# Abstracts of Dissertations June 2014 Exit Assessment Exercise

### ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC UNTWISTING MOTION IN PATIENTS WITH DIABETES MELLITUS BY SPECKLE TRACKING ECHOCARDIOGRAM

Dr Chan Chi Pan, Department of Medicine, Alice Ho Miu Ling Nethersole Hospital (June 2014 Cardiology Exit Assessment Exercise)

**Background** Some of the diabetic patients develop heart failure without apparent causes. This clinical entity is referred to as diabetes cardiomyopathy. Diabetes cardiomyopathy is marked by the development of diastolic dysfunction. But the association between diabetes mellitus and diastolic untwisting is not known. With the development of two-dimension speckle tracking echocardiogram, it is now possible to assess left ventricular diastolic untwisting motion. The aim of this study is to determine if there's any difference between left ventricular untwisting motion in patients with diabetes mellitus and in patients without diabetes mellitus.

**Methods** 92 echocardiograms done in 2013 were analyzed. The left ventricular untwisting rate during isovolumic relaxation time and the left ventricular peak diastolic untwisting rate was calculated using offline analysis tool. These indices were compared between diabetic patients and non diabetic patients.

**Results** The peak diastolic untwisting rate was significantly higher in diabetic patients. It was also influenced by the presence of chronic kidney disease. And this index was independent of the diastolic dysfunction grading in DM patients.

**Conclusions** The peak diastolic untwisting rate may have a role in assessing diabetic patient's diastolic heart function. Further study is needed to assess its role in diagnosing diabetic cardiomyopathy and its prognostic value.

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### PROGNOSTIC VALUE OF THE PRESENCE AND EXTENT OF OBSTRUCTIVE AND NON-OBSTRUCTIVE CORONARY SEGMENTS DETECTED BY CORONARY COMPUTER TOMOGRAPHY ANGIOGRAPHY FOR MAJOR ADVERSE CARDIAC EVENTS

Dr Lau Alexson Tsz Ki, Department of Medicine & Geriatrics, United Christian Hospital (June 2014 Cardiology Exit Assessment Exercise)

**Background** Coronary computed tomographic angiography (CCTA) has emerged as a valuable non-invasive modality for the investigation of chest pain of low to moderate risk due to its excellent negative predictive value.<sup>1,2</sup> Researches have demonstrated the superior prognostic value of CCTA in comparison to traditional clinical predictive models for predicting major adverse cardiac events (MACE).<sup>3</sup> With this ground work, latest researches aim to develop CCTA prognostic scores such as Segment Involvement Score (SIS) which could provide a better guide to management.<sup>4</sup> On the other hand, while the significance of obstructive lesions (>=50% stenosis) has been well recognized, recent researches has suggested that non-obstructive lesions (<50% stenosis) may have an important role in the development of MACE and is a predictor of all-cause mortality.<sup>5</sup> Non-obstruction lesions represent a "blind spot" in the field of functional cardiovascular imaging because they are

unlikely to be detected by stress imaging technique. On the contrary, they are commonly noted on CCTA and their significance remains to be explored.<sup>6,7</sup>

**Objective** The objective of this study is to evaluate the prognostic value of the presence and extent of involvement of obstructive and non-obstructive coronary segments as detected by CCTA to predict cardiovascular outcomes of unstable angina required medical attention, myocardial infarction, unscheduled coronary percutaneous intervention, cardiovascular death and all-cause mortality.

**Methods** All consecutive subjects referred to the United Christian Hospital for CCTA from July 2006 to December 2013 for the diagnosis or risk stratification of coronary artery disease (CAD) were analysed retrospectively. 606 subjects were included and their demographical, clinical characteristics and symptoms were analyzed and their CCTA results reviewed. Severity of stenosis was classified into normal (no lesions), non-obstructive (<50% stenosis) or obstructive (>=50% stenosis). Extent of involvement was represented by the total number of diseased segments, non-obstructive segments and obstructive segments as detected on CCTA. Time to MACE and all-cause mortality were recorded. Kaplan Meier curves were constructed according to CCTA findings. Potential factors were further analyzed by univariable and multivariate Cox regression models.

**Results** After an observation period of a median of 25 months, there were a total of 20 adverse events, 9 unstable angina, 1 unscheduled percutaneous coronary intervention, 1 cardiovascular mortality and 9 non-cardiac mortality. The total number of diseased coronary segments, non-obstructive segments and obstructive segments detected on CCTA were found to be independent predictors for time to MACE event with hazard ratio of 1.54 [ 95% confidence interval ( CI ) = 1.17 - 2.03, p <0.002 ], 1.49 [ 95% CI = 1.08 - 2.53, p =0.014 ], 1.66 [ 95% CI = 1.09 - 2.04, p = 0.027 ] respectively. All subjects with normal angiogram reached MACE event free survival at end of study. This was in contrast to 99% +/- 1% for non-obstructive CAD patients and 84% +/- 4% for obstructive CAD patients.

**Conclusion** The prognostic value of the presence and the extent of involvement of non-obstructive and obstructive coronary segments detected on CCTA for the development of MACE were demonstrated in a cohort of intermediate pretest probability for CAD.

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### LEFT VENTRICULAR TORSION IN PATIENT WITH VARIOUS DEGREES OF MITRAL REGURGITATION WITH APPARENTLY NORMAL LEFT VENTRICULAR EJECTION FRACTION

Dr Tang King Fun, Department of Medicine, North District Hospital (June 2014 Cardiology Exit Assessment Exercise)

**Objective** Mitral regurgitation (MR) is a common valvular disease in clinical practice. Evaluation of cardiac function traditionally based on the left ventricular ejection fraction (LVEF) and left ventricular (LV) dimensions. Due to an increase of preload in MR, worsening of LVEF often developed late in disease course. Recent advance using speckle-tracking imaging (STI) by echocardiogram was developed to assess LV twisting and untwisting mechanics. There is evidence that STI is able to detect early LV dysfunction in those patients. The purpose of this study is to investigate the relationship between LV twisting mechanics with various degrees of mitral regurgitation with apparently normal LVEF.

**Methology & Result** Echocardiographic data were screened in North District Hospital echocardiography laboratory from 1<sup>st</sup> January, 2013 to 31<sup>st</sup> December, 2013. Patients with

different severities of MR and apparent normal EF (Defined as LVEF >=60%) were included. Exclusion criteria are those with history of myocardial infarction, mitral stenosis, significant aortic valve disease (>Mild), previous cardiac surgery, echo evidence of other cardiac diseases, inadequate echo windows, and suboptimal echo quality. Analyses are done including patient's demographic data and torsional parameters (i.e. Peak systolic twist, peak twist/untwist velocity and time, untwisting velocity during IVRT). There are statistically significant difference of peak LV systolic torsion between age-matched control and MR group (control  $12.1\pm4.3^{\circ}$  versus mild MR  $10.3\pm4.2^{\circ}$  versus moderate MR  $9.8\pm4.0^{\circ}$  versus severe MR  $9.0\pm3.8^{\circ}$ , p=0.049), significant difference of untwisting rate during IVRT between disease groups and control group (control  $30.0\pm30.8^{\circ}$ /s, mild  $16.4\pm37.6^{\circ}$ /s, moderate  $2.6\pm27.2^{\circ}$ /s, severe  $-0.2\pm21.1^{\circ}$ /s, p=0.003). However no difference between peak untwisting rates and timing of peak untwisting rates can be detected in this study.

**Conclusion** Novel speckle tackling imaging by 2D strain analysis may play an important role in identifying patients with MR and early subclinical LV incipient dysfunction before the development of LVEF impairment and LV chamber dilatation.

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# PREDICTORS FOR INTENSIVE CARE UNIT ADMISSION IN MYASTHENIA GRAVIS AND REVIEW OF CHARACTERISTICS OF MYASTHENIA GRAVIS PATIENTS IN A LOCAL REGION HOSPITAL IN HONG KONG

Dr Cheung Wing Sze Emily, Department of Intensive Care, Pamela Youde Nethersole Eastern Hospital (May 2014 Critical Care Medicine Exit Assessment Exercise)

**Introduction** Myasthenia gravis (MG) is the commonest neuromuscular junction disorder that requires intensive care. Mortality rate has decreased with the improvement in respiratory care in specialized intensive care unit (ICU). However, limited studies have been done on the predictive factors for ICU admission in MG patients.

**Objective** The primary objective of this study is to identify the predictive factors for ICU admission in a local regional hospital. Secondary objectives included identity risk factors for MG related mortality, evaluate the characteristic of MG patients admitted to ICU and identify the risk factors for extubation failure.

**Methods and Main results** This is a retrospective single center cohort study carried out in a local tertiary hospital between January 1997 and June 2013. All MG patients diagnosed either in-patient or out-patient by our neurology team during this period was included. Patients' demographics, MG diseases characteristics and treatment modalities and ICU clinical informations were collected. A total of 164 patients diagnosed to have MG during this period were included in the analysis. MG related mortality rate was 6.1%. Among the study group, 21 patients (12.8%) required ICU admission. The median ICU length of stay was 7 days (2-26). In multivariate logistic regression analysis, presence of axial symptoms on initial MG presentation was found to be the only independent predictive factors for ICU admission (OR 9.67, 95% CI 2.18-42.79, p = 0.003). Moreover, positivity in repetitive stimulation test (RST) was significantly associated with MG related mortality (OR 11.23, 95% CI 1.34-94.1, p = 0.026).

**Conclusion** This study found that presence of axial symptoms on initial presentation was the only independent predictive factor for ICU admission and positivity in RST was associated with MG related mortality. Early recognition of high risk patients for potential ICU care is critical to improve the clinical outcome.

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### PREDICTORS OF EARLY ADVERSE OUTCOMES FOLLOWING INTRAVENOUS THROMBOLYSIS OR ENDOVASCULAR INTERVENTION FOR ACUTE ISCHEMIC STROKE PATIENTS ADMITTED TO AN INTENSIVE CARE UNIT Dr Fong Man Chi Natalie, Department of Anesthesia and Intensive Care Unit, Tuen Mun Hospital (May 2014 Critical Care Medicine Exit Assessment Exercise)

**Background** The predictors of early adverse outcomes following intravenous thrombolysis or endovascular therapy for acute ischemic stroke are inadequately characterised among patients in Hong Kong. It is essential to identify early prognostic factors to clarify the therapeutic perspective.

**Objective** To determine the clinical features observed in the first 24 hours post-intervention that predict early mortality and poor functional outcomes for stroke patients admitted to the intensive care unit.

**Design** A retrospective cohort study.

**Setting** ICU of an acute regional hospital in Hong Kong.

**Subjects** Patients with acute ischemic stroke who were admitted to the ICU after intravenous thrombolysis or endovascular therapy between 1<sup>st</sup> June 2004 and 31st July 2013 were included in this study.

**Outcomes** The primary outcome was all-cause mortality at 30 days. The secondary outcome was severe disability or death defined as modified Rankin scores (mRS) of 4 to 6 at 90 days.

**Results** A total of 204 ICU patients (median age, 67 years) were included in the study; 164 patients were treated with intravenous thrombolysis alone, and 40 patients were treated with endovascular intervention. The 30-day all-cause mortality rate was 14.7% (n=30), and the 90-day all-cause mortality rate was 17.2% (n=35). 14 patients (6.9%) suffered from symptomatic intracranial haemorrhage. A higher score on the National Institute of Health Stroke Scale (NIHSS) at presentation (adjusted OR, 1.098; 95% CI,1.012-1.191; p=0.018), a higher Acute Physiology and Chronic Health Evaluation (APACHE) II score (adjusted OR, 1.246; 95% CI, 1.127-1.377; p<0.001) and higher first 24-hour systolic blood pressure (adjusted OR,1.054; 95% CI,1.09-1.019; p=0.003) independently predicted 30-day mortality regardless of treatment modality. Additionally, a higher NIHSS score (adjusted OR,1.114; 95% CI 1.053-1.178; p<0.001) at presentation and a higher APACHE II score (adjusted OR,1.12; 95% CI,1.041-1.204; p=0.001) were independently associated with poor functional outcome (modified Rankin scores.4-6). Endovascular therapy was associated with less functional dependence (adjusted OR, 0.232; 95% CI, 0.09-0.598; p=0.001), a significantly decreased requirement of temporary tracheostomy (p=0.027) and less development of in-hospital sepsis (p=0.030) despite a higher initial NIHSS score (median, 15 versus 12).

**Conclusion** Prediction of stroke mortality and functional outcome can be performed as early as within the first 24 hours after receiving intravenous or endovascular therapy for acute ischemic stroke. Endovascular therapy may be superior to intravenous thrombolysis alone, in terms of functional outcome and stroke-related complications.

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# DIAPHRAGMATIC ULTRASONOGRAPHY FOR THE MECHANICALLY VENTILATED PATIENTS

Dr Leung Chi Hung Czarina, Adult Intensive Care Unit, Queen Mary Hospital (May 2014 Critical Care Medicine Exit Assessment Exercise)

**Introduction** Mechanical ventilation (MV) is a crucial intensive care unit (ICU) tool, however its use can cause diaphragmatic atrophy and dysfunction. Previous studies described ultrasound measurements of diaphragm thickness or excursion.

**Objective** We hypothesize that diaphragmatic ultrasonography is a safe and effective tool for predicting ventilator weaning outcome in critically ill patients requiring MV.

**Methods** We performed a prospective observational pilot study to evaluate the relationship of ultrasonographically measured percentage respiratory change of diaphragmatic thickness ( $\Delta$ tdi%) and diaphragmatic excursion with clinical outcome. We recruited 31 ICU patients upon necessitating MV. We performed serial ultrasound on bilateral diaphragm from start until end of MV period.

**Results** For predicting weaning failure, decrease in  $\Delta$ tdi% and excursion at the end of MV period were the best predictors [ROC AUC Left 0.979, Right 1.000; excursion AUC Left 0.986, Right 0.861]. Even first day values showed high negative predictive values ( $\geq$ 88.9%). For predicting MV duration, at least one side of the diaphragm showed increase  $\Delta$ tdi% and excursion to be associated with shorter duration.

**Conclusion** The diaphragmatic ultrasound measurements of  $\Delta tdi\%$  and excursion are safe to perform and feasible predictors of MV outcome. The best predictor of weaning failure is reduction of  $\Delta tdi\%$  and diaphragmatic excursion on last day. Application of these ultrasound parameters may help assess readiness for weaning.

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### PATIENT CHARACTERISTICS, AETIOLOGIES AND RISK FACTORS FOR MORTALITY OF SEVERE COMMUNITY ACQUIRED PNEUMONIA IN A LOCAL INTENSIVE CARE UNIT: A RETROSPECTIVE REVIEW

Dr Yung Sai Kwong, Intensive Care Unit, Queen Elizabeth Hospital (May 2014 Critical Care Medicine Exit Assessment Exercise)

**Background** Community acquired pneumonia (CAP) is a common cause of intensive care unit (ICU) admission. The aim of this study was to identify factors predicting 30-day mortality and to describe the patient characteristics and aetiologies in patients admitted to the ICU for severe CAP.

**Methods** This was a single centre retrospective study. Demographic data, treatment methods, aetiologies and outcomes of patients admitted to the ICU of Queen Elizabeth Hospital for severe CAP from 1st January 2011 to 30th June 2013 were analysed.

**Results** 116 eligible patients were identified. The 30-day mortality rate was 28% (32 patients). Older age (adjusted OR 1.06 per year increase, 95% CI 1.02 - 1.11), need for renal replacement therapy (adjusted OR 12.1, 95% CI 3.92 - 37.4) and admission to ICU during weekends or public holidays (adjusted OR 4.16, 95% CI 1.26 - 13.7, compared to admission during office hours) were independent predictors of 30-day mortality on multivariate logistic regression analysis. Among the pneumonia-specific severity scores examined, pneumonia severity index was most predictive of 30-day mortality (AUC = 0.70 on ROC curve). For the

general ICU severity scores, APACHE II and IV had the same performance in predicting 30-day mortality, both with AUC 0.84 on ROC curves. Of the 80 (71%) patients with an identifiable aetiology, influenza (34 patients, 29.3%) and pneumococcus (30 patients, 25.9%) were the most common.

**Conclusions** Older age, need for renal replacement therapy and admission to ICU during weekends or public holidays were independent predictors of 30-day mortality in patients admitted for severe CAP.

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# PEMPHIGUS VULGARIS: A RETROSPECTIVE REVIEW OF THE CLINICAL FEATURES, TREATMENT AND PROGNOSTIC FACTORS OVER A 13-YEAR PERIOD

Dr Kung Ka Yee, Social Hygiene Service, Department of Health (June 2014 Dermatology & Venereology Exit Assessment Exercise)

**Objective** To review the patient demographic characteristics, clinical features, treatment and clinical course in local patients with pemphigus vulgaris (PV). The prognostic influence of certain epidemiological, clinical and immunological factors on the clinical outcome of PV will be evaluated.

**Method** A retrospective, multi-center, observational study was conducted to review the medical records of all patients diagnosed with pemphigus vulgaris in dermatological clinics under the Department of Health from January 2000 to July 2013.

**Results** A total of 108 patients were recruited in the study. The mean age of onset was 54.47 years and the male to female ratio was 1:1.25. After disease establishment, 73.1% had mucocutaneous involvement, 8.33% and 18.5% had isolated mucosal and cutaneous involvement respectively. The mean starting steroid dose was 33.93mg and adjuvant treatment was used in 75.9% of patients. Complete remission while on therapy was achieved in 77.8% of patients, after a mean duration of 58.51 weeks of treatment. Relapses occurred in 51.2% of patients. A total of 13.9% of patients had recalcitrant disease, compared with 12.0% of patients who achieved complete remission off treatment with no relapse detected till end of study period. Isolated mucosal disease at presentation was significantly associated with longer time to disease control (p=0.005) and complete remission (p=0.006.) Patients who achieved disease control earlier also achieved complete remission earlier (r=0.419, \*p=0.001.)

**Conclusion** Most patients with PV achieved complete remission around 1 year after treatment, though relapses were common. Isolated mucosal disease was associated with worse prognosis than other subtypes of PV. Earlier response to treatment predicted better long term prognosis.

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### STUDY ON KNOWLEDGE OF HUMAN PAPILLOMA VIRUS (HPV), HPV VACCINE, VACCINE ACCEPTANCE AND BARRIERS TO VACCINATION AMONG ATTENDANTS OF SEXUALLY TRANSMITTED DISEASE AND SKIN CLINICS IN HONG KONG

Dr Tang Wing Sen Joyce, Social Hygiene Service, Department of Health (June 2014 Dermatology & Venereology Exit Assessment Exercise)

**Background** Patients attending sexually transmitted disease (STD) clinics often have risky

sexual behaviours which could affect their beliefs and attitudes towards human papilloma virus (HPV) vaccine. Local data on HPV vaccine acceptance of male population and sexual behaviours in relation to vaccine acceptance are lacking.

**Objective** To examine awareness and knowledge of HPV and HPV vaccine, sexual behaviours, attitudes towards HPV vaccine and barriers to vaccination among patients of STD clinics and skin clinics, and lastly factors associated with HPV vaccine acceptance. **Study Design** This is a cross sectional study in Hong Kong.

**Methods** Attendees of STD clinics and skin clinics from August 2013 to October 2013 were invited and recruited after consent. They then completed a questionnaire about their sociodemographics, sexual behaviours, awareness and knowledge of HPV and HPV vaccine, and attitudes and barriers of HPV vaccine.

**Results** A total of 370 patients were recruited and 349 of them were included in the study. 57.9% and 56.9% of STD clinics patients were aware of HPV and HPV vaccine respectively, while 78.9% and 72.9% of skin clinics patients had heard of HPV and HPV vaccine respectively. 73.6% of STD clinics patients and 56.4% of skin clinics patients showed positive acceptance of HPV vaccine. Concern about side effects was the most common barrier to HPV vaccination. The significant independent predictors associated with willingness of selfvaccinating against HPV include younger age (OR: 0.743,95%CI: 0.603-0.916), perceived risk of contracting STD (OR: 2.017, 95%CI: 1.136-3.582), greater number of lifetime sexual partners (OR: 1.282, 95%CI: 1.091-1.506) and positive awareness of HPV vaccine (OR: 3.288, 95%CI: 1.964-5.504).

**Conclusion** STD clinic patients were less aware of HPV and HPV vaccine yet they had greater acceptance of HPV vaccine than patients of skin clinics possibly due to their high-risk sexual behaviours. Awareness of HPV and HPV vaccine should be enhanced especially in the STD clinic patients through education in order to achieve better prevention of HPV related diseases.

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### **RETROSPECTIVE REVIEW ON THE CLINICAL PRESENTATION, TREATMENT AND OUTCOMES OF PATIENTS WITH GASTROENTEROPANCREATIC NEUROENDOCRINE TUMOUR IN A HONG KONG TERTIARY CENTRE**

Dr Chan Ting, Department of Medicine & Therapeutics, Prince of Wales Hospital (May 2014 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Gastroenteropancreatic neuroendocrine tumours (GEP-NETs) are being increasingly recognized due to their wide spectrum of clinical presentations and variable prognosis, and its incidence is notably rising in many parts of the world. There is, however, a paucity of epidemiological data in local Hong Kong Chinese population.

From 1996 to 2013, 126 patients with histopathologically confirmed GEP-NETs at the Prince of Wales Hospital were reviewed. The most common primary sites were pancreas (34.9%), rectum (33.3%), and stomach (8.7%), with the vast majority being non-functional GEP-NETs (91.3%) which presented as incidental finding or with non-specific gastro-intestinal symptoms. The tumours were mostly grade 1 (G1)(87.3%) according to the 2010 World Health Organization classification. Around 20% of cases had metastases on presentation and liver was the most common site of distant metastases. Univariate analysis identified that age less than 55 years, G1 tumours and absence of metastases on presentation as significant favourable predictors for survival; with G2/3 tumours, tumours larger than 2 cm, and

metastases on presentation as significant predictors for disease progression (all p<0.05). In multivariate analysis, age and metastases on presentation were significant predictors of mortality (respective hazard ratios [HR] 1.05 [95% confidence interval {CI} 1.02-1.08] and 6.52 [95% CI 3.22-13.2]) and disease progression (respective HRs 1.05 [95% CI 1.02-1.07] and 4.12 [95% CI 1.96-8.68]), while higher tumour grade also independently predicted disease progression (HR 5.17 [95% CI 2.05-13.05]) (all p<0.05).

Given the high morbidity and potential need for different treatment modalities, multidisciplinary approach in the management of patients with GEP-NETs may help improve the treatment efficacy and outcome, by adopting a more uniform yet individualized management plan based on the current treatment guidelines and trend worldwide.

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# THE MISSING LINK BETWEEN HAEMOGLOBIN A1C AND FRUCTOSAMINE

Dr Hue Siu Man, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (May 2014 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

**Background** HbA<sub>1c</sub> and fructosamine are commonly used in assessment of glycaemic control. The difference between measured HbA<sub>1c</sub> and that predicted from fructosamine is termed as "glycation gap".

**Objectives of this dissertation** 1. To understand the potential factors causing the discrepancy between HbA<sub>1c</sub> and fructosamine 2. To understand the concept of glycation gap and its current evidence 3. To study the glycation gap in our local Chinese diabetic population

**Method** This was a cross-sectional study of local Chinese diabetic patients (n=128). Strict selection criteria were applied. HbA<sub>1c</sub> and fructosamine were measured at  $0^{h}$  and  $4^{h}$  month. Glycation gap (G-GAP) was calculated. Subjects were divided into high, medium and low G-GAP tertiles. Its relationship with albuminuria and its consistency over four months were analyzed.

**Results** HbA<sub>1c</sub> strongly correlated with fructosamine (r=0.786, P<0.001). The glycation gap ranged from -2.17% to +2.51%. The prevalence of albuminuria in high, medium and low G-GAP group was 47.6%, 26.8% and 16.7% respectively. In the high G-GAP group, the odds of having albuminuria was 4.5 times of the low G-GAP group (P=0.003) and 2.5 times of the medium G-GAP group (P=0.053).The mean HbA<sub>1c</sub> did not differ significantly between subjects with and without albuminuria (7.7% vs. 7.3%, P=0.13) whereas the glycation gap did (0.5% vs. 0.0%, P<0.001). Using the multivariate logistic model to control for age, duration of diabetes, body-mass-index and hypertension, G-GAP independently predicted the presence of albuminuria (P=0.005). The glycation gap remained consistent over a period of four months. The first and second G-GAP were highly correlated (r=0.79).

**Conclusions** In our local Chinese diabetic population, glycation gap was associated with albuminuria. Consistency in glycation gap was observed over four months.

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# PREVALENCE OF HEPATITIS B AND CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE PATIENTS IN A HEPATITIS B ENDEMIC AREA

Dr Chan Chi Hey Heyson, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2014 Gastroenterology & Hepatology Exit Assessment Exercise)

**Background** Little is known of the prevalence of chronic hepatitis B virus (HBV) infection and its effect on the course and choice of therapy in patients with inflammatory bowel disease (IBD) in a HBV-endemic region.

**Aim** To assess the prevalence of HBV, determinants of liver dysfunction, and effects of HBV infection on the therapeutic strategy and clinical course of IBD patients

**Methods** In this cross-sectional study, consecutive IBD subjects were recruited over one year. Baseline demographics, IBD disease control and use of IBD medications were recorded. Patients were tested for hepatitis B surface antigen (HBsAg) and HBV DNA level. Liver dysfunction was defined as serum alanine aminotransferase (ALT) level above twice the upper limit of normal. Liver stiffness was measured by Fibroscan in a subset of patients with chronic hepatitis B (CHB).

**Results** A total of 406 patients were recruited (59.4% male, 45.6% Crohn's [CD], 54.4% ulcerative colitis [UC]). The mean age was 44.9. 23 patients (5.7%) had positive HBsAg. Use of steroid (odds ratio [OR] 2.52, p = 0.010) and a previous history of surgery (OR 2.33, p = 0.026) were associated with liver dysfunction in patients with IBD. HBsAg positivity and use of other immunosuppressants were not significantly associated with liver dysfunction. There was no significant difference in the rate of IBD control (p=0.770), hospital admission (p=0.145), history of surgery (p=0.298) and use of IBD medication including 5-aminosalicylate (p=0.199), thiopurines (p=0.093) and steroid (p=0.116) between HBsAg-positive and HBsAg-negative IBD patients. No significant differences were detected for UC or CD location and behavior between these two subgroups of patients. Mean serum HBV DNA level (p=0.319) and liver stiffness measurement (p=0.081) did not differ between CHB patients with or without IBD.

**Conclusion** The prevalence of CHB among patients with IBD in Hong Kong is not higher than that that of the general population. Use of steroid and a history of surgery were associated with liver dysfunction. There was no difference in disease control and choice or use of medications for the underlying disease between IBD subjects with or without CHB.

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### APPLICATION OF THE WATER EXCHANGE METHOD FOR SCHEDULED COLONOSCOPY: SEDATION REQUIREMENT CAN BE MINIMIZED WITHOUT COMPROMISING PATIENT-CENTRED AND PROCEDURE-RELATED OUTCOMES

Dr Chu Wai Ying, Department of Medicine & Geriatrics, Princess Margaret Hospital (June 2014 Gastroenterology & Hepatology Exit Assessment Exercise)

**Background** Water exchange colonoscopy has demonstrated to be effective in reducing sedation requirement and pain score, without compromising cecal intubation rate compared with conventional air method.

**Aim** The aim of this study is to examine whether water exchange method increases proportion of patient completing colonoscopy examination without sedation, reduces sedation use and patient discomfort as compared to conventional air method.

**Methods** A single blinded, randomized controlled trial was carried out in Princess Margaret Hospital from June 2013 to January 2014. One hundred and twenty patients who accepted on-demand sedation were recruited and randomized into either the water group or the air group.

**Results** A total of 178 patients were invited to participate into the study, in which 120 patients who agreed for on-demand sedation were randomized into either the water group or the air group. Cecal inbubation rate was lowered though not statistically significant in the water group 83% compared to 93% in the air group (p=0.15). Cecal intubation time was significantly longer in the water group (24 minutes in the water group verses 19 minutes in the air group, p=0.01). Sedation requirement was significantly lowered in the water group compared to the air group (p=0.03). However, the proportion of patients who completed unsedated colonoscopy was not significantly higher in the water group (52%) compared to the air group (37%) (p=0.31). The pain score was similar between the two groups though a higher proportion of patients were willing to repeat colonoscopy by water exchange method. Learning curve built from the current data was similar compared with previous studies.

**Conclusion** Current data could not demonstrate a significantly higher proportion of patients completing colonoscopy without sedation by water exchange method. However, a lower sedation requirement without compromising cecal intubation might benefit a selected group of patients.

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### THE EFFECT OF TAKING A 15-MINUTE BREAK DURING COLONOSCOPY SESSION ON ADENOMA DETECTION, A PROSPECTIVE, RANDOMIZED CONTROL STUDY

Dr Ho Kai Tin, Department of Medicine, Alice Ho Mui Ling Nethersole Hospital (June 2014 Gastroenterology & Hepatology Exit Assessment Exercise)

**Background** Adenoma detection rate (ADR) has been widely recommended as an important quality indicator of colonoscopy. Recent research suggests that endoscopist fatigue may significantly affect the ADR which is noted to decline in each subsequent hour during a colonoscopy session. However, there are little interventional studies that may reduce endoscopist fatigue so as to improve the colonoscopy performance.

**Objective** To determine whether a 15-minute break in the middle of a colonoscopy session would prevent dropping in ADR due to endoscopist fatigue.

**Methods** This is a prospective, randomized controlled study conducted at the Alice Ho Miu Ling Nethersole Hospital (AHNH). Patients who underwent afternoon colonoscopies during the study period were eligible. Endoscopists would perform six colonoscopies during afternoon session and each endoscopist would be randomized to control and intervention group in 1:1 ratio. Endoscopists who were randomized to the control group would work continuously to complete the list as was the usual practice whereas those who were randomized to the intervention group would take a 15-minute break after the 3rd colonoscopy. The primary outcome was the ADR of the 4<sup>th</sup> to 6<sup>th</sup> colonoscopies between the control and intervention group.

**Results** Total 1379 patients were included, of which 348 and 341 patients were done in later half of the session in the intervention and control group respectively. The ADR was higher in the intervention group than in the control group (37.4% vs. 30.8%) but this did not reach statistical significance (p=0.069). However, after controlling for confounding factors using multivariate logistic regression analysis, taking 15-minute break was significantly associated with an increased ADR (p=0.034).

Conclusion After adjusting for confounding factors, taking a 15-minute break halfway

through a session of six colonoscopies was shown to improve ADR. This may provide a relatively simple, inexpensive and practical way to tackle endoscopist fatigue during a long colonoscopy session.

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# PROSPECTIVE STUDY INTO THE RISK OF COLORECTAL NEOPLASMS IN ASYMPTOMATIC INDIVIDUALS WITH A FAMILY HISTORY OF ADVANCED ADENOMAS

Dr Ng Siew Chien, Department of Medicine and Therapeutics, Prince of Wales Hospital (June 2014 Gastroenterology & Hepatology Exit Assessment Exercise)

**Background and Aim** The risk of colorectal neoplasms among siblings of individuals with advanced adenomas is unclear. We assessed the prevalence of advanced adenomas and cancers in siblings of individuals with advanced adenomas compared with siblings with no such lesions.

**Methods** Colonoscopies were performed in 188 asymptomatic siblings to subjects with advanced adenomas (adenomas  $\geq 10$ mm, high grade dysplasia, villous/ tubulo-villous; cases, age 58±6.4 years) and 323 age- and sex-matched siblings of healthy subjects who had normal colonoscopies (controls, 57.6± 5.9 years). Primary outcome was the prevalence of advanced neoplasms defined as cancers or advanced adenomas.

**Results** The prevalence of advanced neoplasms was 11.7% among siblings of patients and 2.8% among controls (matched odds ratio [mOR], 4.58; 95% confidence interval [CI], 2.07-10.14;  $P \le 0.001$ ). The prevalence of adenomas  $\ge 10 \text{ mm} (11.2\% \text{ vs. } 1.9\%; \text{mOR}, 6.62; 95\%$  CI, 2.61-16.8; P<0.001), villous adenomas (5.9% vs. 1.2%; mOR, 5.01; 95% CI, 1.57-16.04; p=0.007) and all colorectal adenomas (38.3% vs. 21.7%; mOR, 2.27; 95% CI, 1.51- 3.41; P < 0.001) was higher among siblings of patients. Two cancers were detected among siblings of patients; no cancer was detected in controls. The prevalence of advanced neoplasms among siblings of patients was higher when their index case was female (mOR, 6.4; 95% CI, 2.0–20.46) and had large adenomas (mOR, 4.6; 95% CI, 1.9–11.3) or villous adenomas (mOR, 7.6; 95% CI, 1.6-36.1).

**Conclusions** Siblings of patients with advanced adenomas have a more than four-fold increased risk of developing advanced neoplasms. This high risk group should be offered screening colonoscopy.

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# CHARACTERISTIC OF INTERVAL COLORECTAL CANCER: A RETROSPECTIVE COHORT ANALYSIS

Dr Tong Yee Hong Terence, Department of Medicine and Geriatrics, Tuen Mun Hospital (June 2014 Gastroenterology & Hepatology Exit Assessment Exercise)

**Introduction and aims** Colorectal cancers are consistently reported soon after colonoscopy. These cancers are also known as "interval cancers" or "post-colonoscopy colorectal cancers". It is believed that most of them are potentially preventable. This study aimed to examine the rate and possible risk factors of interval cancer in two regional hospitals in Hong Kong.

**Method** All colorectal cancers diagnosed between 1 Jan 2006 and 31 Dec 2013 with a colonoscopy performed 6-60 months prior to the diagnosis are identified as interval cancers; they were compared with all individuals who received two colonoscopies more than 60 months apart between 1 Jan 2001 – 31 Dec 2013 without cancer diagnosis.

**Results** After exclusion, 36 patients fulfilled the criteria of interval cancers among the 3268 colorectal cancers diagnosed within the study period. The rate of interval cancer was 1.1%. Comparing with 187 controls with binary logistic regression, incomplete index colonoscopy (OR = 56.377, P<0.001), colonoscopy done prior to index colonoscopy (OR = 5.926, P=0.002), detection of polyp larger than 1cm at index colonoscopy (OR = 11.524, P=0.001), out-patient bowel preparation (OR=4.951, P=0.014) and age at yearly increment (OR = 1.051, P=0.019) were indentified as independent risk factors for interval cancers.

**Conclusion** The rate of interval cancers in the study population was 1.1% which is comparable with previous studies in other regions. Contributing factors were indentified in the patient characteristics, colonoscopy setting, performance and findings. These results highlight the importance to ensure colonoscopy quality and appropriate post-colonoscopy management.

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# PREVALENCE AND RISK FACTORS OF DEPRESSIVE SYMPTOMS IN ELDERLY PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Dr Lai Tin Lok, Department of Medicine & Geriatrics, Kwong Wah Hospital (May 2014 Geriatric Medicine Exit Assessment Exercise)

**Background** COPD and depression are both common and serious diseases among elders in Hong Kong. Depression is reported to be prevalent among COPD patients, but the data concerning their association is lacking in our locality.

**Objective** The primary aim is to investigate the prevalence of depressive symptoms in elders with clinically stable COPD. The second aim is to determine if the elderly with COPD have more depressive symptoms than controls. The third aim is to identify risk factors associated with depressive symptoms among elders with COPD.

**Methods** This study is a cross-sectional, case-control study. A total of 55 elders with clinically stable COPD from the COPD clinic and 55 elders from the geriatric clinic of Kwong Wah Hospital formed a case and control group. Basic demographic data and clinical characteristics were collected. Depressive symptoms were assessed by using the Chinese version of the Geriatric Depression Scale short form (GDS - 15 items).

**Results** In our study, the prevalence of depressive disorders in elders with COPD and controls were 21.8% and 3.6%, respectively. The median GDS score was 3 (2, 7) in COPD groups and 2 (1, 4) in controls (p = 0.001). Univariate analysis identified that the (1) Borg scale, (2) activity domain score in the St. George's Respiratory Questionnaire (SGRQ), (3) 6-minute walk distance (6MWD), (4) Body Mass Index (BMI), (5) BI-20, (6) MMRC scale and (7) BODE score were associated with depressive symptoms in COPD. The regression model explored that the BODE index was the strong associated factor, with an odd ratio of 1.8, p = 0.003.

**Conclusion** A significant proportion of stable COPD elders were found with depressive symptoms, which was significantly more than the other elderly without COPD. COPD disease seemed to increase the likelihood of a depressive mood compared with other chronic illnesses, and the BODE index was associated with them. Early screening for depressive symptoms among the elderly with COPD might be warranted.

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### MORTALITY AND PROGNOSTIC PREDICTORS IN BULLOUS PEMPHIGOID: AN INTER-SUBSPECIALTY COHORT OF CHINESE NURSING HOME OLDER ADULTS

Dr Li Wing Man Christie, Department of Medicine, Queen Mary Hospital (May 2014 Geriatric Medicine Exit Assessment Exercise)

**Introduction** Bullous pemphigoid (BP) is the commonest autoimmune blistering disease in elderly. It affects primarily frail older patients with dependent activity of daily living. BP is known to be associated with significant long-term all-cause mortality. Data on the effect of BP on the overall mortality in patients living in the Residential Care Homes for the Elderly (RCHE) are, however, lacking. Knowledge on the predictors for poor survival outcomes in Chinese patients with BP is also limited.

**Objective** The objectives of our study were to determine the one-year, two-year and three-year mortality rates of BP in patients living in the RCHE and to identify specific prognostic factors associated with poor survival outcomes. Local epidemiology, functional, clinical, biochemical, immunological characteristics and treatment strategies of the patients with BP were also described.

**Main Outcome Measures** The one-year, two-year and three-year mortality rates of BP in patients living in the RCHEs, the independent predictors for poor survival outcomes and the descriptive data on the local epidemiology, functional, clinical, biochemical, immunological and therapeutic characteristics of patients.

**Method** We conducted a retrospective, case-control cohort study of 266 patients living in the RCHEs who were newly diagnosed with BP within the Hong Kong West Cluster between the period 2001 and 2011. The Hospital Authority Computer Management System (CMS) was used for patient identification. Demographic data, clinical, laboratory and treatment records were reviewed. The mortality rate of the patients was compared with age-, gender-and comorbidity- matched controls at a ratio of 1:3. There were 1078 patients in total with 266 cases and 812 controls.

**Results** The one-year, two-year and three-year mortality rates were 51.9%, 72.9% and 83% respectively. The mean age at diagnosis was  $85.1 \pm 7.9$  years. 94% of the patients had dependent activity of daily living. The mean baseline Charlson Comorbidity Index (CCI) was 2.1  $\pm$  1.1. Multivariate analysis showed that BP was an independent predictor of mortality (hazard ratio [HR], 3.7; 95% confidence interval [C.I.], 3.1 - 4.4) (P<0.001). BP was also associated with a higher rate of infection-related mortality (HR, 4.0; 95% C.I., 3.3 - 4.9) (P<0.001). Older age (Odds ratio [OR], 1.02; P=0.03), increased number of admissions in the preceding year prior to the diagnosis of BP (OR, 1.12; P<0.001), generalized disease (OR, 1.37; P=0.05) and serum albumin level at time of diagnosis (OR, 0.93; P<0.001) were the observed independent predictors for mortality in BP patients. The use of systemic corticosteroid was associated with faster rate of skin recovery (P=0.02), but had no effect on the survival and relapse rate of BP.

**Conclusion** BP is associated with significant risks of the all-cause and infection-related mortality in patients living in the RCHEs. More attentions on the nutritional and general medical needs are warranted among them. Individual predictors exist and may help stratification of the death risk among these patients. Systemic corticosteroid therapy has a role in symptomatic control, while the effect on long term survival remained questionable.

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# EFFECTIVENESS OF MULTIDISCIPLINARYDISCHARGE PLANNING AND COMMUNITY SUPPORT PROGRAM FOR HIGH RISK OLDER PATIENTS

Dr Lin Oi Yee, Department of Medicine, Queen Mary Hospital (May 2014 Geriatric Medicine Exit Assessment Exercise)

**Background** Hospital readmission shortly after discharge on one hand is an important indicator of patient health outcome and healthcare system performance; on the other hand, it contributes significantly to rising healthcare costs. In January 2012, Hong Kong West Cluster has launched the new Integrated Care and Discharge Support for Elderly Patients (ICDS) to attempt at reducing the risk of unplanned hospital re-admission through better discharge planning and post-discharge support. Large scale study is indicated in studying the effectiveness of the ICDS program in preventing readmission and improving overall health outcomes of older patients. In addition, factors affecting its effectiveness should also be analyzed in detail, so that fine adjustment of the ICDS program can be made in future to further boost its effectiveness as well as efficiency.

**Objective** The aim of this study was to investigate the effectiveness of the ICDS program in preventing readmission and improving overall health outcomes of older patients. In addition, factors affecting its effectiveness would also be analyzed.

**Subject and method** It was an 18-month prospective cohort study conducted in the 4 hospitals of the Hong Kong West Cluster (HKWC) from 1<sup>st</sup> April 2012 to 30<sup>th</sup> September 2013. Our subjects were those home dwelling elderly aged 60 or above recruited to the ICDS program from 1<sup>st</sup> April 2012 to 31th March 2013. Baseline demographics, co-morbidity according to Charlson Co-morbidity Index (CCI), Barthel Index [BI (20)], Abbreviated Mental Test (AMT), Modified Functional Ambulation Category scale (MFAC), details of the service received, number of medications and baseline blood test results of included subjects were collected at baseline. Subjects were followed up for 6 months. The number of Accident and Emergency Department (AED) attendance, unplanned acute hospital admissions and length of stay of both acute and convalescent hospitals 6 months before and after recruitment, the 6-month all-cause mortality and rate of institutionalization to residential care home for the elderly (RCHE) were recorded. The AMT score, BI (20), MFAC were also reassessed in all patients when they were discharged from the program.

**Results** 1090 home dwelling elderly joining the ICDS program were included into the study. The median number (inter quartile range) of 6-month AED attendance of included subjects reduced from 2 (1-3) before joining the ICDS program to 1 (0-2) after joining the ICDS program (p<0.001). The median number of unplanned acute hospital admission of these subjects also reduced from 1 (0-2) to 0 (0-1) (p<0.001). The median number of hospital bed days reduced from 11 (4-22) days to 2 days (0-13.5) (p<0.001). The median BI (20) and MFAC of included subjects improved significantly at the end of the program. Only 2.6% of the surviving subjects were being institutionalized to RCHE at 6 months after joining the ICDS. Increasing age and high CCI scores were independent positive predictors for AED attendance 6 months after joining the ICDS program. On the other hand, high albumin level and living alone were negative predictors for AED attendance. Increasing age and increasing number of medications were significant independent positive predictors for no reduction in bed days while higher hemoglobin level was a negative predictor.

**Conclusion** This 18-month prospective cohort study suggested that the ICDS program might be able to reduce AED attendance, hospital readmission and readmission acute and convalescent hospital length of stay. Independent predictors for AED attendance and no reduction in hospital bed days 6 months after joining the ICDS program were identified. Further studies are warranted to examine whether AED attendance, acute hospital admission and hospital bed days among the high risk older patients can be further reduced by modifying some of predicting factors identified in this study. In addition, a detailed cost analysis is needed to show whether ICDS is cost effective and is able to save money by reducing hospital utilization.

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# POLYPHARMACY AND POTENTIAL INAPPROPRIATE MEDICATION IN A GERIATRIC OUTPATIENT CLINIC

Dr Siu Chun Yue, Department of Medicine and Geriatrics, Caritas Medical Centre (May 2014 Geriatric Medicine Exit Assessment Exercise)

**Background** Polypharmacy and potential inappropriate medication (PIM) are common problems in geriatric population. As the population is aging, they become significant problems in the medical care system.

**Objective** The study is to evaluate the prevalence and predictive factors of polypharmacy and potential inappropriate medication in a local geriatric outpatient clinic.

**Method** We conducted an one week cross-sectional retrospective study in a geriatric outpatient clinic in Hong Kong. Polypharmacy was defined as the prescription of five or more medications. Potential inappropriate medication was defined according to the Beers criteria version 2012. The prevalence of polypharmacy and potential inappropriate medication were measured. Multivariate logistic regression was done to determine predictive factors.

**Result** There were 521 patients recruited. Prevalence of polypharmacy was 69.1%. Prevalence of potential inappropriate prescription was 25.1%. Logistic regression revealed number of comorbidity (OR 2.13, 95% CI, 1.70-2.68) and ischaemic heart disease (OR 3.03, 95% CI, 1.21-7.58) were the significant predictors of polypharmacy, while polypharmacy (OR 3.89, 95% CI, 2.04-7.42) and chronic obstructive airway disease (COAD) (OR 2.73, 95% CI, 1.31-5.70) were the significant predictors of potential inappropriate medication. The most common prescribed potential inappropriate medication was alpha one blocker for hypertension (4.4%), followed by first generation antihistamines (4.2%), central alpha agonist for hypertension (3.1%) and H2-receptor antagonists in dementia or cognitive impairment patients (2.7%).

**Conclusion** Polypharmacy and potential inappropriate medication are common problems in Hong Kong. Geriatric patients usually have multiple comorbidities that make them prone to polypharmacy and potential inappropriate medication. The drug regime in geriatric patients need to be individualized.

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# TO CHARACTERISE FEATURES AND RISK FACTORS OF DELIRIUM IN ELDERLY MEDICAL IN-PATIENTS IN A SUB-ACUTE AND REHABILITATION HOSPITAL

Dr Yuk Ka Lok Daniel, Department of Medicine and Geriatrics, Shatin Hospital (May 2014 Geriatric Medicine Exit Assessment Exercise)

**Background** Delirium is an acute confusion state. It can be associated with various risk factors in the elderly population. Delirium is associated with short- and long-term mortality. There are different complications related to delirium if these patients were not managed well. Yet there is no published data on the issue in the local setting.

**Objective** This study aims to study incidence, prevalence, features, risk factors and outcomes of patients with delirium managed in a sub-acute and rehabilitation hospital.

**Methods** Acohort study was done in Shatin Hospital from January to June 2013. Delirium patients were screened by ward visits and performing the CAM (confusion assessment method) score. The background demographics, comorbidities, drug lists, features of delirium and the reported delirium onset time were recorded. Each subject was reviewed at least daily until discharge, to determine the duration of delirium, the features of delirium and complications arising from the delirium. A same number of non-confused subjects were recruited for comparison.

**Results** Prevalence rate of delirium was 1.37% (47/3437), with an incidence rate of 0.73% (25/3437). Background dementia was the most relevant background predisposing comorbidity (p<0.05). In the incident cases, precipitating factors within 2 weeks of delirium onset were any falls or trauma (p<0.05), faecal impaction (p<0.05) and pain (p<0.05). Incident delirium patients used more physical restraints in the acute hospital (p<0.05) and more chemical restraints in the sub-acute and rehabilitation hospital (p<0.01). There was no difference in the length of stay, 28-day readmission, in-patient and 6-month mortality rates between the 2 groups.

**Conclusion** Some precipitants of delirium could be preventable by good nursing care. Iatrogenesis, especially restraints use, still needs to be further studied in larger scale studies on its role in precipitating incident delirium as they are important preventable risk factors.

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**REVIEW OF ADULT HAEMOPHILIA CARE IN HONG KONG: A CROSS-SECTIONAL STUDY OF HEALTH-RELATED QUALITY OF LIFE** Dr Wong Ho Nam, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (May 2014 Haematology & Haematological Oncology Exit Assessment Exercise)

Haemophilia, a rare X-linked inherited disorder, is due to a deficiency in the coagulation factor VIII (in haemophilia A) or factor IX (in haemophilia B). The advent of plasma-derived coagulation factors in the 1960s brought hope to many patients with severe haemophilia who had little prospect of surviving past the age of 40.1 However, by 1980, contaminated factor concentrates had also ravaged those who were infected by the human immunodeficiency virus (HIV) and the hepatitis C virus (HCV).2,3 With the advancements in donor screening and virucidal techniques, HIV and HCV infections have not occurred in patients with haemophilia in the developed world since 1986 and 1992 respectively.4 Thus a new generation was born who may live free from the chronic viral infections and enjoy a near-normal life expectancy. Modern haemophilia care is now beyond the mere safety of therapy or improvement in mortality — health-related quality of life (HRQoL) has emerged as an important tool of measurement of the standard of care. Various studies have been conducted in developed countries in the recent years for the purpose of comparing the HRQoL of haemophilia patients with that of the normal population, or other patients with the burden of chronic diseases.5 The usefulness of these studies in alerting policy makers of the economic and social impact of the treatments in haemophilia has also been highlighted.!!

The first part of this dissertation provides a general overview of the management of haemophilia, with relevant updates in the literature and references to the local data and practice in Hong Kong. In the second part, the findings of an original study on the HRQoL in Hong Kong Chinese patients with haemophilia are presented.

# RISK OF VIROLOGIC REBOUND IN HIV-INFECTED PATIENTS ON HAART WITH VERY LOW-LEVEL VIRAEMIA

Dr Chan Shuk Ying, Department of Medicine, Queen Elizabeth Hospital (May 2014 Infectious Disease Exit Assessment Exercise)

**Background** Current guidelines recommend suppression of plasma human immunodeficiency virus type 1 (HIV-1) RNA viral load to below the limit of assay detection. Newer generations of viral load assays are now able to detect and quantify viral load at very low levels, but the significance of this very low-level viraemia (VLLV) remains unclear.

**Methods** A retrospective cohort study was conducted to analyse the association between VLLV and virologic rebound in 820 HIV-1 infected patients on highly active anti-retroviral therapy (HAART). Patients with viral load < 50 copies/ml were stratified into "VLLV" group (20-49 copies/ml) and "suppressed" group (<20 copies/ml) according to the viral load tested by Roche Molecular Systems COBAS AmpliPrep/COBAS Taqman HIV-1 Test version 2.0. Independent effects of viral load groups, demographic, clinical and laboratory variables on risk of virologic rebound at 104 weeks were investigated by a Cox proportional hazard model.

**Results** There were 626 patients in the "suppressed" group and 194 patients in the "VLLV" group. Median follow-up time was 96 weeks (interquartile range (IQR) 90- 101 weeks), virologic rebound rate were 1.8% and 3.6% in the "suppressed" and "VLLV" group respectively at 48 weeks and 3.2% and 7.2% at 104 weeks. Time to virologic rebound at 104 weeks is significantly shorter in "VLLV" group (log-rank test, p < 0.005). Cox proportional hazard model demonstrated that adjusted hazard ratio for virologic rebound for VLLV at 104 weeks was 3.351 (95% confidence interval, 1.411-7.957, p < 0.01), which is independent of adherence levels. Another independent predictor was suboptimal HAART adherence.

**Conclusion** HIV-1 infected patients on HAART with very-low level viraemia were associated with virologic rebound and this finding was independent of other recognized determinants. The clinical significance of VLLV warrants further study.

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# PREDICTIVE VALUE OF EGFR MUTATION TO WHOLE BRAIN RADIOTHERAPY (WBRT) IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC) BRAIN METASTASIS (BM)

Dr Chan Chiu Yan, Department of Clinical Oncology, Prince of Wales Hospital (June 2014 Medical Oncology Exit Assessment Exercise)

**Objectives** This is a retrospective study of the efficacy of WBRT in NSCLC patients with brain metastasis and known EGFR mutation status. The primary end point is to compare the tumor response rate to WBRT between patients with and without EGFR mutation. The secondary end point is to look at the survival between the two groups.

**Methods** We selected patients with histology confirmed NSCLC, evidence of brain metastasis radiologically and known EGFR mutation status in Prince of Wales Hospital, Hong Kong from 2005 till 2011.

**Results** Ninety patients were recruited into our study. Of the 65 patients who received WBRT, 79.2% in EGFR wild type group responded while 75.6% in EGFR mutant group responded according to the Bezjak response criteria, which were not significant. Also, there

were no significant differences in BM progression free and overall survival between the two groups.

**Conclusions** Contrary to precedent studies, EGFR mutation is neither a predictive biomarker for WBRT nor a prognostic factor for BM survival. EGFR mutation is not a recommendable biomarker in directing the use of WBRT for lung cancer patients with brain metastasis.

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### NOVEL PROGNOSTIC FACTOR IN METASTATIC COLON CANCER

Dr Wong Chi Yan, Department of Clinical Oncology, Prince of Wales Hospital (June 2014 Medical Oncology Exit Assessment Exercise)

**Introduction** There are robust data highlighting the differences between proximal and distal colon cancers in terms of physiology, embryology and molecular features. However, the prognostic significance of tumor location remains uncertain in patients with metastatic colon cancer (mCC).

**Method** This is a retrospective study of 287 patients with mCC. Patients with proximal and distal mCC were compared in terms of response rate (RR) to first-line chemotherapy and overall survival (OS). Multivariate analyses were performed to investigate the relationship between these study endpoints with important prognostic factors.

**Result** Among the 287 patients, there was no association between tumor location with RR or OS. Since *KRAS* mutation status and the number of lines of therapy were potential confounders of survival in multivariate analysis, unplanned subgroup analyses were performed. In the subgroup of 65 patients who had more than 2 lines of chemotherapy and tumors tested for *KRAS* mutation, tumor location was associated with OS with a hazard ratio (HR) of 0.52 (95% CI=0.29-0.93, p=0.027). In a subgroup of 124 patients with *KRAS*-wild-type mCC, tumor location was associated with response rates to chemotherapy, with an odds ratio (OR) of 2.40 (95% CI=1.07-5.41, p = 0.03). A similar trend was observed in a subgroup of 58 patients with *KRAS*-wild-type mCC treated with cetuximab. (OR= 4.13, 95% CI=1.17-14.55, p = 0.03).

**Conclusion** Patients with proximal primaries appeared to have poorer survival and response to first line chemotherapy than those with distal primaries in unplanned subgroup analyses. This result remains exploratory and further investigation in larger cohorts is indicated.

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# GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS (GEP-NET)- A RETROSPECTIVE ANALYSIS OF CLINICAL FEATURES AND SURVIVAL IN A TERTIARY HOSPITAL IN HONG KONG AND TOPIC REVIEW

Dr Yu Kin Chap, Department of Clinical Oncology, Prince of Wales Hospital (June 2014 Medical Oncology Exit Assessment Exercise)

**Objective** Gastroenteropancreatic (GEP) neuroendocrine tumor (NET) is the most common type of NET. There are limited studies of GEP-NET among Chinese patients; therefore, a retrospective review on Chinese GEP-NET patients in the Prince of Wales Hospital in Hong Kong from 2004 to 2013 was performed.

Method A total of 87 case records were reviewed to collect the clinical information

including age, gender, tumor locations, clinical parameters, endoscopic findings, radiological findings, tumor histopathological characteristics, metastatic patterns, treatment modalities and outcomes. The R3.0.1 software was used for statistical analyses.

**Results** The median age was 58 years (28-91 years). Rectum (46%), pancreas (26%) and stomach (13%) were among the 3 most common sites of involvement. The majority were non-functional tumors (95%). The proportion of Grade 1, Grade 2 and Grade 3 NETs were 45%, 5% and 10% respectively. Neuroendocrine tumor (NET), neuroendocrine carcinoma (NEC) and mixed adenoendocrine carcinoma (MANEC) were 70%, 14% and 6% respectively. TNM stage 1, stage 2, stage 3 and stage 4 disease was found in 49%, 22%, 9% and 20% of the patient cohort. The liver was the most common metastatic site (11-17%). Surgery was the main treatment modality (80%) and the overall 5-year survival rate (69%) was compatible with other studies. Tumor type, tumor grade and the stage at diagnosis were found to statistical significantly correlate with the overall survival.

**Conclusion** GEP-NET is a heterogeneous group of tumor with a wide range of clinical presentations. Early diagnosis, proper classification and staging may help to improve the survival outcomes.

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# PREVALENCE AND SEVERITY OF SLEEP APNEA IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE

Dr Chan Chi Wang Gary, Department of Medicine, Queen Mary Hospital (June 2014 Nephrology Exit Assessment Exercise)

**Background and Objectives** Sleep apnea is increasingly being recognized as an important comorbidity in endstage renal disease. However, the prevalence and severity of sleep apnea in the nondialysis chronic kidney disease (CKD) population have not been well characterized. The handful of studies performed to date have yielded highly variable prevalence rates due to cohort heterogeneity and inter-study inconsistencies in sleep apnea definition. Hence, this study sought to determine the association of sleep apnea with non-dialysis CKD by recruiting a uniform cohort to undertake overnight polysomnography (PSG).

**Methods** In total, 141 male patients aged 40 to 60 years old were recruited to undergo overnight PSG. Height, weight, neck girth, estimated glomerular filtration rate, spot urinary protein excretion and Epworth sleepiness scale (ESS) score were collected at baseline. The prevalence and severity of both sleep apnea and associated nocturnal hypoxemia (NH) were determined across the full spectrum of non-dialysis CKD.

**Results** The prevalence of sleep apnea (apnea-hypopnea index  $[AHI] \ge 15$ ) and NH (Sleep Heart Health Study arbitrary definition) was 35.5% and 10.6% respectively in this study population, which had a mean ( $\pm$  SD) age and BMI of 51.44  $\pm$  6.05 y and 26.05  $\pm$  4.22 kg/m2. The adjusted odds ratio (OR) for sleep apnea by body mass index (BMI) and proteinuria were 1.18 (95% confidence interval [CI] 1.02 - 1.37; P  $\le$  0.05) and 2.60 (95% CI 2.56 - 2.61; P  $\le$  0.05) respectively. The adjusted OR for median cohort oxygen desaturation index (ODI) by BMI and proteinuria were 1.23 (95% CI 1.05 - 1.45; P  $\le$  0.05) and 2.60 (95% 2.56 - 2.61; P  $\le$  0.05). In addition, statistically significant mean differences were noted for both AHI and ODI at various levels of proteinuria. However, no significant correlation between prevalence and severity of sleep apnea and NH with progressive renal deterioration could be observed. Furthermore, an ESS score above 10 showed no significant mean difference in AHI and ODI when compared to a score below 10.

**Conclusions** Sleep apnea is prevalent in the Chinese non-dialysis CKD population and strongly correlated with BMI and proteinuria, but not renal function. The study results also indicate that ESS is an investigative tool that lacks discriminatory power in patients with renal insufficiency. Hence, this study supports the need to maintain high clinical vigilance for sleep apnea when attending to CKD patients with significant proteinuria.

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# WEIGHT GAIN AFTER STARTING PERITONEAL DIALYSIS: PREVALENCE, POSSIBLE CAUSES AND PROGNOSTIC SIGNIFICANCE

Dr Choy Shin Man, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2014 Nephrology Exit Assessment Exercise)

**Background** Observational studies suggested that high body mass index is associated with improved survival in dialysis population. Weight gain is common amongst patients newly put on peritoneal dialysis (PD). However, the prevalence, risk factors and long term implications of body weight gain in patients newly started on PD have not been explored.

**Methods** We studied 444 consecutive patients with end stage renal disease newly started on PD therapy. Body weight, measured when the patient was clinically euvolemic, at the time of initiation of PD and 1 year later were reviewed. Clinical factors affecting weight changes were explored.

**Results** Patients were followed up for  $60.9 \pm 32.8$  months. The mean weight change after one year of PD was  $1.34 \pm 3.27$  kg; 109 patients (24.6%) had weight gain >3.0 kg. Patients without any peritonitis episodes during the first year of PD had significantly more weight gain than those who had peritonitis ( $1.58 \pm 3.17$  vs  $0.16 \pm 3.56$  kg, P = 0.001). The number of peritonitis episodes during the first year of PD had inverse correlation with weight gain during this period (r = -0.174, P = 0.0002). In addition, weight change had a modest but statistically significant correlation with the concomitant change in residual renal function (r = 0.137, P = 0.004). However, there were no significant relations between body weight change and glucose load, peritoneal transport characteristics, fasting plasma glucose, HbA1c, dialysis adequacy, or baseline residual renal function. Patients with weight gain >3.0 kg had similar overall survival, technique survival and peritonitis-free survival as compared to those with stable body weight. On the other hand, patients with weight loss >0.5 kg had worse technique survival (P = 0.03) and peritonitis-free survival (P = 0.005) than the others.

**Conclusion** Weight gain is common among Chinese patients during the first year of PD. Weight change is related to peritonitis and decline of residual renal function during the same period, but does not correlate with pre-existing diabetes, glucose load, dialysis adequacy, baseline residual renal function, or peritoneal transport status. Weight gain within the first year of PD is not associated with any adverse clinical outcomes. On the other hand, weight loss more than 0.5 kg is associated with worse technique survival and peritonitis-free survival subsequently.

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# OUTCOME OF THE TUNNELED CUFFED HEMODIALYSIS CATHETER EXCHANGE- A SINGLE CENTRE EXPERIENCE

Dr David Ip, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (June 2014 Nephrology Exit Assessment Exercise)

Background Tunneled cuffed hemodialysis catheters (THCs) are commonly used as the

vascular access worldwide. But complications such as catheter dysfunction, catheter related infections often occur and lead to hospitalisation and require catheter removal then reinsertion of a new one to solve the problem. However, hemodialysis (HD) patients' venous access is limited. An alternative method "over-the-guide wire catheter exchange" which involves creation of a new exit site but reinserts the new catheter into the same venous site. Some studies already suggest this option is feasible to solve the problem of catheter dysfunction with favourable success rate without excess risks. However, for management of catheter related infections including exit site infection or catheter related bloodstream infection, there is still limited data to support its use.

Study Design Retrospective case control study.

**Setting and Participants** From 2009 to 2012, total 41 catheter exchange cases and 41 de novo catheter insertion cases from a single local hospital in Hong Kong were included for analysis and comparison.

**Results** There was only 1 technical failure, giving an overall technical success rate 97.6%. The 40 catheter exchanged functioned well (mean catheter patency 313 days) with similar performance to de novo catheters. Complication rates 25%, infection rates (0.34 infections per catheter; 0.11 infection per 100 catheter days) were similar to the de novo catheter insertion cohort.

**Conclusions** For dysfunctional or infected THCs, catheter exchange is feasible and as safe as de novo catheter insertion. And it can be an good alternative to preserve precious venous access in HD patients.

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# STREPTOCOCCUS PERITONITIS COMPLICATING PERITONEAL DIALYSIS: A REVIEW OF 10-YEAR EXPERIENCE

Dr Kwan Pui Yuen Lorraine, Department of Medicine, Queen Mary Hospital (June 2014 Nephrology Exit Assessment Exercise)

**Background** Streptococcus has emerged to become an important organism causing peritoneal dialysis (PD)-related peritonitis in recent years. Local data regarding this clinical entity is relatively limited.

**Methods** This study retrospectively reviewed all cases of streptococcal peritonitis which occurred in the two dialysis units in Hong Kong West Cluster during the period of 2003 to 2012, and the clinical course and outcomes of these episodes were analyzed.

**Results** A total of 228 episodes of streptococcal peritonitis occurred during a follow-up of 4350 patient-months, accounting for 16.5% of all episodes of peritonitis. *Streptococcus viridans* is the leading strain (90%), followed by *streptococcus bovis* (3.1%) and *streptococcus agalactiae* (2.2%). The primary and secondary response rates were 73.7% and 23.7% respectively. Dialysis duration, and use of concurrent use of immunosuppressive agents and were predictive of poor response to medical therapy. Presence of dental problem is more prevalent in patients with repeat peritonitis (40%). Forty-two percent of the streptococcus strains isolated had complete/partial resistance to penicillin, and were associated with lower primary response rates and higher relapse. Sixty two percent of the streptococcal peritonitis episodes caused by strains with "intermediate resistance" responded to cefazolin, and outcome was good. Compared with *staphylococcus aureas* peritonitis, streptococcal peritonitis was associated with more favorable outcome in terms of response to

medical treatment, primary response rate, relapse rate and mortality.

**Conclusion** Patients with streptococcal peritonitis had favorable response to medical therapy and clinical outcomes. Repeat peritonitis is common and is related to poor dental health. The increase in penicillin non-susceptible stains is also an emerging issue which warrants further attention. Cefazolin is recommended as first line intraperitoneal antibiotics for treatment of penicillin-"intermediate resistance" strains.

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### A COMPARISON OF CLINICAL OUTCOMES ON INCIDENT HOME DIALYSIS-NOCTURNAL HOME HAEMODIALYSIS VERSUS CONTINUOUS AMBULATORY PERITONEAL DIALYSIS A RETROSPECTIVE COHORT STUDY FROM A SINGLE CENTER IN HONG KONG

Dr Li John Wing, Department of Medicine, Queen Elizabeth Hospital (June 2014 Nephrology Exit Assessment Exercise)

**Background** The Hospital Authority of Hong Kong has adopted "Peritoneal dialysis (PD) first" policy as the mode of dialysis for patients with end stage renal failure (ESRF). Nocturnal home haemodialysis (NHHD) was introduced in Hong Kong in 2006 and was shown to deliver superior clinical outcomes when compared with center haemodialysis. However, direct comparison on outcomes of the two different home dialysis modalities, i.e. NHHD versus continuous ambulatory peritoneal dialysis (CAPD), has not been performed systematically before. We hypothesized that both NHHD and CAPD could provide similar clinical benefits and outcomes to ESRF patients in a renal unit of Queen Elizabeth Hospital of Hong Kong.

**Method** A 2-year retrospective cohort study was performed in 12 incident NHHD and 35 incident CAPD patients. The primary outcomes were the differences in infection rate, hospitalization rate and employment rate over the course of dialysis between the two groups. Secondary outcomes included the change in 4 different domains (kidney function, mineral metabolism, anaemia and clinical parameters).

**Results** Baseline demographics were similar. NHHD patients had higher employment rate (50% VS 37.1%), lower serum parathyroid hormone (10.43 VS 41.23 pmol/L, p = 0.002), decreased number of phosphate binder intake (0.63 VS 1.26, p = 0.045) and marginally lower calcium phosphate product (3.46 VS 4.13 mmol<sup>2</sup>/L<sup>2</sup>, p = 0.09) when compared with the CAPD group. However, the residual renal function in NHHD patients declined at a greater magnitude (0.67 VS 3 ml/min, p = 0.03). No differences were noted in infection rate (p = 0.66), hospitalization rate (p = 0.14), haemoglobin level (p = 0.61), weight (p = 0.22), systolic and diastolic blood pressure (p = 0.83 and 0.43 respectively) and number of anti-hypertensive medications (p = 0.11) between the two groups.

**Conclusion** There are benefits in different aspects in both modalities of home dialysis for incident ESRF patients. Higher employment rate in NHHD might be more appealing to younger subjects. One must balance the outcomes and personalize the dialysis regime for these patients in order to maximize their potential and quality of life.

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**COMPARISON OF THREE COMORBIDITY INDICES AS PREDICTORS OF SURVIVAL IN CHINESE INCIDENT PERITONEAL DIALYSIS PATIENTS** Dr Ma King Wing Terry, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2014 Nephrology Exit Assessment Exercise)

**Background** A number of comorbidity indices have been developed to quantify the burden of comorbid conditions and predict survival in dialysis patients, but data on the use of these indices in Chinese peritoneal dialysis (PD) patients are limited. The aim of this study is to compare the performance of the Charlson Comorbidity Index (CCI), Hemmelgarn index and Liu index in predicting survival in incident Chinese PD patients.

**Methods** In this retrospective study, 461 incident PD patients were recruited. Clinical information and presence of comorbid conditions were obtained by chart review and cross-checking. Cox regression models were used to compare the prognostic value of the three indices.

**Results** The mean age was  $57.7 \pm 13.7$  years. The median Charlson, Hemmelgarn, and Liu scores were 4 (inter-quartile range [IQR] 2 to 5), 1 (IQR 0 to 2), and 4 (IQR 2 to 5), respectively. Patients were followed for  $45.5 \pm 33.0$  months. Cox regression analysis showed that after adjusting for confounding factors, CCI was the best predictor of patient survival, with each point increase in Charlson score associated with 31% increased risk of mortality. The Hemmelgarn index was the best one to predict technique survival and peritonitis-free survival. However, over 70% of patients scored 0 or 1 by this system, limiting its role as a prognostic marker.

**Conclusion** The CCI was the best predictor of patient survival in incident Chinese PD patient. Further prospective studies are required to determine the role of comorbidity indices on hospitalization and medical expenditure in Chinese PD patients, as well as the application of comorbidity index for serial monitoring of PD patient.

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# OUTCOMES IN ISCHAEMIC STROKE PATIENTS WITH COEXISTING INTRACRANIAL LARGE ARTERY ATHEROSCLEROTIC STENOSIS: A RETROSPECTIVE STUDY

Dr Chan Wai Lun Larry, Department of Medicine, Alice Ho Miu Ling Nethersole Hospital (June 2014 Neurology Exit Assessment Exercise)

**Background/Aims** Strokes related to intracranial large artery stenosis (ILAS) are known to have adverse outcomes, but data on outcomes of asymptomatic ILAS are limited. This study aims to determine the risk of ischaemic events related to asymptomatic ILAS. The secondary end-points include risk of ischaemic events in any other cerebral vascular territories, mortality and risk of other vascular events.

**Methods** Patients admitted to a local hospital for ischaemic cerebral events from 1 Jan 2009 - 31 Aug 2010 were studied. Patients with moderate or severe ILAS unrelated to the index ischaemic event would be the study group while patients with no or only mild stenosis would be the control group. All the patients were followed for 3 years or till their deaths.

**Results** Total 534 adult patients were studied. The mean follow-up time was  $33.28 \pm 8.31$  months. Age (p<0.0001) and diabetes mellitus (p=0.032) were independent risk factors for development of ILAS. More patients in the study group had large vessel disease causing their index ischaemic events while more patients in the control group had small vessel disease (p<0.0001). More patients in the study group received dual anti-platelets upon discharge (p=0.020). At 3-year, 5 patients (1.9%) in the study group and 2 patients (0.7%) in the control group reached the primary outcome (p=0.233). All secondary outcomes did not

show any statistically significant difference.

**Conclusions** Asymptomatic ILAS in stroke patients does not increase risk of cerebral ischaemic events, mortality or other vascular events within subsequent 3 years.

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# PREDICTORS OF OUTCOME IN ISCHAEMIC STROKE PATIENTS RECEIVING INTRAVENOUS THROMBOLYSIS

Dr Chang Carlin, Department of Medicine, Queen Mary Hospital (June 2014 Neurology Exit Assessment Exercise)

**Background** Intravenous thrombolytic, tPA, is widely used and the best available first-line treatment for acute ischaemic stroke when presented within the 4.5 hours of onset. This treatment has been found to minimize the area of ischaemic infarct to enable maximum recovery and minimum disability. This study aims to identify the potential prognostic predictors of stroke outcome in cases that received IV tPA.

**Methods** This study included all patients who received IV tPA at the Queen Mary Hospital in Hong Kong. Clinical data of 161 subjects were analyzed and multiple logistic regression analysis was used to determine which variables could predict the eventual outcome.

**Results** The most important predictors of IV tPA outcome were the history of antiplatelet use when tPA was administered as well as the final NIHSS score. The presence of atrial fibrillation was highly predictive of post thrombolytic intracerebral hemorrhage while fasting glucose levels was correlated with the presence of symptomatic hemorrhage in post tPA cases. However, advanced age was not a poor indicator of post tPA outcome.

**Conclusion** When ischaemic stroke patients are admitted as potential candidates for IV tPA, careful assessment should be made to determine not only whether the patient is eligible for tPA but more importantly who would best benefit from tPA. Based on the results of this study, no specific factor is able to precisely predict the eventual outcome, but particular caution should be made if the patient has been taking an antiplatelet or if the patient has a high serum glucose level in the background of atrial fibrillation as these are associated with a poor tPA outcome (mRS 4-6).

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# LATE ONSET POMPE DISEASE IN HONG KONG

Dr Chu Yim Pui, Department of Medicine & Geriatrics, Princess Margaret Hospital (June 2014 Neurology Exit Assessment Exercise)

**Background** Late onset Pompe disease (LOPD), a rare inherited disease, affects the musculoskeletal system due to reduced  $\alpha$ -glucosidase enzyme activity in lysosome. The clinical manifestation is diverse but Chinese population tends to show a more aggressive form of the disease. Enzyme replacement therapy (ERT) was associated with symptoms improvement but it varies among individuals. Here we aimed at performing an in-depth review of natural history and investigating the treatment response of all LOPD patients in Hong Kong.

**Methods** We reviewed all case records and conducted a face-to-face interview to complete a detailed questionnaire regarding clinical manifestation and diagnosis of the disease. We studied the clinical outcomes of ERT by 6 minute walking test (6MWT), forced vital capacity

(FVC), Medical Research Council (MRC) sum score, muscle enzymes and SF-36 questionnaires.

**Results** Between 2000 and 2013, 11 patients were identified and one was lost to follow up. Age of diagnosis ranged from 9 to 44 years. Median age of first symptoms was 22.5 (6-44) years while median age of first medical attention was 29 (9-44) years. The most common initial complaint was decrease exercise tolerance. One fifth of patients' first complaint was difficulty to get up from lying position and fail to perform sit up. The mean time from first medical attention to diagnosis was 1.3 years but one patient was diagnosed 8 years later. Half of patients sought medical attention due to progressive shortness of breath and all of them developed type 2 respiratory failure requiring ventilator support during the first admission. 30% patients were chair-bound and 70% patients required ventilation support. Six patients were put on ERT. They showed a mean absolute increase of 62 m in 6MWT and 2.4% of FVC predicted after 12 months of treatment. The results were sustained at 24 months.

**Conclusion** In our population, LOPD patients tend to have an earlier and more aggressive clinical presentation with respiratory insufficiency and they showed a sustained improvement in lung function and walking distance after ERT.

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# AN EVALUATION OF HEMODYNAMICS ACROSS INTRACRANIAL STENO-OCCLUSIVE LESIONS BY COMPUTATIONAL FLUID DYNAMICS Dr Fan Sin Ying, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2014 Neurology Exit Assessment Exercise)

**Background** Intracranial atherosclerotic steno-occlusive disease is a major cause of stroke worldwide and portends a high risk of recurrence. Although the degree of arterial stenosis might predict stroke recurrence, it is likely not the sole determining factor for relapse. Notably, collateral flow and the hemodynamics across the culprit lesion may pose a significant impact on stroke risk. Computational fluid dynamics (CFD) is a novel technique developed to solve and analyze the dynamic effects of fluid flow. While CT cerebral angiography (CTA) provides non-invasive anatomical assessment on intracranial atherosclerotic steno-occlusive disease, processing of CTA images by CFD offers functional hemodynamic assessments across the stenosis. We aimed to process CTA images by CFD and explore the correlation between the degree of arterial stenosis and hemodynamic flow status across intracranial atherosclerotic steno-occlusive lesions.

**Methods** We recruited patients with stroke and transient ischemic attack attributed to intracranial atherosclerotic steno-occlusive disease from Acute Stroke Unit, Prince of Wales Hospital. All participants received definitive vascular imaging including CTA and digital subtraction angiography (DSA). We first delineated the hemodynamic parameters, including pressure difference, pressure ratio, pressure gradient, shear strain rate ratio (SSR), wall shear stress (WSS) ratio and velocity ratio, across the stenosed vessels, and then we correlated the degree of arterial stenosis with these hemodynamic parameters.

**Results** Among the 53 recruited patients (mean age 62.9 years, 69.8% males), 45 (85%) had stroke or TIA in the carotid circulation. The anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.392, p=0.004), pressure ratio (rs=-0.429, p=0.001) and pressure gradient (rs=0.419, p=0.002). There was no significant correlation between the anatomical severity of stenosis with SSR ratio, WSS ratio and velocity ratio. Among patients with anterior circulation stroke or TIA, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity of stenosis showed a weak-to-moderate correlation with pressure difference (rs=0.381, the anatomical severity seve

p=0.01), pressure ratio (rs=-0.426, p=0.004) and pressure gradient (rs=0.407, p=0.005). For patients with posterior circulation stroke or TIA, the anatomical severity of stenosis was strongly correlated with pressure difference (rs=0.714, p=0.047) and pressure ratio (rs=-0.714, p=0.047); and very strongly correlated with velocity ratio (rs=0.833, p=0.01).

**Conclusions** The severity of intracranial steno-occlusive disease showed weak-to-moderate correlation with pressure difference, pressure ratio and pressure gradient across the culprit lesion. As determination of furture stroke risk and treatment based solely on stenotic severity may be inadequate for patients with symptomatic intracranial stenoocclusive disease, our findings may guide further research in the field, specifically, studies on estimating stroke risks and selection of high-risk patients who may benefit from adjunctive treatment like plaque stabilization or cerebral re-vascularization. This study also illustrated the potential role of CTA as a non-invasive imaging modality in providing both anatomical and functional assessments for intracranial steno-occlusive disease.

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# FACTORS AFFECTING MOTOR DETERIORATION IN ACUTE DEEP WHITE MATTER INFARCTION

Dr Ismail Moamina, Department of Medicine, Queen Elizabeth Hospital (June 2014 Neurology Exit Assessment Exercise)

**Background and objective** A substantial amount of patients with acute deep white matter infarction suffered from progressive motor deficits. This study aims to determine its predictors, so as to generate hypothesis of the underlying pathogenesis and potential preventive or therapeutic strategies.

**Methods** 54 patients with acute deep white matter infarction were prospectively evaluated by daily National Institutes of Health Stroke Scale (NIHSS) motor score. Motor deterioration was defined as drop in NIHSS motor score of more than or equal to 1 point during the first 7 days. Patients with and without motor deterioration were compared on their clinical and radiological parameters.

**Results** 11 patients (20.4%) had motor deterioration. They had higher mean diastolic blood pressure in the first 24 hours (88.1±17.2mmHg; vs. 79.0±10.9mmHg, p = 0.033); elevated haemoglobin level (14.6±1.2g/dL vs. 13.2±1.6g/dL, p = 0.007elevated haematocrit level (0.433±0.035 vs. 0.392±0.043, p = 0.005); elevated white cell count (7.1 [6.0-7.9]; vs. 8.5 [7.3-9.2], p = 0.025); elevated total protein (73 [70-75] vs. 76 [73-81], p = 0.03); elevated total cholesterol level (5.5±1.5mmol/L; vs. 4.6±1.0mmol/L, p = 0.01); elevated low density lipoprotein (LDL) cholesterol level (3.6±1.3mmol/L vs. 2.7±0.8mmol/L, p = 0.005) and elevated urine albumin to creatinine ratio (5.1mg/mmol [2.0-8.4]; vs. 1.45mg/mmol [0.7-2.6], p = 0.019). After logistic regression analysis, LDL cholesterol higher than 3.2mmol/L (relative risk 11.85; 95% CI 1.95-72.09; p = 0.007; table 2) and urine albumin to creatinine ratio higher than 3.5 (relative risk 8.02; 95% CI 1.32-48.8; p = 0.024) were independent predictive factors for progressive motor deterioration.

**Conclusion** Progressive motor deterioration in acute deep white matter infarction was independently associated with elevated LDL cholesterol and urine albumin to creatinine ratio, supporting the role of endothelial dysfunction as the underlying mechanism of such deterioration

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# PROGNOSIS AND CRISIS IN GENERALIZED MYASTHENIA GRAVIS AMONG HONG KONG CHINESE

Dr Lee Chi Yan, Department of Medicine, Queen Mary Hospital (June 2014 Neurology Exit Assessment Exercise)

**Objectives** To study the clinical features of local gMG patients, the independent predictors for good long-term outcome and for development of MG crisis, and potential role of cytokines as biomarkers of MG disease activity.

**Methods** Local gMG patients managed in Queen Mary Hospital from 1997 to 2012 were retrospectively reviewed. Serum or plasma levels of a number of inflammatory cytokines were measured in a small portion of gMG patients to compare between patients with stable disease and those with MG exacerbation or crisis.

**Results** 123 Chinese gMG patients were recruited. 96 (78.0%) patients had good outcome. The use of azathioprine was the only independent predictor of good outcome (OR 3.57, 95% CI 1.05-12.10, p=0.042). 35 (28.5%) patients had experienced MG crisis and two died. More than half of the MG crisis episodes occurred beyond 2 years from clinical onset. Moderate to severe weakness at clinical onset (OR 5.79, 95% CI 1.29-25.96, p=0.022) and presence of major comorbid illness (OR 3.70, 95% CI 1.29-10.65, p=0.015) were independent predictors for development of MG crisis. Serum/plasma levels of interleukin-17A (IL-17A) and interferon- $\gamma$  (IFN- $\gamma$ ) were higher in patients in MG exacerbation or crisis.

**Conclusions** Long-term outcome of gMG among Hong Kong Chinese is satisfactory and use of immunosuppressive therapies especially azathioprine is crucial. MG crisis remains an important potentially fatal complication and is unexpectedly common even in the later course of disease.

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### A REVIEW OF PROGNOSTIC FACTORS AND TREATMENT MODALITIES IN SMALL CELL LUNG CANCER: RESULTS FROM A LOCAL DISTRICT HOSPITAL

Dr Szeto Ching Ho, TB and Chest Unit, Wong Tai Sin Hospital (June 2014 Respiratory Medicine Exit Assessment Exercise)

**Introduction** Small cell lung cancer (SCLC) has high mortality and research on the prognostic factors of SCLC is important. Seventy-seven patients with SCLC had been managed in Yan Chai Hospital Medical Department during the period 1st January, 2001 to 31st December, 2010 as identified by the Clinical Data Analysis and Reporting System (CDARS).

**Method and statistical means** Seventy-seven patients were observed from 1st January, 2001 to 30th September, 2011. Patients' survival was counted starting from the time of pathological diagnosis. Seventy two patients succumbed and five patients survived for more than 55 months during the period of observation by 30th September, 2011. Kaplan-Meier survival plot showed up the association between various prognostic attributes and survival. Univariate Log-rank test and multivariate Cox regression analysis showed up the clinical significance of 24 pretreatment attributes on survival.

# Results

1. Considered all cases of SCLC, the extent of disease (according to the Veterans Administration Lung Study Group (VALG) definition of limited disease (LD) and extensive

disease (ED)) and anemia were significant prognostic factors. In subgroup analysis, male gender or percentage weight loss of more than 10% in the last 3 months in LD was adversely associated with clinical outcome and adrenal metastasis in ED at diagnosis was a significant adverse prognostic factor.

2. Renal impairment necessitating chemotherapeutic dosage reduction was associated with increased mortality whereas chemotherapy (CT), thoracic radiotherapy (TRT), prophylactic cranial irradiation (PCI), and the increasing number of treatment modalities reduced the mortality.

In addition to the treatment data of medical patients with SCLC from Yan Chai Hospital, the SCLC treatment protocols of two major oncology units from Princess Margaret Hospital and Tuen Mun Hospital involved in treatment were also reviewed.

The second part of this dissertation is dedicated to a literature review on CT, TRT, PCI, surgical resection, and molecular therapy that will be presented in five basic areas—LD, ED, recurrent disease, elderly patients, remarks on treatment with emphasis on platinumbased therapy, topotecan, amrubicin, and phase III treatment trials. Oncology treatment has evolved to a more explicit one stating the regimen and the dosage in different situation. Patients' tolerability and chemotherapy toxicity should be considered. Potential candidate drugs for treatment of SCLC (phase II trials) are shown in appendix.

**Conclusion** Prognostic factors for survival and survival rate of SCLC patients in this locality were similar to National Cancer Institute (NCI), USA and other international data suggesting the uniqueness of SCLC across different countries. Chemotherapy regimes are similar for LD and ED and topotecan is useful in treatment of SCLC relapse. TRT is offered to LD only whereas PCI is offered to LD and ED patients who showed complete response to chemotherapy. Many therapeutic trials aiming to improve treatment response and survival of patients with this dreadful disease are under way.

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# A PROSPECTIVE STUDY OF FACTORS RELATED TO READMISSION AND MORTALITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS IN A REGIONAL HOSPITAL IN HONG KONG

Dr Tsui Sui Na, Department of Medicine & Geriatrics, United Christian Hospital (June 2014 Respiratory Medicine Exit Assessment Exercise)

**Background** Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide with a high burden on healthcare resources. Study investigating modifiable factors related to readmission and mortality of COPD patients can help formulate better management plan.

**Methods** A prospective observational study was performed to investigate factors related to readmission and mortality of COPD patients. From August 2011 to August 2012 consecutive patients admitted for acute exacerbation of COPD (AECOPD) were screened for recruitment to the study. The time to first readmission for AECOPD, number of readmission and time to death in the ensuing year were recorded and analyzed against potential risk factors collected during the index admission.

**Results** 250 patients admitted for AECOPD were recruited. The mean age was  $76.7\pm7.7$  years and the mean FEV1 was  $43.1\pm15.8\%$  predicted. 183 patients (73.2%) were readmitted at least once for AECOPD in the ensuing year and 41 patients (16.4%) died. Use of long-acting

bronchodilators (HR 1.800, 95% CI 1.163–2.786), use of high dose inhaled corticosteroids (HR 1.609, 95% CI 1.119–2.314), number of admission for AECOPD in the previous year (HR 1.103, 95% CI 1.049–1.161) and 6-minute walk distance (HR 0.998, 95% CI 0.996–0.999) were independently associated with time to first readmission for AECOPD. Older age (HR 1.079, 95% CI 1.020–1.142), higher BODE index (HR 1.547, 95% CI 1.224–1.955) and history of using acute non-invasive ventilation (HR 2.624, 95% CI 1.229–5.599) were independently associated with shorter time to death. Subgroup analysis found that anxiety (OR 3.957, 95% CI 1.444-10.841), use of high dose inhaled corticosteroids (OR 2.695, 95% CI 1.135-6.398) and higher number of admission for AECOPD in the previous year (OR 1.917, 95% CI 1.513-2.428) were independently associated with very frequent readmissions (defined as  $\geq 4$  in 1 year).

**Conclusion** AECOPD is associated with high rate of readmission and significant 1-year mortality. Anxiety is found to have a strong association with very frequent readmissions.

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# **EXPERIENCE OF MANAGING MALIGNANT PLEURAL EFFUSION WITH INDWELLING PLEURAL CATHETER**

Dr Wong Wai Mui, Department of Medicine, Queen Mary Hospital (June 2014 Respiratory Medicine Exit Assessment Exercise)

**Background** Indwelling pleural catheter (IPC) has become a treatment option for malignant pleural effusion (MPE) in Queen Mary Hospital (QMH) since 2010. Besides effective symptom relief and reduced hospitalizations, the possibility of spontaneous pleurodesis (SP) is another unique outcome of IPC.

**Aims** To review the safety and complication profile of IPC in our unit, and attempt to explore what clinical factors could associate with spontaneous pleurodesis and IPC removal.

**Methods** The clinical records of all patients had IPC inserted for MPE were retrospectively evaluated and their in-patient record and drainage diaries were reviewed.

**Results** There were a total of 19 IPCs inserted in 18 patients with MPE, since 2010 until Feb 2014 in QMH. There were no major IPC related complications or pleural infection. Minor complications include cellulitis over entry/exit site of IPC in four patients (21%) and mild wound infection at IPC removal site in one patient. Symptomatic and asymptomatic pleural loculations occurred in two patients (10.5%) and four patients (21%) respectively. Tumor seeding at IPC tract developed in one patient (5.3%). Clinical factors associating with higher likelihood of IPC removal were identified, including higher pleural fluid total cell count (p = 0.03) and longer duration from IPC insertion to patients' death/end of study (whichever was earlier) (p = 0.001).

**Conclusions** IPC was safe and complications were generally mild. Based on the limited number of subjects in this study, patients who had higher pleural fluid total cell count were more likely to achieve spontaneous pleurodesis and subsequent IPC removal. The duration from IPC insertion until patients' death/end of study was also longer in patients who had IPC removed.

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# AN INCEPTION COHORT OF PATIENTS WITH ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS IN A TERTIARY

# CENTRE IN HONG KONG - A STUDY OF CLINICAL MANIFESTATIONS, SURVIVAL AND PROGNOSTIC FACTORS

Dr Ho Chup Hei, Department of Medicine, Queen Elizabeth Hospital (May 2014 Rheumatology Exit Assessment Exercise)

**Background** Despite advancement in the treatment of ANCA-associated vasculitis (AAV), there are still considerable morbidities and mortalities resulting from treatment-related complications. Overseas studies have identified various prognostic factors of AAV in order to stratify patients' risks and thus to determine the suitable treatment strategy. Given the difference in epidemiology of AAV over the world, a new scoring system for prognostication of AAV in local population is needed.

**Objectives** To review the clinical profile and survival of AAV in local Chinese population; to look for any predictors for mortality, renal outcome and adverse events; and to formulate a prognostic scoring system derived from local data in this study.

**Methods** A total of 81 patients with AAV diagnosed between January 2000 and December 2012 in Queen Elizabeth Hospital were included in this study. Demographic data, background medical comorbidies, clinical profile related to AAV of these patients were reviewed and compared with overseas studies. Survival was analysed with Kaplan-Meier method and Cox proportional hazards model. Predictors of renal outcome and adverse events were determined by multivariate analysis. The five-factor score (FFS) proposed by the French Vasculitis Study Group (FVSG) was calculated for our patients and compared with the local version prognostic score.

**Results** Local patients had an older age of disease onset compared with data from European studies. Median survival was 80 months. The commonest cause of death was infection. Overall 1-year and 5-year mortality of ANCA-associated vasculitis in local population were 87% and 52% respectively, which were similar to and worse than those reported in European trials respectively.

Age older than 68-year-old (HR 3.99, p = 0.008), haematuria (HR 3.42, p = 0.007), pulmonary haemorrhage (HR 10.02, p = 0.003), background of cardiovascular risk factors (HR 2.71, p = 0.024) and pre-existing malignancy (HR 3.95, p = 0.018) were found to be significant predictors of overall and 12-month mortalities. Plasma exchange was associated with a lower risk of 12-month (HR 0.126, p = 0.022) and in-hospital mortalities (HR 0.08, p = 0.025). No predictor of renal outcome was identified in this study. Age (OR 1.053, p = 0.014) and use of cyclophosphamide (OR 8.649, p = 0.005) predicted infective complications. Age (OR 1.072, p = 0.028) and peaked serum creatinine level (OR 1.002, p = 0.031) predicted future cardiovascular events. No significant predictor of secondary malignancy was found.

The local prognostic score "Hong Kong Five-Factor Score" (HKFFS) was formulated. The 1-year mortality rate of HKFFS scores 0, 1 and >2 were 0%, 15% and 51% respectively; and the 5-year mortality rate of HKFFS scores 0, 1 and >2 were 0%, 19% and 74% respectively. (p < 0.001).

**Conclusion** Local Chinese patients with AAV tended to be older and had different prognostic factors compared with their western counterparts. The HKFFS had a better ability to differentiate local patients with mild and severe disease than the original FFS. A strategy of tailoring treatment according to disease severity should be adopted to strike a balance between adequate disease control and prevention of treatment-related complications.

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# PREVALENCE OF CARDIOVASCULAR DISEASE AND RISK FACTORS IN CHINESE PATIENTS WITH PSORIATIC ARTHRITIS

Dr Law Mei Yan, Department of Medicine & Geriatrics, Tai Po Hospital (May 2014 Rheumatology Exit Assessment Exercise)

**Objectives** To describe the cardiovascular (CV) morbidities, the prevalence of CV disease in Chinese patients with PsA and compare these parameters with a group of age- and sexmatched healthy controls. The relationships among the CV risk factors associated with CV disease in PsA were also studied.

**Methods** PsA patients fulfilling the Moll and Wright criteria or the Classification of Psoriatic Arthritis study group (CASPAR) criteria were recruited for a cross sectional comparative study. Patients with CV risk factors and CV disease including myocardial infarction (MI), acute coronary syndrome (ACS), ischemic heart disease (IHD), congestive heart failure (CHF), hypertensive heart disease, transient ischemic attack (TIA) and cerebrovascular accident (CVA) were studied. The prevalence of CV morbidities in these patients was compared with data collected from twice the number of age- and gender-matched healthy control subjects.

**Results** 91 Chinese patients with PsA were recruited. The most common CV risk factor was overweight or obesity (70%). Hyperlipidemia (66%) was the second most common CV risk factor, followed by hypertension (HT) (51%) and diabetes mellitus (DM) (20%).

Independent sample t-tests revealed significantly higher prevalence of CV risk factors in all domains (p-value ranged from 0.006 to <0.001) and higher prevalence of overall CV disease than healthy controls (14% vs. 3%, p-value <0.005). Among all the CV disease entities, CVA was significantly more prevalent in PsA patients than controls (10% vs. 1 %, p-value <0.001). However, in this study, PsA patients did not show statistically significant although higher prevalence of coronary artery disease than controls (6% vs. 3%, p-value 0.309).

Multivariate analysis exhibited raised white cell count (odds ratio [OR] 4.902), HT (OR 27.453) and regular use of nonsteroidal anti-inflammatory drugs (NSAID) (OR 11.542) were the independent predictors of overall CV disease. In separate, Framingham risk score (OR 1.115) and hyperlipidemia (OR 72.035) were independent predictors of coronary artery disease in PsA patients, whereas regular use of NSAID (OR 7.901) was the only independent predictor of CVA in PsA patients.

**Conclusion** Chinese patients with PsA have higher prevalence of CV disease as well as CV risk factors than the general population without PsA. Apart from traditional CV risk factors, novel risk factors such as raised white cell count and regular NSAID use are associated with the development of CV disease in patients with PsA. These results support inflammatory process plays a significant role not only in the development of atherosclerosis but also in CV outcomes like vascular occlusion.

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# RADIOLOGICAL IMAGING AND CLINICAL MEASURES OF DISEASE ACTIVITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Dr Tsang Hoi Lun Helen, Department of Medicine, Queen Mary Hospital (June 2014 Rheumatology Exit Assessment Exercise)

**Introduction** Spondyloarthritis is a chronic disorder characterized by progressive ankylosis of the axial skeleton. The early diagnosis and monitoring of disease status are hampered by the lack of accurate and objective assessment tools. Traditionally, assessment of

spondyloarthritis relies on self-reported clinical measures by patients. The advent of magnetic resonance imaging (MRI) permits earlier diagnosis and comprehensive evaluation of spinal inflammation whereas conventional radiography allows assessment of structural damage.

**Objectives** The aim of the study was to determine the relationship between axial inflammation on MRI and plain radiograph structural damage with traditional clinical measures of disease activity and serum inflammatory markers in patients with axial spondyloarthritis.

**Methods** This was a cross-sectional study of patients with axial spondyloarthritis who were newly referred to Queen Mary Hospital. All recruited subjects had conventional radiographs and MRI to determine their radiographic damage and axial inflammation respectively. Correlations with clinical and biochemical measures of disease activity were performed.

**Results** Forty-five Chinese subjects were included for analysis. MRI inflammation in the sacroiliac joint was significantly associated with Bath Ankylosing Spondylitis Metrology Index [regression coefficient (B) = -2.49, p=0.03] while MRI inflammation in the spine was not significantly associated with any clinical measures. Radiographic damage on x-rays was significantly associated with a longer symptom duration (B=0.66, p<0.01) and history of smoking (B=9.60, p=0.004).

**Conclusion** This study demonstrated that MRI and radiographic findings are more reliable than traditional clinical measures in delineating disease activity and structural damage. Clinicians should include objective measures like MRI and conventional radiographs to gauge disease activity and monitor progress.

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Note: For obtaining the full dissertation, please contact the author directly.