.06.012. [Epub ahead of print]

10. Chan AWH, Tong JHM, Kwan JSH, Chow C, Chung LY, Chau SL, Lung RWM, Ng CSH, Wan IYP, Mok TSK, To KF. Assessment of programmed cell death ligand-1 expression by 4 diagnostic assays and its clinicopathological correlation in a large cohort of surgical resected non-small cell lung carcinoma. Mod Pathol. 2018 Apr 30. doi: 10.1038/s41379-018-0053-3. [Epub ahead of print]

11. Li JY, Ho JC, Wong KH. T790M mutant copy number quantified via ddPCR predicts outcome after osimertinib treatment in lung cancer. Oncotarget. 2018 Jun 15;9(46):27929-27939. doi: 10.18632/oncotarget.25332. eCollection 2018 Jun 15.

12. Soria JC, Ho SN, Varella-Garcia M, Iafrate AJ, Solomon BJ, Shaw AT, Blackhall F, Mok TS, Wu YL, Pestova K, Wilner KD, Polli A, Paolini J, Lanzalone S, Green S, Camidge DR. Correlation of extent of ALK FISH positivity and crizotinib efficacy in three prospective studies of ALK-positive patients with non-small cell lung cancer. Ann Oncol. 2018 Jul 13. doi: 10.1093/annonc/mdy242. [Epub ahead of print]

13. Loong HH, Raymond VM, Shiotsu Y, Chua DTT, Teo PML, Yung T, Skrzypczak S, Lanman RB, Mok TSK. Clinical Application of Genomic Profiling With Circulating Tumor DNA for Management of Advanced Non-Small-cell Lung Cancer in Asia. Clin Lung Cancer. 2018 May 7. pii: S1525-7304(18)30104-9. doi: 10.1016/j.cllc.2018.04.022. [Epub ahead of print]

14. Muruganandan S, Azzopardi M, Fitzgerald DB, Shrestha R, Kwan BCH, Lam DCL, De Chaneet CC, Rashid Ali MRS, Yap E, Tobin CL, Garske LA, Nguyen PT, Stanley C, Popowicz ND, Kosky C, Thomas R, Read CA, Budgeon CA, Feller-Kopman D, Maskell NA, Murray K, Lee YCG. Aggressive versus symptom-guided drainage of malignant pleural effusion via indwelling pleural catheters (AMPLE-2): an open-label randomised trial. Lancet Respir Med. 2018 Jul 20. pii: S2213-2600(18)30288-1. doi: 10.1016/S2213-2600(18)30288-1. [Epub ahead of print]

15. Ho KY, Li WHC, Wang MP, Lam KKW, Lam TH, Chan SSC. Comparison of two approaches in achieving smoking abstinence among patients in an outpatient clinic: A Phase 2 randomized controlled trial. Patient Educ Couns. 2018 May;101(5):885-893. doi: 10.1016/j.pec.2018.02.003. Epub 2018 Feb 8.

16. Chen J, Ho SY, Wang MP, Lam TH. Parental smoking, rejection of parental smoking, and smoking susceptibility and behaviors in Hong Kong adolescents. Addict Behav. 2018 Jul;82:19-22. doi: 10.1016/j.addbeh.2018.02.019. Epub 2018 Feb 13.

17. Yu WC, Yu EL, Kwok HC, She HL, Kwong KK, Chan YH, Tsang YL, Yeung YC. Endobronchial valve for treatment of persistent air leak complicating spontaneous pneumothorax. Hong Kong Med J. 2018 Apr;24(2):158-165. doi: 10.12809/hkmj176823. Epub 2018 Apr 4.

18. Luk TT, Wang MP, Leung LT, Chen J, Wu Y, Lam TH, Ho SY. Perceived family

relationship quality and use of poly-tobacco products during early and late adolescence. Addict Behav. 2018 Oct;85:38-42. doi: 10.1016/j.addbeh.2018.05.011. Epub 2018 May 24.

19. To KKW, Lu L, Fong CHY, Wu AKL, Mok KY, Yip CCY, Ke YH, Sze KH, Lau SKP, Hung IFN, Yuen KY. Rhinovirus respiratory tract infection in hospitalized adult patients is associated with TH2 response irrespective of asthma. J Infect. 2018 May;76(5):465-474. doi: 10.1016/j.jinf.2018.02.005. Epub 2018 Feb 15.

20. To KK, Yip CC, Lai CY, Wong CK, Ho DT, Pang PK, Ng AC, Leung KH, Poon RW, Chan KH, Cheng VC, Hung IF, Yuen KY. Saliva as a diagnostic specimen for testing respiratory virus by a point-of-care molecular assay: a diagnostic validity study. Clin Microbiol Infect. 2018 Jun 12. pii: S1198-743X(18)30468-3. doi: 10.1016/j.cmi.2018.06.009. [Epub ahead of print]

21. L ee ACY, To KKW, Zhang AJX, Zhu H, Li C, Zhang RR, Hung IFN, Kao RYT, Chan KH, Yuen KY. Triple combination of FDA-approved drugs including flufenamic acid, clarithromycin and zanamivir improves survival of severe influenza in mice. Arch Virol. 2018 May 7. doi: 10.1007/s00705-018-3852-4. [Epub ahead of print]

22. Ng YP, Yip TF, Peiris JSM, Ip NY, Lee SMY. Avian influenza A H7N9 virus infects human astrocytes and neuronal cells and induces inflammatory immune responses. J Neurovirol. 2018 Jul 9. doi: 10.1007/s13365-018-0659-8. [Epub ahead of print]

23. Hui KPY, Ching RHH, Chan SKH, Nicholls JM, Sachs N, Clevers H, Peiris JSM, Chan MCW. Tropism, replication competence, and innate immune responses of influenza virus: an analysis of human airway organoids and ex-vivo bronchus cultures. Lancet Respir Med. 2018 Jul 9. pii: S2213-2600(18)30236-4. doi: 10.1016/S2213-2600(18)30236-4. [Epub ahead of print]

24. To KW, Kam KM, Chan DPC, Yip WH, Chan KP, Lo R, Ng S, Ngai J, Lee SS. Application of GeneXpert on bronchoalveolar lavage samples in the clinical management of patients suspicious of tuberculosis in an intermediate-burden setting. J Infect. 2018 Jun 28. pii: S0163-4453(18)30189-0. doi: 10.1016/j.jinf.2018.06.011. [Epub ahead of print]

25. Lange C, Chesov D, Heyckendorf J, Leung CC, Udwadia Z, Dheda K. Drug-resistant tuberculosis: An update on disease burden, diagnosis and treatment. Respirology. 2018 Jul;23(7):656-673. doi: 10.1111/resp.13304. Epub 2018 Apr 11.

26. Chang KC, Nuermberger E, Sotgiu G, Leung CC. New drugs and regimens for tuberculosis. Respirology. 2018 Jun 19. doi: 10.1111/resp.13345. [Epub ahead of print]

27. Mugweru J, Liu J, Makafe G, Chiwala G, Wang B, Wang C, Li X, Tan Y, Yew WW, Tan S, Zhang T. Mutation EthAW21R confers co-resistance to prothionamide and ethionamide in both Mycobacterium bovis BCG and Mycobacterium tuberculosis H37Rv. Infect Drug Resist. 2018 Jun 13;11:891-894. doi: 10.2147/IDR.S163965. eCollection 2018.

28. Yew WW, Yoshiyama T, Leung CC, Chan DP. Epidemiological, clinical and mechanistic perspectives of tuberculosis in older people. Respirology. 2018 Jun;23(6):567-575. doi: 10.1111/resp.13303. Epub 2018 Apr 1.

29. Yew WW, Chang KC, Chan DP. Oxidative Stress and First-Line Antituberculosis Drug-Induced Hepatotoxicity. Antimicrob Agents Chemother. 2018 May 21. pii: AAC.02637-17. doi: 10.1128/AAC.02637-17. [Epub ahead of print]

30. Hsin MKY, Wong CF, Yan SW, Fan KY, Ho CKL, Bhatia I, Au TWK. The history

of lung transplantation in Hong Kong. J Thorac Dis. 2018 Jun;10(Suppl 16):S1899-S1904. doi: 10.21037/jtd.2018.04.118.

Report on Evening Scientific Symposium

"The importance of latent TB infection control: from policy to implementation" on 15th May 2018

The evening scientific symposium took place on 15th May 2018, at the Sheraton Hotel, Tsim Sha Tsui. The educational activity was co-organized by the Hong Kong Thoracic Society, and CHEST Delegation Hong Kong & Macau. ***Dr. Chi-Chiu LEUNG*** was the chairman of this evening symposium. ***Dr Yi-Wn HUANG,*** Director of Taiwan Society of Tuberculosis and Lung Disease, delivered his talk on epidemiology, implications of latent TB infection, as well as the evidence on various treatment regimens. The latest advance on the use of Rifapentine and Isoniazind combination was extensively discussed. The lecture was well received by more than 100 members.

Dr. CC Leung and Dr. Yi-Wen HUANG

'Asthma – what are the new to know & to-do?' on 3rd July 2018

The evening scientific symposium took place on 3rd July 2018, at the Sheraton Hotel, Tsim Sha Tsui. The educational activity was co-organized by the Hong Kong Thoracic Society, and CHEST Delegation Hong Kong & Macau. More than 130 members & associate members of Hong Kong Thoracic Society have attended the symposium. ***Dr. Maureen Wong*** was the chairman of this evening symposium. ***Professor Ronald Dahl***, consultant at the Aarhus University Hospital Denmark, delivered his talk on the lately published data on inhaled corticosteroids plus long acting beta-agonist. Audiences were refreshed on the practical insights and management strategies to achieve asthma control in our patients.

Professor Ronald Dahl

LEISURE CORNER

Joy and challenge of becoming a father

Dr Ryan YF Cheng

Department of Medicine & Geriatrics

Tuen Mun Hospital

Sigmund Freud said, 'Love and work, work and love, that's all there is.' This is particularly true for me while I became a father and a higher physician trainee at the same time. The very first time my wife announced to me this magnificent news was actually over our celebration dinner for finally passing the PACES examination. I was much more than joyful and especially grateful that I was so lucky to have passed the exam on time, or else I may end up raising up my baby while studying for PACES.

In the upcoming few months, we were busying around for preparing the coming of our first baby girl: baby bed, baby car, toy, clothes, diaper, milk powder, hiring a babysitter, you name it. Honestly, I was not a very good husband, as my wife handled most of the things. With all the joy and excitement, one thing came to worry us. Morphological scanning show that the body weight of our baby girl is around 4 weeks smaller than expected. Frequent ultrasound monitoring was done subsequently, but showing persistent low body weight though she seems growing normally. At the third trimester, our doctor eventually suggested induction at 37th weeks of gestation

Induction of labour was a total chaos. After nearly 20 hours of pain, our baby girl finally was born on the 24th of October 2016. My wife was so brave and great that she went through the delivery without even having an epidural anesthesia, which we originally planned to have. The birth weight of Athena was only 2.5kg, which was less than 10th percentile of full term babies. What make things even worse, the first set of blood tests show elevated WCC and she also experienced hypothermia, she was then kept inpatient for IV antibiotics injection for 5 days. After all these little stormy peripartum things, Athena could finally be brought home with a cute smiling face.

We named our first baby girl as Athena, who was an ancient Greek goddess of wisdom. Instead of wishing her to be clever, we hoped she would have the desire for freedom, persistence in justice, roll-up-the-sleeves attitude in life, and a never give up spirit in chasing dreams. As we believe, 'attitude is more important than aptitude to determine your altitude'. Fortunately, Athena is kid who is outgoing, sociable, playful and cheerful. But she might sometimes be too "playful" to refuse eating and sleeping. It was quite happy and enjoyable for us to bring her out to play, and we even went hiking together. Athena caught chickenpox at the age of 5 months, and I still remembered clearly how she looked with vesicles all over her face and body. However, it was so amazing and fortunate that with just a little fever and itchy skin, the rash subsided in a week's time.

After having our 1st baby girl, we planned to have the 2nd one. So, by the time Athena was 6 months old, my wife was pregnant again. It was actually unexpectedly earlier than what we thought, as Athena was still on breastfeeding at that time. Not sure if we were more experienced or what, the second pregnancy went quite smoothly. When my wife's tummy got bigger, it was so amazing that Athena actually knew her sister was about to come. Athena would always go to kiss her mummy's tummy, which we both felt so sweet and warm.

On the night my wife went into labour, I was on call in the hospital till 10pm. When my wife called me saying she felt regular uterine contractions, I was still in the hospital. I rushed home, prepared the things and quickly took taxi with my wife to the labour ward. By the time we arrived, cervix was already at 8 degrees. The midwives asked why we were so late as it was really chaotic to go into labour immediately upon arrival. Our 2nd baby girl Hebe was born just around 1 hour after we arrived the hospital, on the 17th of January 2018. It was an unforgettable day for my wife, our baby girl and Hebe was a healthy newborn,

with the quick and smooth delivery, we all went home on day 2.

Athena was so excited to see Hebe, she kept saying Hi to Hebe and kissing her on her cheek, this scene was so unforgettable and amazing. It is great that Athena is still loving Hebe and always treating her well now. We named our 2nd baby as Hebe, partly because I am lazy, but also we want a name with simple meaning. It was also an ancient Greek goddess, who represented youth. And for us, Hebe simply means happy. Hebe was growing quite well, unlike Athena, Hebe ate well, slept well, and her body weight thrives much more than Athena. We were so blessed to have a healthy and happy baby. Hebe is less outgoing than Athena. She likes music and pictures, and she can usually play by herself quietly for a rather long time. It really lessens our burden on taking care of two babies at the same time.

After becoming father of two adorable daughters, I experienced and celebrated life, and learnt to faith, and be able to overcome challenges, may it be big or small. I also worried less, as it only make you feel bad while not helping you to solve the problem. I learnt to be more open-mind and let my babies to choose their own way. Athena and Hebe grew up together but they developed their own unique characters. They might not be brilliant in learning one thing while was superb in learning another; this really did remind me that every child is different and we should treasure and explore their own talents. Albert Einstein said, 'If you judge a fish by it's ability to climb a tree, it will spend it's whole life believing that it is stupid'. Moreover, I also learnt to cherish the time with my family. When Athena took her first step on her own, I was on call and I was just able to see her walking the other day when I was finally back from work, which I still pity to have missed. I know exactly what is important to me, and I learnt to live and enjoy every moment, as everyday counts.

With all these, I really hope my two babies grow up healthily, and to be honest, righteous, happy, and loving towards things and people. Last but not least, I am numerously thankful to my wife for all the tough time taking care of the two babies.

Designed and Prepared by:
Dr. L H Shek
AC, CMC M&G

Clinical Meetings 2018

JUL

Sun	Mon	Tue	Wed	Thu	Fri	Sat
1 HKSAR Establishment Day	2 Day after HKSAR Establishment Day	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

AUG

Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

SEP

Sun	Mon	Tue	Wed	Thu	Fri	Sat
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23 30	24	25 Day after Mid-Autumn Festival	26	27	28	29

19th: HKTS^ Clinical Meeting

Venue: Ruttonjee Hospital
Speakers: United Christian Hospital & Haven of Hope Hospital
Organiser: HKTS^, CHEST Delegation HK & Macau

1-2nd: Symposium on Asthma and COPD: Now and Future

Venue: Meeting Room S421, Level 4, Phase 1 (Old Wing), Hong Kong Convention and Exhibition Centre, Hong Kong
Organizer: HKTS^, CHEST Delegation HK & Macau

15-19th: ERS International Congress 2018

Venue: Paris, FRANCE
Organizer: European Respiratory Society (ERS)

27th: HKTS Clinical Meeting

Venue: Ruttonjee Hospital
Speakers: Tuen Mun Hospital & Tseung Kwan O Hospital
Organizer: HKTS^, CHEST Delegation HK & Macau

Clinical Meetings 2018

OCT

Sun	Mon	Tue	Wed	Thu	Fri	Sat
	1 National Day	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17 Chung Yeung Festival	18	19	20
21	22	23	24	25	26	28
28	29	30	31			

6-10th: Chest 2018

Venue: Henry B. Gonzalez Convention Center
San Antonio, Texas, US
Organizer: American College of Chest Physicians

NOV

Sun	Mon	Tue	Wed	Thu	Fri	Sat
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

17th: Workshop on Pleural Diseases

Venue: Jockey Club Building, Hong Kong
Organizers: Pleural chapter under IP SIG, HKTSˆ, CHEST Delegation HK and Macau

18th: Autumn Respiratory Seminar

Venue: Hong Kong Convention & Exhibition Centre, HONG KONG
Organizers: HKTSˆ, CHEST Delegation HK & Macau

29/11-2/12: 23rd Congress of Asian Pacific Society of Respirology (APSR)

Venue: Taipei International Convention Center (TICC), Taipei, TAIWAN
Organizer: APSR

DEC

Sun	Mon	Tue	Wed	Thu	Fri	Sat
2	3	4	5	6	7	1
9	10	11	12	13	14	8
16	17	18	19	20	21	15
23	24	25 Christmas Day	26 Boxing Day	27	28	29
30	31					

ˆ Hong Kong Thoracic Society

WELCOME!

Hong Kong Thoracic Society would like to welcome the following new members

Ordinary Members:

Dr	Lee	Yin Ling	李燕玲	HHH
Dr	Kwong	Kin Keung	鄺建強	Royal Darwin Hospital
Dr	Wong	Ho Sum Cally	汪可心	HHH
Dr	Tang	Yiu Hung	鄧耀雄	KWH

Associate Members:

Ms	Li	Kwan Fong	利群芳	Nurse
Ms	Wong	Lai Fan	黃麗芬	Nurse
Ms	Wu	Sin Yi	胡善儀	Nurse
Ms	Luk	Lai Sheung	陸麗嫦	Nurse
Ms	Lee	Ka Wai	李嘉慧	Physiotherapist
Mr	Liu	Ka Nam	廖家楠	Nurse
Mr	Cheung	Ka Lun Paul	張嘉倫	Physiotherapist
Ms	Lee	Wai Chun	李惠珍	Nurse
Ms	So	Man Lan	蘇文蘭	Physiotherapist
Ms	Li	Ching Ting	李政婷	Nurse
Mr	Tam	Cheuk Kit	譚卓傑	Nurse
Mr	Wong	Man Lai	黃文禮	Nurse
Ms	Chan	Long Yee	陳朗兒	Nurse
Ms	Lai	Yuen Man	黎婉雯	Nurse
Ms	Cheung	Wing Yee	張泳怡	Nurse
Ms	Fung	Wing Yu	馮詠瑜	Nurse

USEFUL WEBSITES

Medical Societies

Hong Kong Thoracic Society	http://www.hkresp.com
CHEST Delegation Hong Kong and Macau	http://www.hkresp.com
American College of Chest Physician	http://www.chestnet.org/
American Thoracic Society	http://www.thoracic.org/
Asian Pacific Society of Respirology	http://www.apsresp.org/
British Thoracic Society	http://www.brit-thoracic.org.uk/
Canadian Lung Association	http://www.lung.ca/
European Respiratory Society	http://www.ersnet.org/
National Heart, Lung and Blood Institute	http://www.nhlbi.nih.gov/
American Association for Respiratory Care	http://www.aarc.org/index.html
Hong Kong Society of Critical Care Medicine	http://www.hksccm.org
The Federation of Medical Societies of HK	http://www.fmshk.org/fmshk.pp

Publications

American Journal of Respiratory and Critical Care	http://ajrccm.atsjournals.org/
American Journal of Respiratory Cell and Molecular Biology	http://ajrcmb.atsjournals.org/
British Medical Journal	http://www.bmj.com/
Canadian Respiratory Journal	http://webserver.pulsus.com/Respir/home.htm
Chest	http://www.chestjournal.org/
Clinical and Experimental Allergy	http://www.wiley.com/bw/journal.asp?ref=0954-7894
Current Opinion in Pulmonary Medicine	http://www.co-pulmonarymedicine.com/
European Respiratory Journal	http://erj.ersjournals.com/
Journal of Allergy and Clinical Immunology	http://www.jacionline.org/
Journal of Bronchology	http://www.bronchology.com/pt/re/jbronch/
Lung Cancer	http://www.journals.elsevierhealth.com/periodicals/lung/home
Morbidity and Mortality Weekly Report	http://www.cdc.gov/mmwr/
Respiration	http://www.karger.com/Journal/Home/224278
Respiratory Care Online	http://www.rcjournal.com/

MEMBERSHIP

Hong Kong Thoracic Society

Member Categories: ordinary (doctor), associate (nurses and allied health), student, honorary and life. Please refer to the website for more information, and downloading application/renewal forms: -

http://www.hkresp.com/index.php/about-joomla/48-membership .

By joining as members, you will enjoy the privilege to join the activities organized by the society at discounted rates, newsletter access with inclusion of update and advances in the specialty, networking with various professionals in the field, access to funds, sponsorships and grants for conferences, training and research. You are welcome to refer to our website for more information: http://www.hkresp.com/.

To be eligible for Life membership, three years of full membership prior to the application is necessary. Please write to the Honorary Secretary of Hong Kong Thoracic Society and send the letter with a cheque of HK$2,000 (payable to Hong Kong Thoracic Society Ltd) as stated in the application form. Acceptance will be decided in the Hong Kong Thoracic Society council meetings.

CHEST

To become a CHEST Member: You must complete a membership application. Membership application is open to the medical, nursing, allied health and paramedical professions involved in the field of pulmonary, critical care and sleep medicine. You can find more information regarding the application procedures at https://www.chestnet.org/Get-Involved/Membership/Join. You can enjoy the privilege of on-line access to the official CHEST journal and many other benefits by joining CHEST as members. You are welcome to refer to the official website for more details. http://journal.publications.chestnet.org/ . CHEST Members residing in Hong Kong and Macau are ex-officio members of CHEST Delegation Hong Kong and Macau.

FUNDS AND GRANTS

Hong Kong Lung Foundation Fellowship

The fellowship is open to medical practitioners, allied health professionals, scientists, students and others for travelling aboard to engage in research, study and training in order to gain experience in modern methods of diagnosis, prevention and treatment of diseases of the respiratory system. Please note that priority will be given to *active* members of the Hong Kong Thoracic Society.

The Hong Kong Lung Foundation Fellowship has three types of Awards:

1. Members of the medical profession granting a sum up to HK$120,000
2. Members of the nursing or allied health professions granting a sum up to HK$80,000
3. Members of the medical, nursing and paramedical profession granting a sum up to HK$50,000 for attending conference or short training course of 3 months or less.

Hong Kong Lung Foundation Fellowship opens its application **twice a year in June and December.** Applicants should submit the application forms to the Hon Secretary of the Hong Kong Lung Foundation**.**

Application procedures and forms can be downloaded from the HKLF Website: http://www.hklf.org/index/hklf-fellowship/fellowship-application-and-form or obtain from Hon secretary: Dr. HO Chung-Man James, Department of Medicine, Queen Mary Hospital. Email: jhocm@hku.hk

Pneumoconiosis Compensation Board (PCFB) Research Fund

The Pneumoconiosis Compensation Board (PCFB) set up a research fund in 1996 with the purpose to support projects that are related to the prevention, diagnosis, assessment of disability and treatment of pneumoconiosis in Hong Kong. Interested parties may visit the website for more information: http://www.pcfb.org.hk/prevention_fund_application.php or contact the PCFB secretariat, tel: 3578 8109, fax: 2116 0116, email: research@pcfb.org.hk

The Hong Kong Lung Foundation Research Grant

Hong Kong Lung Foundation was established in 1996 to nurture advancement in clinical practice in the field of lung diseases in the Hong Kong Special Administration Region. As from January 2001, the foundation awards research grants, on an annual basis, to fund research projects being performed in the HKSAR. This aims to enhance the research culture and standards of local clinicians and health-care professionals in the field of respiratory medicine and related disciplines.

Please refer to the Hong Kong Lung Foundation Research grant regulations, which must be strictly adhered to. Application procedures and application form of the research Grant can be downloaded from the Hong Kong Lung Foundation Website: http://www.hklf.org/index/research-grants/research-grants-application-and-form. You are welcome to contact the Honorary secretary for more information: Dr. HO Chung-Man James, Department of Medicine, Queen Mary Hospital. Email: jcmho@hku.hk

Pneumoconiosis Compensation Board (PCFB) Training Grant

The Pneumoconiosis Compensation Board (PCFB) has established a training grant to facilitate health-care workers and occupational safety and health personnel to enhance their knowledge and skills in pneumoconiosis. This scheme aims to encourage eligible applicants to attend overseas training programs or conferences that are related to the topic of pneumoconiosis. A maximum grant of HK$ 100,000 will be allowed for a suitable course longer than 6 months, and $50,000 for a course of 6 months or less. Interested applicants may contact the Board Secretariat at Tel: 2541 0032, Fax: 2541 0211 or E-mail: contact@pcfb.org.hk.