Abstracts of Dissertations
June 2016 Exit Assessment Exercise

APIXABAN VERSUS WARFARIN IN CHINESE PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION

Dr Chan Kwong Yue Eric, Department of Medicine, Queen Mary Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background and Objective There is a paucity of data in the use of non-vitamin K antagonist oral anticoagulants (NOAC) compared with warfarin in Chinese patients with atrial fibrillation. This study investigated clinical outcomes in a real-world cohort of Chinese patients receiving warfarin compared with apixaban, the latest NOAC in Hong Kong.

Methods This was a retrospective, single-centre, observational study based on a hospital registry.

Results A total of 752 Chinese patients (76.8±11.4 years; female 48.7%) with non-valvular AF were included in the study with mean CHA2DS2-VASc and HAS-BLED scores of 4.1±1.7 and 2.3±1.0 respectively. There was no statistically significant difference between the apixaban and warfarin group in terms of the primary outcome of ischaemic stroke (HR 1.25, 95% CI 0.28-5.60, P=0.774), secondary outcomes of intracranial haemorrhage (HR 0.71, 95% CI 0.12-4.25, p=0.707), major bleeding (HR 0.83, 95% CI 0.42-1.64, p=0.594), myocardial infarction (HR 0.37, 95% CI 0.10-1.38, p=0.138), death (HR 0.76, 95% CI 0.42-1.37, p=0.355), and composite endpoint of ischaemic stroke, ICH and death (HR 0.71, 95% CI 0.41-1.22, p=0.213). Subgroup analysis including patients on apixaban 5mg BD only showed a statistically significant difference in the composite endpoint (HR = 0.36, 95% CI 0.14-0.92, P=0.032).

Conclusion Among local Chinese patients with non-valvular atrial fibrillation, apixaban is similar to warfarin in stroke prevention in terms of efficacy, bleeding risks and all-cause mortality.

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A RETROSPECTIVE STUDY OF THE CORRELATION BETWEEN IFR AND FFR IN ANGIOGRAPHIC INTERMEDIATE CORONARY LESIONS IN A LOCAL CHINESE POPULATION

Dr Chung Yat Kiu, Department of Medicine, Tseung Kwan O Kwan Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background Assessment of intermediate coronary lesions by coronary angiography alone is sometimes challenging and error-prone. Therefore, physiological assessment of these intermediate lesions is recommended. Fractional flow reserve (FFR) is a well validated and useful tool to provide information about the functional significance of intermediate lesions. FFR requires the administration of adenosine to induce intracoronary vasodilatation and hyperemia. However, adenosine has the side effects of inducing chest tightness, shortness of breath or nausea, and it is contraindicated in some conditions, such as asthma, bradycardia or hypotension. Instantaneous wave-free ratio (iFR) is a novel method to assess the functional significance of intermediate lesions. It measures the trans-stenotic pressure gradient during a "wave-free" period, without the use of adenosine.

Objectives To retrospectively assess the diagnostic accuracy of iFR in characterizing the severity of stenosis, as defined by FFR ≤0.80. The correlation between iFR and FFR in acute coronary syndrome and diabetic patients would be tested respectively in the subgroup analysis. The hybrid iFR-FFR approach would be tested retrospectively based on the data obtained in this study.

Methods Both iFR and FFR were performed in 95 intermediate coronary stenoses in 71 patients. Receiver-operating characteristic (ROC) curves were used to assess the accuracy of the cutoff points for iFR in predicting FFR ≤0.80. Sensitivity and specificity were determined. The correlation between iFR and FFR in acute coronary syndrome (ACS) vs. stable coronary artery disease (SCAD) and diabetic (DM) vs. non-diabetic (non-DM) patients were compared.

Results The mean age was 62.5 ± 10.9 years and 80.3% of them were male patients. At ROC analysis, the area under the curve was 0.95 (95% CI: 0.90-0.99) which confirmed a strong correlation between iFR and FFR in all patients. The optimal iFR cutoff point to predict FFR ≤0.80 was 0.89, with a sensitivity of 93.6% and specificity of 83.3% (95% CI: 0.91-0.99). The correlation between iFR and FFR was strong in both acute coronary syndrome and diabetic patients. The hybrid iFR-FFR approach could further increase the diagnostic accuracy and reduce the use of FFR by nearly 60% of the cases.

Conclusions iFR demonstrated a strong correlation with FFR in the local Chinese population. iFR had a strong correlation with FFR in both acute coronary syndrome and diabetic patients. This study supports the diagnostic value of iFR in establishing the functional significance of coronary stenoses. The hybrid iFR-FFR approach increased the overall diagnostic accuracy and reduced the usage of FFR effectively.

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DEVICE DETECTED ATRIAL TACHYARRHYTHMIAS AND THE CLINICAL OUTCOME

Dr Leung Chun Yu, Department of Medicine, Tseung Kwan O Kwan Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background Devices detected subclinical atrial tachyarrhythmias of at least 6 minutes are reported to be associated with increased risk of ischemic stroke. However, consensus has not been reached regarding the best management strategy for this population, especially those with very brief episodes of atrial tachyarrhythmias which lasted for less than 6 minutes.

Objectives To evaluate the diagnostic performance provided by dual chamber cardiac implantable electronic devices and the clinical outcome of devices detected atrial tachyarrhythmias of different durations.

Methods All patients who had active follow up in Tseung Kwan O hospital for their dual chamber pacemakers or implantable defibrillators by the time of 1st July 2013 were screened. Patients who received anticoagulation or have atrial fibrillation more than 48 hours were excluded. Clinical information and devices retrieved data were reviewed. Comparison of clinical outcome was performed between subgroups with different durations of devices detected atrial tachyarrhythmias.

Results A total 230 patients were included in this study. Atrial tachyarrhythmia of at least 6 minutes was associated with increased risk of stroke and systemic embolism (OR 5.56, 95% CI 2.10-14.62, P<0.001). Similar association was found when the cut off threshold of 30 seconds was used (OR 3.34, 95% CI 1.28-8.74, P=0.010). Patients with brief atrial tachyarrhythmia of < 6 minutes had lower risk of thromboembolism compared with those with atrial tachyarrhythmia of >= 6 minutes (OR 4.0, 95% CI 1.13-14.22, P=0.024) but no significant difference when compared with patients without atrial tachyarrhythmia (OR 1.61, 95% CI 0.45-5.73, P=0.461).

Conclusion Patients with atrial tachyarrhythmia of less than 6 minutes had lower stroke risk when compared to patients with more prolonged atrial tachyarrhythmia. Conventional CHA_2DS_2-VASc model may not be helpful to guide anticoagulation therapy and individualized stroke prevention strategy is required for different patients.

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HOW TO REFINE THE RISK OF STROKE IN ATRIAL FIBRILLATION PATIENTS WITH CHA2DS2-VASC SCORE OF 1

Dr Li Cho Shan, Department of Medicine & Geriatrics, Tuen Mun Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background__CHA2DS2-VASc score (congestive heart failure, hypertension, age 65-74 or >=75, diabetes, stroke, vascular disease, sex category) is preferred to refine the ischaemic stroke risk in patients with atrial fibrillation (AF) to the traditional CHADS2 score. However, according to American, European and Canadian guidelines, there is still no consensus on the best antithrombotic strategy in AF patients with CHA2DS2-VASc score of 1. Also, the stroke risk related to individual components of CHA2DS2-VASc score is unclear. Noteworthy, Age 65-74 is consistently shown to be a significant risk factor, it is logical to explore whether the age limit could be further lowered down.

Objective__The objective of this study is to look at the stroke risk in AF patients with CHA2DS2-VASc score of 1. Also, I will find out the ischaemic stroke risk contributed by the 6 individual factors constituting CHA2DS2-VASc score, and to explore the stroke risk in female aged 60-64.

Methods and Results This is a retrospective study. From Apr 1, 2009 to June 30, 2009, 2255 patients from Tuen Mun Hospital with the diagnosis code of AF have been identified by using the computer-based clinical data analysis and reporting system (CDARS). The dates of first diagnosis of AF are traced in the Clinical Management System (CMS). 260 patients who get CHA2DS2-VASc score 0 and 1 at their first diagnosis of AF are recruited. 73 patients score 0 (male only), 187 score 1 (124=male, 63=female). The annual incidence of ischaemic stroke in patients with CHA2DS2-VASc score of 0 and 1 are 3.1% and 4.5% respectively. Out of the six factors that contribute to CHA2DS2-VASc score of 1, hypertension (HT) (Hazard ratio {HR}: 2.2, 95% Confidence interval {CI}: 1.1-4.7) and age 65-74 (HR: 2.0, CI: 1.0-4.0) are associated with ischaemic stroke. While in female patients, age 60-64 is also found to be a significant risk factor (HR: 2.5, CI: 1.0-5.9)

Conclusion Among the six individual factors in CHA2DS2-VASc score, HT and age 65-74 are significant risk factors for stroke. More aggressive use of anti-thrombotic is indicated in AF patients with CHA2DS2-VASc score of 1 due to HT or age 65-74. Also, age 60-64 is a potential risk factor in female patients.

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THE BLEEDING RISK FACTORS FOR PATIENTS ON NOVEL ORAL ANTICOAGULATION: A MODIFIED BLEEDING RISK SCORE: A2BCD

Dr Ng Lok Hang Canice, Department of Medicine & Geriatrics, Princess Margaret Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background The availability of Novel Oral Anticoagulants (NOAC) has changed the landscape for stroke prevention in atrial fibrillation (AF) and management of venous thromboembolism (VTE). These drugs offer better efficacy, safety and convenience but any related major bleeding could result in disaster. Therefore, it is important to identify bleeding risk factors for patient on NOAC. Until now, HASBLED score has not been validated in patients on NOAC. In this study, the association of major bleeding with clinical risk factors in HASBLED score in an Asian population on NOAC for AF and/or VTE was evaluated. The objective of this study was to evaluate HASBLED score and to incorporate additional risk factors as relevant. Finally, the performance of HASBLED score and the modified bleeding risk score would be evaluated.

Method This was a retrospective cohort observational study conducted in Princess Margaret Hospital. The patients on NOAC and with a primary diagnosis of atrial fibrillation (AF), deep

vein thrombosis (DVT) or pulmonary embolism (PE) between 1 July 2012 and 30 June 2015 were recruited. Patient information including sex, age, body weight, history of stroke, history of bleeding, medication history (antiplatelet and NSAID), renal function test, liver function test and history of alcoholism was collected. The study endpoint was major bleeding within 1 year after initiation of NOAC. Major bleeding was defined according to the International Society on Thrombosis and Haemostasis (ISTH) criteria. Univariate and Multivariate logistic regression were used to obtain the odds ratio of different risk factors. Statistical analysis for the subgroup of patients taking full dose NOAC (i.e. dabigatran 150mg BD, dabigatran 110mg BD, rivaroxaban 20mg daily and apixaban 5mg BD) for AF was also performed. Receiver-operating characteristic (ROC) analysis (C statistics) was used to assess the performance of HASBLED score and the modified bleeding risk score.

Results A total 806 patients were identified via Clinical Data Analysis and Reporting System (CDARS). 35 patients were excluded because they actually did not take NOAC after prescription. In 771 patients on NOAC, there were 45 patients with major bleeding (5.83%, 6.6/100 patient-years). The mean duration of NOAC therapy was 10.6 months. The male to female ratio was 1.08. There were 502 patients on dabigatran (65.1%), 233 patients on rivaroxaban (30.2%) and 36 patients on apixaban (4.7%). Variables associated with major bleeding were age ≥ 80 years (OR:6.98, CI:1.576-30.901, p-value:0.011), history of bleeding (OR:3.16, CI:1.656-6.023, p-value:<0.001), moderate to severe renal impairment CrCl <50 ml/min1.73 m^2 (OR:2.64, CI:1.256-5.551, p-value:0.010) and concomitant use of NSAID and/or antiplatelet (OR:2.59, CI:1.130-5.938, p-value:0.025). Based on the results of multivariate logistic regression analysis, a modified bleeding risk score: A2BCD (A: Age, 1 point for Age >=65-79 years, 2 points for Age >= 80 years, B: history of bleeding, C: CrCl <50 ml/minute/1.73 m^2, D: drug including antiplatelet or NSAID) was developed. The A2BCD score performed better in predicting major bleeding than HASBLED score in patients on NOAC for AF and/or VE (C statistics: 0.755 vs 0.626, p value: 0.007) and in patients on full dose NOAC for AF (C statistics: 0.772 vs 0.637, p value: 0.004)

Conclusion Bleeding risk of Asian patients on NOAC was found to be higher when compared with non-Asians patient. A modified bleeding risk score: A2BCD (A: Age, 1 point for Age ≥65-79 years, 2 points for Age ≥ 80 years, B:history of bleeding, C: CrCl <50 ml/minute/1.73 m^2, D: drug including antiplatelet or NSAID) may have better predictive value for major bleeding and a prospective validation study is required to validate our findings.

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TRADITIONAL AND INNOVATIVE METHODS FOR ASSESSMENT OF VENTRICULAR PERFORMANCE IN PATIENTS WITH IMPAIRED LEFT VENTRICULAR FUNCTION: COMPARISON BETWEEN 2D-ECHOCARDIOGRAPHY AND CARDIAC MAGNETIC RESONANCE IMAGING

Dr Poon Wai Ling Jessica, Integrated Medical Service, Ruttonjee Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background Ventricular function assessment is important for diagnosis, prognostication and treatment in cardiovascular medicine. Currently, there are different echocardiographic (ECHO) and cardiac magnetic resonance imaging (CMR) techniques in the assessment of bi-ventricular systolic function. Beside traditional methods, myocardial deformation analysis using 2D speckle-tracking echocardiography (STE) and CMR tissue-tracking (TT) are novel techniques for assessing ventricular performance. However, the clinical applicability of these imaging techniques requires further exploration.

The main objectives of this study are:

I) To evaluate the accuracy of visual estimation, modified Biplane Simpson's method and the newer semi-automated speckle-tracking based method such as AutoEF for left ventricular (LV) ejection fraction (EF) assessment using CMR LVEF as the reference standard.

II) To correlate right ventricular (RV) fractional area change (FAC), tissue Doppler of lateral

tricuspid annular motion (S'), tricuspid annular plane systolic excursion (TAPSE), RV global longitudinal strain (GLS) and RV free wall longitudinal strain (FWS) with CMR RVEF; and to derive cut-off values of RV strain in predicting RV systolic dysfunction.

III) To compare CMR tissue-tracking (TT) with 2D speckle-tracking echocardiography (STE) for myocardial deformation (strain) analysis.

Methods Cardiac magnetic resonance and 2D-transthoracic ECHO were performed within 48 hours of each other in 30 patients with impaired LVEF. Left ventricular systolic function was assessed separately using visual estimation of LVEF by an experienced cardiologist, modified Biplane Simpson's LVEF, and AutoEF. Right ventricular systolic function was assessed by RV FAC, tricuspid S' and TAPSE. Echo LV GLS, RV GLS and RV FWS were measured off-line. LV and RV volumes and EF were obtained using CMR while CMR LV GLS and RV GLS were obtained using CMR tissue-tracking technique.

Results Excellent correlations and agreement were observed between visual eyeballing LVEF estimation, modified Biplane Simpson's LVEF, AutoEF and CMR LVEF ($r = 0.93$; $r= 0.89$ and $r= 0.90$ respectively, $p <0.001$).

Good correlations were observed between RV FAC, TAPSE, S', RVGLS, RV FWS and CMR RVEF ($r= 0.80$, $p<0.001$; $r= 0.58$, $p<0.01$; $r= 0.48$, $p<0.01$; $r= -0.79$, $P< 0.001$; $r=-0.78$, $P<0.001$). Of the five parameters studied, RV GLS, RV FWS and RV FAC have stronger correlation with CMR RVEF than S' and TAPSE. The best cutoff value of RV GLS for predicting RV dysfunction was -17% [area under the curve (AUC) = 0.86, $p< 0.01$] with a sensitivity of 75% and specificity of 79%. The best cutoff value of RV FWS for predicting RV dysfunction was -22 % (AUC= 0.88, $p< 0.001$] with a sensitivity of 75% and specificity of 79%.

There was excellent correlation and good agreement between CMR LV GLS and ECHO LV GLS ($r=0.87$, $p<0.001$). A weaker correlation ($r=0.57$, $p<0.01$), with significant bias of - 4.53 +/- 13.0% ($p<.001$) between CMR RV GLS and ECHO RV GLS was observed.

Conclusion

In patients with impaired LVEF,

I) AutoEF and visual estimation of LVEF showed better correlation and agreement with the reference standard of CMR LVEF compared with the guideline-recommended modified Biplane Simpson's LVEF. Thus, both of them are also reliable and pragmatic methods in LV functional assessment.

II) 2D-STE and RV FAC provided reasonably good reflection of RV systolic function compared to TAPSE and S'. Both of which can serve as useful techniques to evaluate RV performance.

III) CMR tissue-tracking measurements correlated and agreed well with 2D speckle-tracking echocardiography for LV GLS but less so for RV GLS. It is a potential tool for clinical use in the future. Further validation studies will be required.

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EVALUATION OF USING A RAPID GENOTYPING GUIDED APPROACH TO THE SELECTION OF P2Y12 RECEPTOR BLOCKERS IN CHINESE PATIENTS WITH ACUTE CORONARY SYNDROME

Dr Shea Puigi Catherine, Department of Medicine, Queen Mary Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background CYP2C19 genetic polymorphism is shown to affect on-treatment platelet reactivity and cardiovascular outcomes in patients taking clopidogrel for acute coronary syndrome (ACS). Ticagrelor with a more rapid onset and more pronounced platelet inhibition, has been shown to have better anti-ischemic effect at the expense of increased non-procedural

major bleeding. However, its use is not popular in East Asian patients probably due to perceived higher baseline bleeding risk. As CYP2C19 loss-of-function (LOF) alleles are present in half of East Asian population, we sort to investigate whether a rapid genotyping guided approach is feasible and efficacious to select antiplatelet agents in Chinese patients suffering from ACS.

Methods and Results This is a single-center, prospective, randomized, open-label study. 132 patients were randomized into rapid genotyping guided group (GG, N=65) or conventional group (CG, N=67). All patients were given loading doses of clopidogrel and then patients in GG were genotyped by Verigene system (Nanosphere, Northbrook, IL). 40 patients with CYP2C19 LOF alleles were switched to ticagrelor and all remaining patients continued on clopidogrel. High on-treatment platelet reactivity (HTPR) was defined by platelet reactivity unit (PRU) >208 as measured by VerifyNow P2Y12 assay (Accumetrics) at 24 hours after first loading dose of clopidogrel and one month afterwards. The incidence of HTPR in GG vs CG were 9.2% vs 40.3% (24 hour, $p<0.001$) and 6.5% vs 32.3% (one month, $p<0.001$).

Conclusions Rapid genotyping guided approach to select P2Y12 receptor blockers is feasible and able to reduce the incidence of HTPR in Chinese patients with ACS. Further studies are needed to investigate whether such a pharmacogenetics approach can lead to better clinical outcomes.

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GENDER DIFFERENCES IN BASELINE CHARACTERISTICS, CLINICAL FEATURES AND PROGNOSIS IN PATIENT WITH ACUTE CORONARY SYNDROME: A RETROSPECTIVE OBSERVATIONAL STUDY IN A LOCAL DISTRICT HOSPITAL

Dr Yuen Sze Man, Department of Medicine, North District Hospital (June 2016 Cardiology Exit Assessment Exercise)

Background Acute coronary syndrome is one of the leading causes of death globally. Several published trials investigated gender disparity in acute coronary syndrome. Local data are limited.

Objective To investigate the impact of sex difference on acute coronary syndrome, in terms of baseline characteristics, disease presentation, treatment and clinical outcomes.

Method 420 patients, including 280 males and 140 females, who were admitted to North District Hospital due to acute coronary syndrome between 1st July, 2013 and 30th June, 2014 were recruited. The baseline characteristics, presenting symptoms, investigation results, treatment and clinical outcomes were retrieved from the written and electronic medical records.

Results Women recruited in this study were significantly older than men, as well as having more co-morbidity and poorer functional status. They were less likely to present with typical symptoms as chest pain and sweating. Treatment, including medication and invasive procedure, was more conservative when compared with their male counterparts. The unadjusted in-patient mortality was higher in female patients compared with male ones (female 25% Vs male 8.2%, Odds ratio 3.72, p-value <0.001). The in-hospital mortality difference was not significant after adjusting other potential covariates (odds ratio 1.29, 95% C.I. 0.54 to 3.05, p-value = 0.568).

Conclusion This study revealed the impact of gender on acute coronary syndrome, from baseline characteristics, disease presentation, treatment discrepancy and clinical outcomes, particularly in that women might be easily misdiagnosed due to the atypical presentation and they were more likely to receive conservative treatment. It provides better understanding on disease identification and management, with a view to improving women's health.

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PREDICTIVE VALUE OF QUADRICEPS MUSCLE WASTING IN PATIENTS UNDER THE INTENSIVE CARE UNIT.

Dr Chan Shung Kay Samuel, Department of Medicine, Queen Mary Hospital (May 2016 Critical Care Medicine Exit Assessment Exercise)

Muscle wasting is one of the most commonly encountered and disabling conditions faced by patients under the Intensive Care Unit. There is evidence that muscle wasting is associated with mortality and morbidity. Ultrasonography represents a novel and newly validated tool in assessing this phenomenon. This study aims to further delineate muscle wasting in the ICU and study its interaction with patient outcome locally. A total of 28 subjects entered into final analyses. Main results included muscle wasting affecting all subjects with a mean reduction of 24.47%in quadriceps muscle layer thickness (QMLT) during ICU stay. A statistically significant logarithmic relationship with duration of stay ($p<0.01$) was demonstrated. Measurements were more reliable with muscle compressed, reducing the effect of edema. Age was associated with a lower QMLT at all time points including baseline ($p=0.03$). Caloric deficit was shown to have a significant association with the rate of muscle wasting ($p=0.048$), which also had a moderate discriminative performance to ICU mortality, but inferior to that of APACHE II derived risk of death (area under ROC= 70% vs 74%). We proposed that muscle wasting could a potential variable to adjunct traditional scoring system in conveying more accurate prognostic information.

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THE USE OF SALIVARY CORTISOL AND CORTISONE IN THE DIAGNOSIS OF CUSHING'S SYNDROME – A LOCAL PROSPECTIVE STUDY

Dr Lam Tsz King, Department of Medicine, Queen Elizabeth Hospital (May 2016 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Background Endogenous Cushing's syndrome results from excessive glucocorticoid production from the hypothalamic-pituitary-adrenal axis. It is difficult to diagnose Cushing's syndrome correctly due to non-specific clinical manifestations and lack of a single biochemical test to serve as a gold standard for diagnosis.
The Endocrine Society's Clinical Practice Guidelines had recommended late night salivary cortisol as one of the screening tests for Cushing's syndrome. Local data on diagnostic performance on late night salivary cortisol measured by LC-MS/MS is however lacking. This prompts us to study its sensitivity, specificity and the optimal cutoff value.

Objective The aim of this dissertation is to assess the diagnostic performance of salivary cortisol and salivary cortisone in the diagnosis of Cushing's syndrome, and identify the optimal cutoff values in our local Chinese population.

Study design This is a prospective study to evaluate the role of salivary testing in patients referred for assessment of hypercortisolism using a protocol of biochemical investigations including blood, salivary and urine samplings.

Result 101 patients were recruited, yielding 111 sets of biochemical investigations for analysis. 14 patients were classified as 'disease group' (8 adrenal Cushing, 3 pituitary Cushing, 3 ectopic ACTH syndrome) according to predefined criteria. 45 patients who had normal overnight dexamethasone suppression test, normal 24 hours urine for free cortisol and normal 24 hours urine for steroid profile were classified as 'control group'. 42 patients were categorized as 'indeterminate group' and their results were excluded from subsequent analysis, because of discordant or borderline results, and absence of suggestive clinical features.
For making a diagnosis of Cushing's syndrome, the optimal cutoff values for late-night salivary cortisol, late-night salivary cortisone, post-ONDST salivary cortisol and post-ONDST salivary cortisone, when measured by LC-MS/MS, are 2.85 nmol/L (AUC 0.943,

sensitivity 83.3%, specificity 93.3%), 9.8 nmol/L (AUC 0.922, sensitivity 100%, specificity 73.7%), 1.15 nmol/L (AUC 0.979, sensitivity 92.9%, specificity 97.8%) and 5.9 nmol/L (AUC 1.000, sensitivity 100%, specificity 100%) respectively. At these cut-off values, the late night salivary cortisol, ONDST salivary cortisol and ONDST salivary cortisone all showed good diagnostic performance.

Conclusion From our study, we conclude that late night salivary cortisol, ONDST salivary cortisol and ONDST salivary cortisone can be used in diagnosing Cushing's syndrome

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THE USE OF SALIVARY CORTISOL AND CORTISONE DURING LOW DOSE CORTICOTROPIN STIMULATION TEST IN THE DIAGNOSIS OF ADRENAL INSUFFICIENCY - A LOCAL STUDY

Dr Mak Yin Fung Ingrid, Department of Medicine, Queen Elizabeth Hospital (May 2016 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Background An accurate diagnosis of adrenal insufficiency is clinically important because adrenal crisis may result in lethal consequences. However, there have been controversies in the literature regarding the diagnostic values of different tests and the corresponding optimal cut-off levels for adrenal insufficiency. The potential role of salivary cortisol and cortisone has also been studied over the recent years.

Objectives The main goals of this dissertation are: 1) to establish the reference cut-off value for peak serum cortisol in the low dose corticotropin stimulation test (LDCST), and 2) to explore the utility of salivary cortisol and cortisone during LDCST in the diagnosis of adrenal insufficiency.

Methods This prospective study was conducted in a regional hospital (Queen Elizabeth Hospital) in Hong Kong. Chinese healthy volunteers and patients suspected of having adrenal insufficiency were recruited. All participants underwent a LDCST, in which their serum cortisol, salivary cortisol and cortisone levels were assessed at baseline, 30 and 60 minutes after an intravenous injection of 1 microgram Synacthen 1-24. Their serum cortisol binding globulin (CBG) levels were also explored. The free cortisol index (FCI), which is the ratio of serum total cortisol/CBG, was calculated in patients with discordant serum and salivary results.

Results Using the data from 56 healthy volunteers, the reference cut-off value for post-LDCST peak serum cortisol was found to be 376 nmol/L (mean–2SD). We then analyzed the data of 171 patients, who presented with clinical findings suggestive of adrenal insufficiency and/or risk factors for the impairment of hypothalamic-pituitary-adrenal axis. 59 of them were classified into the adrenal insufficient (AI) group (post-LDCST peak serum cortisol <376 nmol/L) and 112 were in the non-AI group (≥376 nmol/L). From the ROC curve analysis, both peak salivary cortisol and cortisone had a larger AUC (0.914±0.026 and 0.926±0.022 respectively) than their basal counterparts and basal serum cortisol. The best cut-off value with the highest accuracy for peak salivary cortisol was 8.6 nmol/L and that for salivary cortisone was 33.5 nmol/L. Combination of basal test results alone increases the specificity and may be useful to rule in the diagnosis of adrenal insufficiency. In patients with low CBG levels and discrepancies between serum and salivary results, salivary tests and FCI might be more reliable than serum total cortisol in reflecting the free cortisol status.

Conclusion A lower method-specific reference cut-off value for post-LDCST peak serum cortisol was suggested. Both stimulated salivary cortisol and cortisone yielded excellent test performances in diagnosing adrenal insufficiency and they may be useful alternatives especially when a non-invasive test is desired or an abnormal CBG level is suspected.

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CHRONIC HEPATITIS B INFECTION IN RENAL TRANSPLANT RECIPIENTS: A SINGLE-CENTRE RETROSPECTIVE OBSERVATIONAL STUDY FOR 11YEARS

Dr Lam Yau Yui**,** Department of Medicine, Queen Elizabeth Hospital (June 2016 Gastroenterology and Hepatology Exit Assessment Exercise)

Background Natural course of illness and long term prognosis regarding liver and renal outcomes of renal transplant recipients with chronic hepatitis B (CHB) infection might have been improved in the era of effective oral antiviral agents. Recent local data was lacking.

Methods Data of all patients with active or past HBV infection who had renal transplantation done from Feb 2002 to Jan 2013 (N=60) were extracted from the Organ Registry and Transplant System for retrospective analyses. Primary outcome was defined as the occurrence of any significant adverse liver event.

Results The five-year cumulative incidence of primary outcome after renal transplantation was 1.7%. With a median follow-up of 6.6 years, it occurred in 6.7% (N=4) of all subjects. All were baseline HBsAg-positive patients. Detection of significant HBV DNA level (≥2000 IU/ml) after transplantation (p=0.016) was associated with more primary outcomes in univariate analysis. The five-year patient and graft survival rates were 80.0% and 78.3% in all subjects whilst 91.7% and 87.5% in HBsAg-positive ones respectively.

Conclusion In this local study, long term prognosis after renal transplantation among CHB patients in the era of effective oral antiviral agents was better than previously reported. However larger prospective study was needed to have a better evaluation.

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OUTCOME OF COLONOSCOPY IN PATIENTS WITH HIGH THROMBOEMBOLIC RISK RECEIVING HEPARIN BRIDGING ANTICOAGULATION

Dr Lam Yip Shun, Department of Medicine, Queen Elizabeth Hospital (June 2016 Gastroenterology & Hepatology Exit Assessment Exercise)

Background & Aims Heparin bridging therapy is commonly used in patients with high thromboembolic risk undergoing colonoscopy. Specific data on its use remains limited. We aim to evaluate the safety and efficacy of bridging therapy in this group of patients.

Methods Consecutive warfarinized patients who underwent colonoscopy in a regional hospital from Jan 2006 to Dec 2015 were retrieved. Unfractionated heparin (UFH) group was compared with low-molecular-weight heparin (LMWH) group for assessment of thromboembolic risk. The 2 bridged groups were compared as a whole to a control group of those who received warfarin anticoagulation but not bridging for assessment of the bleeding risk.

Results A total of 392 patients who was taking warfarin underwent colonoscopic procedure. Half of them (50.5%) received bridging therapy and in which 62.1% of them were given LMWH. For those patients with a high thromboembolic risk, an overall 1% of thromboembolic event and an overall post-polypectomy bleeding rate of 16.7% were noted. Though the post-polypectomy bleeding (PPB) rate was similar between UFH and LMWH groups (17.1% vs. 16.4%; P=0.92), the whole bridged populations had a significantly higher PPB rate than the controls who did not receive bridging therapy (3.6%; P<0.01). On multivariate analysis, risk factors of post-polypectomy bleeding included a polyp size ≥10 mm (OR 3.58; CI 95% 1.32-9.72; P=0.01) and the use of bridging therapy (OR 5.03; CI 95% 1.39-18.2; P=0.01). The use of LMWH as bridging therapy in elective colonoscopy was associated with a shorter median length of stay. (5 vs. 7 days for UFH; P=0.01).

Conclusion The use of UFH and LMWH were comparable as bridging therapy for patients

who underwent colonoscopy. However, under the effect of anticoagulation, the post-polypectomy bleeding risk remained high and special precautions should be taken to minimize such adverse events.

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PREDICTION OF ESOPHAGEAL VARICES BY TRANSIENT ELASTOGRAPHY (TE) AND NON-INVASIVE BLOOD TESTS IN CIRRHOTIC PATIENTS

Dr Lau Ka Ki, Department of Medicine & Geriatrics, Kwong Wah Hospital (June 2016 Gastroenterology & Hepatology Exit Assessment Exercise)

Background Patients with cirrhosis were recommended to receive periodic oesophagogastroduodenoscopy (OGD) for esophageal varices screening. Detection of high risk esophageal varices (HREV) defined as medium to large size esophageal varices and small size varices with red wale marks or in decompensated Child B or C cirrhosis were indicated for primary propylactic treatment1. However, OGD examination is invasive and therefore the identification of non-invasive methods for predicting the presence of HREV would be valuable.

Methods In this cross-sectional study, 92 consecutive cirrhotic patients were recruited. They had all undergone liver stiffness measurement (LSM) by transient elastography, blood investigations and endoscopic examinations. Serum fibrosis biomarkers include AST to ALT ratio (AST/ALT), AST to platelet ratio index (APRI), FIB-4 index and Lok index were calculated. Univariate and multivariate analysis were used to identify the independent predictors for HREV. The values of LSM by transient elastography, platelet count and the serum fibrosis biomarkers in predicting the presence of HREV were studied.

Results 26 (28.3%) out of 92 cirrhotic patients had HREV. On multivariate analysis, platelet count, Child-Pugh class and LSM by transient elastography were independent predictors for HREV. LSM by transient elastography performed the best for predicting the presence of HREV (AUROC=0.845). At the cut-off point of 20.15kPa, it give a sensitivity of 87%, specificity of 72.3%, positive predictive value of 52.6% and negative predictive value of 94%.

Conclusion LSM by transient elastography may be useful as a screening tool to screen out patients who are unlikely to have high risk esophageal varices (HREV).

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CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING UNDERGOING CAPSULE ENDOSCOPY: 10-YEAR EXPERIENCE IN A LOCAL HOSPITAL

Dr Liu Hin Wai Henry, Department of Medicine, Queen Elizabeth Hospital (June 2016 Gastroenterology & Hepatology Exit Assessment Exercise)

Aim To determine the clinical characteristics, prognostic factors and outcome of patients who underwent small bowel capsule endoscopy for obscure gastrointestinal bleeding

Method A total of 90 patients with obscure gastrointestinal bleeding and small bowel capsule endoscopy done were retrospectively included in the present study. Logistic regression was carried out to define predictive factors for presence of small bowel lesion and incomplete capsule examination. Risk factors for rebleeding in those with negative capsule result were identified using Cox regression analysis. Factors that influenced the small bowel transit time were analysed. The safety profile of the procedure was also assessed.

Results The diagnostic yield in our cohort was 46.7%, with positive rate similar between overt and occult bleeding groups. Patients with congestive heart failure had a higher diagnostic yield. History of myocardial infarction, moderate to severe renal or liver disease,

overt bleeders and hemoglobin <8g/dL on presentation were independent predictors of rebleeding. Suboptimal bowel preparation, prior abdominal radiotherapy and higher Charlson Index were risk factors for incomplete examination. Small bowel transit time was prolonged in patients with prior abdominal surgery or suboptimal bowel preparation. Only one patient experienced capsule retention (1.1%) and the procedure was as safe in elderly as in younger adults.

Conclusion Small bowel capsule endoscopy is a safe procedure with satisfactory diagnostic yield for patients presenting with obscure gastrointestinal bleeding. It is equally useful in overt and occult bleeders. Patients with negative capsule examination still carry a considerable rebleeding risk and should be closely observed.

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DEVELOPING FAECAL NUCLEIC ACID MARKERS FOR DETECTION OF COLORECTAL CANCER AND ADVANCED COLORECTAL NEOPLASIA

Dr Wong Hei Sunny, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2016 Gastroenterology & Hepatology Exit Assessment Exercise)

Colorectal cancer (CRC) is the third most common cancer worldwide, and carries a significant health burden in Asia. Screening for CRC can reduce cancer mortality. Nevertheless, the best strategy for CRC screening is not known. Colonoscopy is associated with a small but definite procedural risk, while faecal occult blood tests (FOBT) have limited sensitivity for pre-cancerous lesions like advanced adenoma (AA). A simple, affordable and accurate screening test for colorectal neoplasia is lacking. With the increasing evidence of microbial alternations in colorectal neoplasia, we evaluated faecal microbial markers for their clinical utility in detecting CRC and AA. We quantitated three microbial markers on *Fusobacterium nucleatum* (*Fn*), *Peptostreptococcus anaerobius* (*Pa*) and *Parvimonas micra* (*Pm*) in CRC patients, AA patients and healthy controls using quantitative PCR (qPCR) assays, and evaluated the diagnostic potential of these biomarkers with respect to faecal immunochemical test (FIT). We observed a higher abundance of all three microbial markers in CRC patients than controls (p<0.001), and for marker *Fn* in AA patients than controls (p=0.030). The best marker *Fn*, when combined to FIT, showed superior sensitivity (92.3% *vs* 73.1%, p<0.001) and area under the receiver-operating curve (AUC) (0.95 *vs* 0.86, p<0.001) than standalone FIT in detecting CRC. Addition of the marker *Fn* to FIT significantly increased its detection rate of AA from 15.5% to 42.7% (p<0.001). This study identified faecal *Fusobacterium* quantification as a useful biomarker for detecting CRC and AA, especially when combined with a standard FIT. Our study takes one step further towards a non-invasive, accurate and affordable diagnosis of colorectal neoplasia.

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PREVALENCE OF MINIMAL HEPATIC ENCEPHALOPATHY IN HONG KONG CIRRHOTIC PATIENTS: DATA FROM LOCAL HOSPITALS

Dr. Wong Tin Long Marc, Department of Medicine & Geriatrics, Princess Margaret Hospital (June 2016 Gastroenterology & Hepatology Exit Assessment Exercise)

Background Minimal hepatic encephalopathy (MHE) describes a state of cognitive impairment in patients with cirrhosis which is not detected by routine neurological examination. Psychometric Hepatic Encephalopathy Score (PHES) and Critical flicker frequency (CFF) are widely used to detect MHE. Prior standardization of PHES norm is required before being applied in each cultural group. While being increasingly recognized internationally, the data of MHE in Hong Kong is lacking. Moreover, the PHES norm in Hong Kong population has yet to be sought.

Aim This study aims to standardize the PHES norm in Hong Kong population and to evaluate the prevalence of MHE among Hong Kong patients with liver cirrhosis using PHES and CFF, as well as to identify the clinical parameters associated with the presence of MHE.

Methods 250 healthy individuals were recruited to perform the PHES test. Based on their results, the PHES test in Hong Kong population was standardized. 250 cirrhotic patients without overt hepatic encephalopathy then underwent both PHES and CFF tests for diagnosing MHE.

Results The standardization cohort consisted of 111 male (44.4%) and 139 female (55.6%). The mean age was 45.1 ± 16.4 with 47 (19%), 126 (50%) and 77 (31%) attained primary, secondary and tertiary education level respectively. The PHES score was -0.08±1.905. The cut-off of PHES test was set at -4. The patient group consisted of 166 male (66.4%) and 84 (33.6%) female. The mean age was 58.8 ± 10.7 with 94 (37.6%), 128 (51.2%) and 28 (11.2%) attained primary, secondary and tertiary education level respectively. The most common aetiology of cirrhosis was Hepatitis B infection (75.2%). Two hundred and twenty nine (91.6%) patients were of Child-Pugh class A, and 21 (8.4%) cases of Child class B cirrhosis.

A total of 120 (48%) patients were diagnosed with MHE, failing PHES or CFF test. The PHES results between patient and control group were significantly different ($p<0.001$). Age ($p<0.001$), Platelet count < 100 x 109/L ($p=0.009$) and presence of varices ($p=0.005$) were significantly associated with presence of MHE.

Conclusion Minimal hepatic encephalopathy affects a significant proportion of cirrhotic patients. Low platelet count (<100 $x10^9$/L) and presence of varices, both surrogate markers of portal hypertension, are strongly correlated with presence of MHE. Standardization of PHES test in Hong Kong enables local application of this test in diagnosing MHE.

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DELIRIUM AND SUBSYNDROMAL DELIRIUM IN CHINESE ELDERLY MEDICAL PATIENTS

Dr Yam Ka Keung, Department of Medicine, Queen Mary Hospital (May 2016 Geriatric Medicine Exit Assessment Exercise)

Background Delirium is prevalent in hospitalized elderly patients, and it is associated with numerous adverse outcomes. Subsyndromal delirium (SSD) is a condition characterized by the presence of symptoms of delirium but not fulfilling its criteria. There is limited study of the prevalence and outcomes of delirium and SSD of Chinese elderly presenting with acute medical problems to the hospital, therefore further research on this topic is indicated.

Objective The aim of this study is to study the prevalence and outcomes of delirium and SSD in Chinese elderly patients who presented with acute medical problems and admitted to general medical wards in a regional hospital in Hong Kong.

Subject and method Patients were recruited from the acute general medical wards of Queen Mary Hospital from January 2014 to September 2014, and they were screened by the Confusion Assessment Method (CAM) on admission to classify them into three groups, namely without delirium, delirium and SSD. Baseline demographics, co-morbidity according to Charlson Co-morbidity Index (CCI), Barthel Index [BI(20)], Mini-mental statue examination (MMSE), potential predisposing factors and precipitating factors were collected at baseline. Subjects were followed up in hospital till they were discharged from the hospital and then for 12 months after discharge. Outcomes including all-cause mortality, hospitalization and number of new institutionalization were recorded.

Results 575 patients older than 65 years of age were recruited. 15.8% patients satisfied the diagnostic criteria of delirium and 11.3% patients satisfied the diagnostic criteria of subsyndromal delirium. Delirium on admission was an independent predictor for death in the index admission (hazard ratio [HR] 1.71, 95% confidence interval [CI] 1.13 –2.60, $p = 0.011$), institutionalization upon discharge from the index admission (Odds ratio 25.76, 95% CI 7.04-94.29,$p < 0.001$)and institutionalization within 12 months (OR 5.36, 95% CI 2.19-13.10,$p < 0.001$). SSD was an independent predictor of death within 12 months (HR 1.75,

95% CI 1.14-2.67, p = 0.01). Among patients with resolved delirium or resolved SSD upon discharge, the mortality in the following 12 months did not differ from the mortality of patients with no delirium.

Conclusion Delirium and SSD are common among elderly patients admitted into acute medial ward. They predict adverse short and long term outcomes. Prompt recognition and management of delirium and SSD might improve the prognosis of these patients.

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CLINICAL OUTCOME OF HEMATOPOIETIC STEM CELL TRANSPLANT IN MULTIPLE MYELOMA PATIENTS

Dr Wong Hiu Yan Hilda, Department of Medicine, Queen Mary Hospital (May 2016 Haematology and Haematological Oncology Exit Assessment Exercise)

Background In eligible multiple myeloma patients, upfront autologous hematopoietic stem cell transplantation (HSCT) following induction therapy is a standard of care, but most patients eventually relapse. This dissertation aims to: i) summarize demographics, tumor characteristics, treatment and HSCT data in our patient cohort; ii) assess clinical outcomes, including overall survival (OS), progression-free survival (PFS), tumor response rate (RR) and treatment-related complications; iii) compare clinical outcomes of autologous and allogeneic HSCT; and iv) evaluate predictors of outcomes.

Methods Clinical data of 248 consecutive HSCTs (autologus: 182; allogeneic: 66) performed for myeloma patients in Queen Mary Hospital, Hong Kong, from August 1991 to August 2015, were retrospectively reviewed.

Results Median patient age was 54 years, with a slight male predominance. In the upfront setting, all patients ≤ 40 years old responded after HSCT, with OS and PFS significantly favoring the allogeneic group (median OS: 105.3 *versus* 45.7 months, p=0.002; median PFS: 91.0 *versus* 40.0 months, p=0.003). In contrast, RR and OS were superior in the autologous group for patients older than 40 years. On multivariate analysis of the autologous group, creatinine ≤177umol/L, calcium ≤2.99mmol/L, and non-progressive disease at transplantation were independent prognostic factors, whereas in the allogeneic group, age ≤40 years and response after HSCT were associated with favorable OS and PFS, with response after HSCT being an independent predictor.

Conclusion Patients ≤40 years old may benefit from an upfront allogeneic HSCT. Early transplantation in patients with at least stable disease after primary treatment, is associated with superior outcome.

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ROLE OF SERUM PROCALCITONIN (PCT) MONITORING IN BLOODSTREAM INFECTIONS

Dr Li Chun Man, Department of Medicine & Therapeutics, Prince of Wales Hospital (June 2016 Infectious Disease Exit Assessment Exercise)

Background Bloodstream infections are common and cause significant morbidity and mortality. Reliable biomarkers for monitoring response and predicting prognosis are necessary for optimal treatment outcomes. Over the past decade, serum procalcitonin (PCT) has emerged as a promising biomarker for infections.

Method A single-centre prospective observational study was conducted on adult patients (age ≥ 18) admitted to the Prince of Wales Hospital during July to December 2015 with culture confirmed bloodstream infections (n=50). Serial monitoring of serum PCT levels was performed thrice weekly with the Roche Elecsys BRAHMS PCT assay. Electronic and written records were reviewed for collection of clinical data. Severity and outcome measures analysed

included major complications (septic shock, acute kidney injury, and acute respiratory distress syndrome), length-of-stay (LOS), requirement of intensive care, death during hospitalization and death within 30 days of recruitment. Comparison of performance with serum C-reactive protein (CRP) and white blood cell (WBC) was done.

Results Among the 50 patients, 64% had bloodstream infections due to Gram negative organisms, 32% had Gram positive infections, 2% had polymicrobial infections (both Gram positive and Gram negative) and 2% had fungemia. Crude all-cause mortality within 30 days was 10%. The mean and median length-of-stay among survivors was 16.3 days (SD 15.9) and 11 days (IQR 7-17), respectively. One subject required intensive care. Forty-two percent of the patients developed at least one major complications. The mean and median baseline PCT were 9.52 (SD 17.7) and 2.8 (IQR 0.64-8.10) respectively. The mean and median peak PCT were 15.61 (SD 25.4) and 5.15 (IQR 0.80-18.58) respectively. In general PCT showed about 90% reduction from baseline by the end of the first week. The AUC of using baseline PCT for prediction of 30-day mortality was 0.778 (95% CI = 0.595-0.961, p=0.043). A cut-off of 8μg/L had a 80% sensitivity and 82.2% specificity in predicting 30-day mortality. Baseline PCT of 8μg/L or above was associated with a higher rate of septic shock and death within 30 days of recruitment. The kinetics and prognostication value of PCT appear superior to CRP and WBC.

Conclusion Serum PCT is a potentially useful marker for monitoring and prognostication in patients with bloodstream infections.

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CLINICAL PRESENTATION AND OUTCOME OF CRYPTOCOCCAL MENINGITIS IN A LOCAL HOSPITAL FROM 2002 TO 2014

Dr Ting Wan Man, Department of Medicine, Queen Elizabeth Hospital (June 2016 Infectious Disease Exit Assessment Exercise)

Background Cryptococcal meningitis is associated with significant morbidity and mortality but there has been no recent local study focused on cryptococcal meningitis.

Objective To describe the clinical presentation and outcome of local cryptococcal meningitis patients, to review the use and tolerance of combination antifungal induction therapy, and to compare the clinical presentation and outcome of cryptococcal meningitis between HIV-infected and non-HIV infected patients.

Method A retrospective review of patients with cerebrospinal fluid (CSF) culture confirmed cryptococcal meningitis admitted to Queen Elizabeth Hospital (QEH) from 2002 to 2014.

Results Thirty-nine patients were identified. Thirty-four patients (87.2%) had underlying immunocompromised conditions. Nineteen of them were HIV-infected. Fever and headache were the most common symptoms. Overall, 33 patients (86.8%) were prescribed with amphotericin B and flucytosine combination as induction therapy. Drug discontinuation within 2 weeks due to drug toxicity was observed in 7.9% of patients given amphotericin B and 30.3% of patients given flucytosine. The overall mortality at 10 week was 35.1%. Seven patients had the first lumbar puncture performed by more than 10 days after admission. A trend towards shorter median survival time was observed in these patients when compared with those having lumbar puncture performed within 10 days (26 days versus 1964 days; p=0.101). When compared with the non-HIV infected patients, the HIV-infected ones were significantly younger (median age of 43.0 years versus 58.5 years; p=0.006). They presented with higher serum cryptococcal antigen titre (≥1:64 in 100% versus 72.2%; p=0.022). Furthermore, HIV-infected patients were more likely to have cryptococcaemia (68.4% versus 20.0%; p=0.002), positive CSF fungal stain (100% versus 55%; p=0.001), and less likely to have CSF lymphocytic pleocytosis (17.6% versus 60.0%; p=0.009) in the first lumbar puncture. Hydrocephalus was more commonly found in the non-HIV infected patients (21.1%

versus 0%; p=0.034). The median time from antifungal commencement to CSF sterilization was significantly longer in HIV-infected patients (26 days versus 11 days; p<0.001) but there was no difference in mortality between the 2 groups.

Conclusions The majority of patients with cryptococcal meningitis had underlying immuncompromised conditions. The recommended combination antifungal regimen was given to most of our patients as the induction therapy, but drug discontinuation due to toxicities was commonly observed. Although HIV-infected patients had higher initial fungal load, the mortality rate was similar to non-HIV infected patients. Timely diagnosis and antifungal initiation may improve the survival of patients with cryptococcal meningitis.

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PREDICTIVE FACTORS OF POOR OUTCOME OF PSEUDOMONAS EXIT SITE INFECTION IN CAPD PATIENTS IN A REGIONAL HOSPITAL

Dr Tai Wai Ching, Department of Medicine & Geriatrics, Tuen Mun Hospital (June 2016 Nephrology Exit Assessment Exercise)

Introduction Continuous ambulatory peritoneal dialysis (CAPD) is the commonest form of renal replacement therapy for patients with end-stage renal failure in Hong Kong. Catheter related infections, including exit site infections are common complications in CAPD. If exit site infections are not well treated, they can progress to tunnel tract infections and peritonitis requiring urgent catheter removal. Pseudomonas aeruginosa is one of the most common organisms causing exit site infections. However it is difficult to treat and prone to relapse and even requiring catheter removal. The aim of the study is to study factors predicting poor outcome of pseudomonas exit site infections so that we can intensify or initiate treatment or consider early catheter removal according to these predictive factors.

Methods The records of patients who attended renal ward and exit site clinic in Tuen Mun Hospital dialysis centre with the diagnosis of Pseudomonas aeruginosa exit site infections were retrospectively generated through clinical case notes, the Organ Transplant Registry and the Clinical Management System in Tuen Mun Hospital from the period between 1st January 2006 to 31st July 2015. Patient's demographics, comorbidities, baseline characteristics, laboratory and microbiological results were obtained. Predictive factors were obtained by univariate analysis and logistic regression model.

Results A total of 189 episodes of pseudomonas aeruginosa exit site infections occurred in 147 individuals. On univariate analysis, predictive factors for poor responses to antibiotic treatment included longer duration of dialysis, antibiotic use in recent 3 months, longer interval between diagnosis of infection and treatment, isolation of drug resistant strain, poor drug compliance, external cuff extrusion, history of Pseudomonas exit site infections (excluding relapses) and the presence of exit site granulomas. After using binary logistic regression to determine the independent predictive factors of poor response to Pseudomonas aeruginosa exit site infections, history of Pseudomonas exit site infections (OR 0.213; 95% CI 0.087 to 0.523) and presence of exit site granulomas (OR 0.171; 95% CI 0.071-0.410) are the only significant predictive factors.

Conclusions Exit site granuloma and history of Pseudomonas aeruginosa exit site infections are predictive factors of poor response to antibiotic treatment in Pseudomonas aeruginosa exit site infections in peritoneal dialysis patients. With acknowlegement of these factors, we can consider earlier treatment, stepping up antibiotic therapy or low threshold for Tenckhoff catheter removal.

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RISK FACTORS AND OUTCOMES OF VANCOMYCIN-RESISTANT *ENTEROCOCCUS* COLONIZATION IN PATIENTS ON PERITONEAL DIALYSIS

Dr Yeung Ching Shan Jason, Department of Medicine, Queen Elizabeth Hospital (June 2016

Nephrology Exit Assessment Exercise)

Background Vancomycin-resistant *Enterococcus* (VRE) colonization is common among patients with chronic renal diseases, including those undergoing peritoneal dialysis (PD). The aim of this study is to evaluate the risk factors and various clinical outcomes for VRE colonization among PD patients within a tertiary dialysis centre in Hong Kong.

Methods This is a single-centered retrospective cohort study of 166 hospitalized patients who used PD as mode of renal replacement therapy from 1st August 2013 to 31st July 2014. All patients were screened for VRE colonization status via rectal swabs or stool specimen during hospitalization. They were categorized into two groups: VRE-positive group and VRE-negative group. Baseline characteristics and other potential risk factors were analyzed in both groups. Clinical outcomes including all-cause mortality, infection with VRE, peritonitis-free survival, length of hospitalization, VRE spontaneous clearance rate and VRE relapse rate were also analyzed.

Results Among the 166 PD patients, 28 (16.9%) were VRE-positive. Multivariate analysis showed that previous contact history with VRE-positive patients (OR: 417.86; 95% CI: 17.21-10147.26, p<0.01), previous use of vancomycin in 3 months (OR: 130.32; 95% CI: 5.35-3176.30, p<0.01) and age (OR: 1.13; 95% CI: 1.02-1.24, p=0.02) were the three independent risk factors for VRE colonization. Patients in VRE-positive group had significantly longer length of hospitalization stay but there was no significant difference in all-cause mortality and peritonitis-free survival.

Conclusions VRE-colonization is an important issue among hospitalized PD patients. Cautious use of antibiotics and infectious control measures may be necessary to prevent spreading of VRE especially in those higher risk patients.

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COGNITIVE SCREENING IN THE CHINESE HUMAN IMMUNODEFICIENCY VIRUS POPULATION IN HONG KONG – A CROSS-SECTIONAL & LONGITUDINAL STUDY

Dr Chan Chong Ching, Department of Medicine, Queen Elizabeth Hospital (May 2016 Neurology Exit Assessment Exercise)

Objectives & Methods Cognitive impairment is a significant complication of human immunodeficiency virus (HIV) infection. This is the first cross-sectional and longitudinal observational cohort study to investigate the prevalence, pattern and progression of cognitive impairment in the local Chinese HIV population.

98 adult Chinese HIV individuals were assessed cognitively with a screening questionnaire, the International HIV Dementia Scale (IHDS) and the Montreal Cognitive Assessment (MoCA). 57 subjects underwent a cognitive review and were analysed longitudinally.

Results Baseline cognitive impairment was present in 39% of subjects, and was associated with lower education level (p=0.030) and an inpatient HIV diagnosis (Odds ratio 2.3, 95% confidence interval 1.005-5.417, p=0.047). Subjects with an inpatient HIV diagnosis had more advanced HIV infection and more severe immunosuppression, but none of those factors had significant association with cognitive impairment individually.
There was a small but significant overall cognitive improvement on follow-up (p=<0.001). One-fourth of the subjects improved from baseline cognitively impaired to become cognitively preserved, while the others were cognitively static. No association was found between cognitive change and the HIV severity or control, comorbidities, or other host or social factors. Cognitive change was not associated with whether combined antiretroviral therapy (cART) was used, or the central nervous system penetration-effectiveness (CPE) index of the regime.

Conclusion Cognitive impairment is common in HIV individuals, especially in those with lower education level. There was an overall cognitive improvement on follow-up, but the current study found no significant predictor. Neither cART nor its CPE index had association with cognitive change.

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5-YEAR OUTCOME OF VERTEBROBASILAR TERRITORY ISCHEMIC STROKE ATTRIBUTED TO LARGE ARTERY DISEASE

Dr Ma Sze Ho, Department of Medicine & Therapeutics, Prince of Wales Hospital (May 2016 Neurology Exit Assessment Exercise)

Background and Purpose Vertebrobasilar (VB) territory infarct with Large Artery Disease (LAD) is an important subset of ischemic stroke. While previous studies demonstrated an increased risk of recurrence in short-term, data regarding the long-term prognosis is lacking

Method We conducted a retrospective analysis in a cohort of 282 patients with VB territory infarct. We evaluated the 5-year restroke rate, functional outcome and mortality and assessed the effect of an optimal control of conventional risk factors. Optimal risk factor control was defined as a combination of Low Density Lipoprotein (LDL) ≤1.8mmol/l, systolic Blood Pressure ≤140mmHg, glycosylated hemoglobin (HbA1c) ≤6.5%.

Result The 5-year restroke risk was 21.4% for LAD group versus 11.8% in non-LAD group (OR 2.03; 95% CI 1.05-3.91, P=0.032). LAD group was also associated with a poor functional outcome (OR 2.19, 95% CI 0.97-7.13, P=0.05) and a higher morality (OR 2.41, 95% CI 1.26-4.76, P<0.01). Optimal risk factor control was associated with a significant risk reduction (20.9% vs 6.1%, OR 0.24, 95% CI 0.61-0.98, RR 3.42, P< 0.01). Absolute risk reduction is 24.7% and the Number needed to treat is 4.

Conclusion LAD in VB territory ischemic stroke portends a poor long-term prognosis with a high recurrence. Optimal risk factor control might significantly reduce the recurrent risk.

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ANTIPLATELET RESUMPTION AFTER ANTIPLATELET-RELATED INTRACEREBRAL HEMORRHAGE

Dr Teo Kay Cheong, Department of Medicine, Queen Mary Hospital (May 2016 Neurology Exit Assessment Exercise)

Background Antiplatelet resumption in survivors of antiplatelet-related ICH represents an important medical dilemma as these patients have a high risk for both recurrent intracerebral hemorrhage (ICH) and ischemic vascular event. The increased risk of recurrent ICH and the high mortality of ICH lead to the reluctance among clinicians to resume antiplatelet medicine. OBJECTIVES: To investigate whether antiplatelet medicine should be resumed in survivors of antiplatelet-related ICH, and to identify the risk factors for recurrent ICH.

Method This was a single-centre retrospective longitudinal cohort study involving antiplatelet-related ICH survivors who were admitted to Queen Mary Hospital from July 2002 to June 2013. Antiplatelet exposure and follow-up data were retrieved from the electronic patient record system. The clinical end points were recurrent ICH, ischemic vascular event and vascular death (death due to ICH or ischemic vascular event). Predictors of recurrent ICH and vascular death were derived using multivariable Cox regression model.

Results There were a total of 109 survivors of antiplatelet-related ICH. The median follow-up duration was 3.5 years (total time of 518.2 patient-years). Thirty seven patients were subsequently found to have been resumed on antiplatelet medicine, out of which 16 were resumed antiplatelet after an ischemic vascular event. The recurrent ICH rate was similar between the antiplatelet exposure and no antiplatelet exposure groups (3.1 per 100

patient-years vs. 2.4 per 100 patient-years; p=0.658). In patients not resumed on antiplatelet, the rate of ischemic vascular event was higher than the rate of recurrent ICH (7.6 per 100 patient-years vs. 2.4 per 100 patient-years; p=0.026). Antiplatelet exposure was shown not to be associated with an increased risk of recurrent ICH (HR 1.10, p=0.893) or vascular death (HR 0.85, p=0.825). A mean follow-up systolic blood pressure of >140 mmHg was associated with increased risk of recurrent ICH (HR 5.18, p=0.034) and vascular death (HR 11.14, p=0.001). Cerebral amyloid angiopathy (HR 28.05, p=0.003) was an independent predictor for recurrent ICH.

Conclusion Antiplatelet resumption after antiplatelet-related ICH was not associated with a significant increased risk of recurrent ICH or vascular death. The risk of recurrent ICH and vascular death were increased with inadequate blood pressure control during follow-up. Cerebral amyloid angiopathy was an independent predictor for recurrent ICH. In patients not resumed on antiplatelet medicine, there was a high rate of ischemic vascular event. Antiplatelet resumption should be considered, especially in survivors with low risk of recurrent ICH (hypertensive ICH and patients with adequate blood pressure control). Adequate BP control during follow-up is pivotal in order to reduce the risk of both recurrent ICH and vascular death.

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EFFECT OF SERUM 25-HYDROXYCHOLECALCIFEROL LEVEL ON THE SEVERITY AND PROGNOSIS IN ACUTE ISCHAEMIC STROKE PATIENTS

Dr Wong Wa Tai, Department of Medicine & Geriatrics, Princess Margaret Hospital (May 2016 Neurology Exit Assessment Exercise)

Background Vitamin D deficiency is a common condition in stroke patients. Serum 25-hydroxycholcalciferol [25(OH)D] level is the best indicator of vitamin D status. Low serum 25(OH)D levels have been reported to be possibly associated with poor neurological outcome in stroke patients.

Objective This study aimed to evaluate the effect of serum 25(OH)D level on the initial severity and neurological outcome in acute ischaemic stroke patients.

Methods From March 2015 to October 2015, consecutive first-ever acute ischaemic stroke patients admitted to the Princess Margaret Hospital, Hong Kong, were identified. Serum 25(OH)D levels were measured at baseline. Patients were dichotomized into vitamin D deficient group and non-deficient group using a cut off of 25(OH)D level <50 nmol/l for deficiency. Severe stroke was defined as National Institute of Health Stroke Scale score ≥6 upon admission (D0 NIHSS ≥6). Poor neurological outcome was defined as modified Rankin Scale ≥3 at day-90 after admission (D90 mRS ≥3). Multivariate analyses were performed using logistic regression.

Results A total of 192 patients were enrolled in this study, 120 patients (62.5%) were classified into vitamin D deficient group. The percentages of patients having severe stroke upon admission and poor neurological outcome at day-90 were significantly higher in the vitamin D deficient group than non-deficient group (38.3% vs 19.4%, p = 0.006; and 39.2% vs 19.4%, p = 0.006 respectively). In multivariate analyses, a low serum 25(OH)D level of < 50nmol/l was independently associated with both D0 NIHSS ≥6 [odds ratio (OR) 2.25 (95% confidence interval (CI) 1.09 – 4.66), p = 0.028] and D90 mRS ≥3 [OR 2.36 (95% CI 1.13 – 4.93), p = 0.022] after adjustment of covariates.

Conclusion Vitamin D deficiency is associated with higher stroke severity and worse neurological outcome in acute ischaemic stroke patients. Whether vitamin D supplementation can improve the outcome of stroke patients warrants further research.

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OCCURRENCE OF MULTIPLE SCLEROSIS AND ITS INVESTIGATIONS: A RETROSPECTIVE OBSERVATIONAL STUDY

Dr Young Pui Hong Terence, Integrated Medical Service, Ruttonjee Hospital (May 2016 Neurology Exit Assessment Exercise)

The prevalence of multiple sclerosis is rising and new therapies are becoming available, with a number of drugs undergoing clinical trials. We performed a retrospective observational study in the West Midlands region, United Kingdom, looking into the occurrence of multiple sclerosis, and the investigation modalities involved in making the diagnosis. We concluded that the incidence of multiple sclerosis was 4.5 in 100,000, comparable to the national average. Anti-nuclear antibody titre had a tendency to be positive in multiple sclerosis patients, but it was not significantly useful as a diagnostic tool. Further studies on true prevalence and use of disease modifying therapy would help in planning service provision for the future. Comparison is made with a regional population in Hong Kong, and the latest investigations and management are discussed.

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EFFECTIVENESS OF AN INPATIENT PULMONARY REHABILITATION PROGRAMME FOR ELDERLY COPD PATIENTS

Dr Lam Pui Shan, Department of Rehabilitation & Extended Care, Wong Tai Sin Hospital (June 2016 Rehabilitation Exit Assessment Exercise)

Background Pulmonary rehabilitation improves exercise capacity, symptoms, quality of life for chronic obstructive pulmonary disease (COPD) patients, and is therefore recommended in all stages of the COPD patients. This study aims to evaluate the effectiveness of inpatient pulmonary rehabilitation programme for elderly COPD patients, and to compare its effects on young-elderly (age 65-74 years) and old-elderly (age 75 years or older) COPD patients.

Methods A retrospective study of an inpatient pulmonary rehabilitation programme with 79 patients aged ≥65 with COPD was conducted. Outcome parameters were forced expiratory volume in 1 second (FEV1), serum albumin level, body mass index (BMI), the modified Medical Research Council dyspnoea scale (mMRC), the COPD Assessment Test (CAT), the Chinese (Hong Kong) version of St George's Respiratory Questionnaire (SGRQ), the Chinese (Hong Kong) version of the Medical Outcomes Study 36-item Short-form Health Survey (SF-36) (Version 2) and the 6 minute walk distance (6MWD).

Results Significant improvements were found for serum albumin level, mMRC scale, CAT score, SGRQ score, SF-36-PCS, SF-36-MCS, and 6MWD at discharge and up to 6 months after when compared with baseline. However, for SGRQ score and 6MWD at 6-months post-discharge, only the old-elderly group showed significant improvements. A number of baseline measures were significantly correlated with the improvements (Δ) during the rehabilitation programme.

Conclusion Elderly patients with COPD exhibit clinically meaningful improvements when undergoing pulmonary rehabilitation. Age should not be a limiting factor for pulmonary rehabilitation and old-elderly should not be excluded from pulmonary rehabilitation.

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A RETROSPECTIVE STUDY ON THE OUTCOMES OF POST STROKE PATIENTS WITH DYSPHAGIA DIAGNOSED BY FEES AND THE PREDICTORS OF PERSISTENT DYSPHAGIA

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Background and objectives Stroke is one of the most common causes of death in Hong Kong and stroke patients with dysphagia experience increased mortality and morbidity. Strategy to predict the outcome of stroke patients with dysphagia can help us formulate treatment plans, set up realistic goals, and better allocate public resources. Fiberoptic endoscopic evaluation of swallowing (FEES) is an increasingly popular technique that is used to assess dysphagia in order to promote safe and efficient swallowing. Local data about the outcome of stroke patients with dysphagia as diagnosed by FEES is scarce. The objectives of the study were to assess possible predictors for pneumonia and persistent dysphagia at six months post stroke, to evaluate the outcomes of stroke patients with different dysphagia severity as detected by FEES (included physical outcome, length of stay, discharge destination and survival rate), and to look for the safety of FEES examination.

Methods The clinical records of all post-acute stroke patients who were admitted to rehabilitation wards of Kowloon Hospital and had undergone FEES from 1 January 2010 to 31 December 2012 were analyzed retrospectively. Exclusion criteria were a history of a pre-existing dysphagia or having conditions other than stroke that might cause dysphagia. At the end, 137 subjects were recruited and their demographics, clinical characteristics, FEES findings, and clinical outcomes were reviewed and analyzed.

Results Using binary logistic regression analysis, it was found that higher grading of oropharyngeal secretion (OR = 1.6, p = 0.04) and present of aspiration (OR = 2.91, p < 0.01) in FEES were independent predictors of pneumonia incidence over six months post stroke. Among the initial tube feeding patients, 96 out of 117 (82%) were able to resume oral feeding with subsequent weaning off tube feeding over the three-year observation period. The median time to resume oral feeding was 37.5 days, and 79 patients (67.5%) were weaned off tube feeding before discharge. For those who were able to wean off tube feeding, 95% (*n*=91) patients weaned off by 192 days (i.e., 27 weeks). Female sex (OR=3.48, *p= 0.04*), delayed oral transit time (OR=3.02, *p = 0.04*), and delayed pharyngeal swallowing reflex (OR = 7.35, p = *0.01*) were all independent predictors for persistent tube feeding at six months post stroke. For physical outcome, the mean Barthel Index (BI) gain between admission and discharge in mild dysphagia patients was 23.2 ± 16.3 which was statistically better than moderate dysphagia (BI gain = 12.6; p = 0.04) and severe dysphagia patients (BI gain = 10.1; p < 0.01) with adjusted to age and baseline BI scores. We found that age (OR = 12.7, *p= 0.01*), baseline Barthel Index (OR = 9.57, *p= .02*), motor Functional Independent Measure (OR=20.2, *p < 0.01*), and dysphagia severity by FEES (OR 4.32, *p= 0.02*) were independent predictors of post stroke dependency (defined as modified Rankin Score 4-6) at six months post stroke. After FEES examination, there was one suspected case of aspiration pneumonia (0.7%) and three patients (2.2%) had self-limiting nasal-mucosal bleeding; however no procedure-associated mortality was noted.

Conclusion In the present study, we found that oropharyngeal secretion and present of aspiration were risk factors of pneumonia occurrence in post stroke patient. Delayed oral transit time and delayed pharyngeal swallowing reflex were independent endoscopic predictors of persistent tube feeding. Patients with more severe dysphagia were associated with poorer physical outcome. Mild dysphagic patients had better improvement in functional scores than the moderate and severe dysphagic patients. In addition to these variables (i.e., age, baseline BI and motor FIM), severity of dysphagia diagnosed by FEES was an independent predictor of dependency at six months post stroke. FEES examination is a very safe procedure that may provide valuable information on stroke management.

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VALIDATION OF CODEX INDEX IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN HONG KONG

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Background The CODEX (age adjusted Charlson index, obstruction, dyspnoea,

exacerbation) index has been developed recently to predict the 1 year mortality and readmission rate of chronic obstruction pulmonary disease (COPD) patients after an index hospitalization. The aim of this study was to validate this index in a group of local COPD patients.

Methods A prospective study of 281 COPD patients with recent hospitalization for COPD exacerbation (AECOPD) was performed. Baseline parameters including comorbidities(C), spirometric results (O), dyspnoea score (D) and frequency of exacerbations in the past one year (EX) were collected, and the CODEX scores were calculated. One year mortality and exacerbation rates between patients with CODEX score < 5 (group A) and ≥ 5 (group B) were compared. The optimal CODEX cutoff score was also determined. The predictive capacity of the CODEX index was compared with the updated ADO, BODE and DOSE indices.

Results Among 161 and 141 patients had AECOPD required systemic corticosteroid use and hospitalization respectively in one year, 33 patients died. Group B patients had significantly higher mortality (23 [18.3%] vs 10 [6.5%], p = 0.003) and exacerbation rate (systemic corticosteroid use: 94 [74.6%] vs 67 [43.2%], p < 0.001; hospitalization:91 [72.2%] vs 50 [32.3%], p < 0.001), shorter time to death (hazard ratio [HR] 3.1, 95% confidence interval [CI] 1.5 – 6.5, p = 0.003) and shorter time to exacerbation (systemic steroid use: HR 2.6, 95% CI 1.9 – 3.6, p = 0.002; hospitalization: HR 3.4, 95% CI 2.4 –4.9, p < 0.001). A score of 5 was determined as the best index cutoff value. The CODEX index was superior to other indices in prediction of 1 year exacerbation rate, but not 1 year mortality.

Conclusion The CODEX index is useful for prediction of the mortality and exacerbation rate over 1 year for patients with recent hospitalization due to AECOPD.

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CLINICAL PRESENTATION, MANAGEMENT AND OUTCOMES OF PATIENTS WITH LIFE-THREATENING HAEMOPTYSIS IN A REGIONAL GENERAL HOSPITAL

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Background Life-threatening haemoptysis in the absence of appropriate treatment carries high mortality and multi-disciplinary approach has been employed in handling cases with life-threatening haemoptysis. Pulmonary tuberculosis and bronchiectasis had been reported to be the most common underlying aetiologies in Hong Kong and bronchial artery embolisation (BAE) has been increasingly used as first-line treatment.

Objectives To study the aetiologies, management and outcomes of patients with life-threatening haemoptysis, and examine the effectiveness and safety of BAE in a local regional hospital.

Methods It is a retrospective review of the adult patients who presented with life-threatening haemoptysis and admitted to the Department of Medicine, Queen Elizabeth Hospital from 1/1/2010 to 31/12/2014. Patients with either principal or secondary diagnosis of haemoptysis were identified by Clinical Data Analysis and Reporting System and patients with procedural codes to manage conditions suggestive of life threatening haemoptysis were also studied. Clinical information from hospital records and Clinical Management System (CMS) were reviewed. Patients admitted due to haemoptysis leading to any one of the following features were defined as “life-threatening haemoptysis”: 1) haemoptysis of 200ml or more in 24 hours; 2) haemoptysis resulting in hypotension (BP<90/60mmHg or required inotropes); 3) blood transfusion; 4) tracheal intubation; 5) need of intensive care. Descriptive analysis was performed for the aetiologies, computed tomography angiogram (CTA) and BAE. Cox regression analysis was used to evaluate any possible factors associated with mortality and recurrence.

Results One hundred and sixty-two patients were admitted due to life-threatening haemoptysis during the study period, contributing to 19.4% of all haemoptysis cases. The most common aetiologies were bronchiectasis (27.2%), pneumonia (24.1%) and pulmonary tuberculosis (16.1%). Bronchoscopy was being performed in 47 (29%) cases; among those bleeding site could be lateralised in 23 cases (48.9%) while endobronchial lesions were identified in 6 cases (12.8%). CTA was performed in 89 patients (54.9%) and abnormalities were identified in 62 cases (69.7%) with a sensitivity of 87.9%. BAE was attempted in 70 cases (43.2%) and was able to achieve an immediate control in 63 cases (90% immediate control rate). The 6-month, 1-year and 2-year recurrence rate after BAE were 22.9%, 27.1% and 31.4% respectively and factors which were independently associated with recurrences were age <60, haemoptysis due to bronchiectasis, active intrapulmonary malignancy, abnormal non-bronchial systemic artery and presence of bronchopulmonary shunt.

Conclusion Bronchiectasis, pneumonia and TB were the most common aetiologies of life-threatening haemoptysis in Hong Kong. BAE was a safe and effective procedure in controlling haemoptysis though long term recurrences were still a concern. Patients of age<60, with underlying bronchiectasis, active intrapulmonary malignancy, presence of abnormal non-bronchial systemic artery and bronchopulmonary shunt were independently associated with recurrence of major haemoptysis after BAE. Presence of these risk factors may warrant more frequent and prolonged follow-up visits or definitive treatment for underlying conditions, where possible.

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