

Abstracts of Dissertations

June 2010 Exit Assessment Exercise

CLINICAL CHARACTERISTICS AND OUTCOMES OF CRITICALLY ILL PATIENTS WITH SEPSIS FROM THE MAINLAND REQUIRING INTENSIVE CARE ADMISSION IN A HONG KONG ICU

Dr Ho Chun Ming, Department of Medicine, North District Hospital (May 2010 Critical Care Medicine Exit Assessment)

Objectives To review the characteristics, outcomes, patterns of infection, and predictors of mortality in critically ill patients with sepsis from the Mainland China

Design Retrospective cohort study

Setting A regional hospital in Hong Kong

Patients Critically ill patients who lived in the Mainland and were admitted to the Intensive Care Unit (ICU) of North District Hospital (NDH) from September 2007 to August 2009

Intervention None

Measurements and Results Eighty six patients (median age, 68 years) were analyzed. It accounts for 7.4% of our annual ICU admission. The APACHE II and SOFA scores were 24 and 11 respectively. 27.9% of these patients died before ICU and 47.7% died during their hospital stay. The median length of ICU and hospital stay was 6 and 22 days respectively. The most common cause of sepsis was respiratory infection (n=58, 67.4%). Pathogenic organisms can be identified in most of these patients (n=65, 75.6%). The most common organism was Escherichia coli. Poor prognostic factors included smoking habit, mechanical ventilator or vasopressors use from the Mainland, respiratory infection, mechanical ventilator support in our ICU and higher APACHE II / SOFA scores.

Conclusions Sepsis is a common cause of intensive care admission among patients living in the Mainland with a significant mortality. The incidence of extended spectrum beta-lactamases (ESBL) producing enterobacteriaceae infection was high. Better understandings of their characteristics are important.

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FACTORS AFFECTING TREATMENT OUTCOME OF METHOTREXATE IN PATIENTS WITH MODERATE-TO-SEVERE PLAQUE PSORIASIS

Dr Loo King Fan Steven, Social Hygiene Service, Department of Health (June 2010 Dermatology & Venereology Exit Assessment Exercise)

Background Methotrexate (MTX) is a standard systemic treatment in moderate-to-severe psoriasis worldwide. Its use, however, is limited by the unpredictable variation of efficacy. Clinical factors such as demographics, disease characteristics, phenotypes and associated cardiovascular co-morbidities in relation to the treatment outcome of methotrexate are unknown.

Methods In this 20-week prospective observational study, 72 consecutive patients receiving methotrexate were recruited in Tuen Mun Social Hygiene Clinic between 1st October 2007 and 31st March 2009. Demographic data and cardiometabolic risk factors were compared between treatment responders (at least 75% improvement in psoriasis area and severity index [PASI 75]) and non-responders.

Results Mean age of the patients was 48.1±12.2 years old and 83.3% of them were male. Average age of disease onset was 35.6±14.2 years old, and 13 of them (18.1%) had their onset after 50 years of age. They had high prevalence of obesity [body mass index≥25kg/m²] (58.3%) and metabolic syndrome (48.6%). The mean baseline C-reactive protein (CRP) was in the range of high cardiovascular risk (3.1±1.8mg/L). Sixty one patients (61/72, 84.7%) completed the 20-week study and 32 of them (52.5%) achieved PASI 75 at week 20. Presence of metabolic syndrome (MES) (OR_{Multivariate}=4.9, 95%CI 1.3-18.4, p=0.02), CRP ≥3mg/L (OR_{Multivariate}=5.9, 95%CI 1.6-22.5, p=0.008) and age of disease onset ≤50 years old (OR_{Multivariate}=8.9, 95%CI 1.4-55.7, p=0.02) were independently associated with the non-responders.

Conclusion Methotrexate is an effective treatment in our local patients with psoriasis. Age of disease onset younger than 50 years old, presence of metabolic syndrome (MES) and baseline C-reactive protein (CRP) level greater than 3mg/L are independent predicting factors for the treatment outcome of methotrexate. Optimizing the components of MES and reduction of systemic chronic inflammation may be beneficial to the treatment of psoriasis, in addition to their cardio-protective effects. Our study was limited by small sample size and larger prospective study with longer follow period would be useful in further clarification of the issues.

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PREVALENCE OF SEXUALLY TRANSMITTED INFECTIONS AND ASSOCIATED SOCIO-DEMOGRAPHIC AND BEHAVIOURAL RISK FACTORS AMONG FEMALE SEX WORKERS ATTENDING SOCIAL HYGIENE CLINICS IN HONG KONG

Dr Wong Shiao Yi, Social Hygiene Service, Department of Health (June 2010 Dermatology & Venereology Exit Assessment Exercise)

Background Studies from different regions of the world have demonstrated variable socio-demographic and behavioural risk factors for sexually transmitted infections (STIs) among female sex workers (FSWs). Local data is however scarce.

Objectives The study aims to determine the prevalence of different STIs among the local population of FSWs attending our Social Hygiene Clinics (SHCs), and to identify socio-demographic and behavioural characteristics that may increase their risks for STIs. The study also aims to document cervical smear results, hepatitis B surface antigen status and STI related knowledge of the studied subjects.

Methods 201 FSWs attending Yaumatei Social Hygiene Clinic (YMT(F)) and Wanchai Social Hygiene Clinic (WC(F)) were recruited from March 2009 to July 2009. Subjects underwent sexually transmitted infections screening, their hepatitis B surface antigen status and latest cervical smear results were also recorded. A standardized questionnaire on socio-demographic, behavioural characteristics and STI related knowledge were administered by trained nursing staff.

Results The three most prevalent STIs identified among FSWs in SHCs in Hong Kong were non-specific genital infections(43.5%), Chlamydia trachomatis(5.5%) and syphilis(10%). Abnormal cervical smears were found among 20.4% of FSWs and 11% of the FSWs were HepatitisB surface antigen positive. Age, education level, ethnicity, and condom use were not found to be associated with risk for STIs among FSWs in our study. Knowledge of preventative measures for STIs were limited, and misconceptions about STIs were prevalent among FSWs.

Conclusions STIs remained to be common among FSWs attending SHCs in Hong Kong. Our study was unable to confirm risk factors established in overseas studies. Nonetheless, the study substantiated the need for continual efforts in STI screening, behavioural surveillance and educational counselling among FSWs.

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TESTS USED IN THE SUBTYPE CLASSIFICATION AND OUTCOME OF TREATMENT IN PRIMARY ALDOSTERONISM – LITERATURE REVIEW AND A LOCAL RETROSPECTIVE STUDY

Dr Au Yeung Yick Toa Benjamin, Department of Medicine, Queen Elizabeth Hospital (May 2010 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Background Clinical guidelines state that it is important to differentiate between the different subtypes of primary aldosteronism (PA), notably between unilateral adenoma (APA) and bilateral hyperplasia (BAH). Treatment recommendations for these two subtypes differ. Adrenal venous sampling (AVS) is considered the reference standard for this purpose, though imaging studies can also be helpful.

Objective The aim of this dissertation is to review the evidence base for the need to differentiate between APA and BAH, and the evidence base for the tests used for this purpose.

Methods Literature search as well as a retrospective analysis of the experience in our centre are performed.

Results The difference in prognostic implications between APA and BAH is uncertain. Medical therapy of APA appears to be less effective in terms of cardiovascular outcome than surgical therapy. Whether surgical therapy for BAH is a viable option awaits future exploration. For the time being, it is still worthwhile to differentiate between unilateral and bilateral disease in view of the difference in treatment recommendations.

For differentiation, imaging studies and posture stimulation test both have good positive predictive value for APA. AVS is helpful when these two tests are negative, or show discordant results. AVS can lead to false lateralization in 10% of cases. A cut-off lateralization ratio of > 3:1 should suffice for diagnosing APA. A contralateral ratio of <1 is also very useful. It is a difficult procedure, and failure to cannulate the adrenal veins, especially the right adrenal vein, can occur in 25 to 50%. However, suboptimal cannulation can also produce useful data, and blood samples should always be obtained from the nearest site.

Conclusion The need for differentiating APA and BAH should be further studied. Diagnosis of PA subtypes should depend on a combination of imaging and biochemical studies.

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HYPOTHERMIA IN ELDERLY PATIENTS: CHARACTERISTICS AND PROGNOSIS

Dr Lam Ching Yu, Department of Medicine, Queen Elizabeth Hospital (June 2010 Geriatric Medicine Exit Assessment Exercise)

Study objectives To assess the characteristics of patients admitted for hypothermia, and to identify the risk factors for in-patient mortality.

Methods All patients aged 60 or above admitted from of 1st January, 2005 to 31st December, 2008 were included. Records were retrieved and analysed retrospectively. Hypothermia was defined as either one measurement of core body temperature lower than 35°C by rectal thermometer, or the average of two tympanic body temperature readings, measured within 1 hour after the arrival at Accident and Emergency Department, lower than 34°C. Cases were excluded if the body temperature was not rechecked within the first hour of admission, and if the hypothermia was developed intra-operatively, post-operatively, or during hospitalization.

Results Eight-one patients were eligible to our study. Their mean (\pm standard deviation) age was 80 ± 9 years and 37 (46 percent [%]) of them were male. Multivariate analysis showed that bradycardia on admission (OR, 5.26; 95% CI, 1.31 to 21.10; $p = 0.02$), a higher serum urea level (29.9 ± 22.6 mmol/L in non-survivor group vs. 19.2 ± 11.9 mmol/L in survivor group; OR, 1.04; 95% CI, 1.00 to 1.08; $p = 0.05$), and hypoalbuminaemia (27 ± 5 g/L in non-survivor group vs. 35 ± 9 g/L in survivor group; OR, 0.79; 95% CI, 0.69 to 0.90; $p = 0.001$) were the independent predictors of mortality in elderly hypothermic patients.

Conclusion Hypothermia is a condition associated with high in-patient mortality. Bradycardia, hypoalbuminaemia and high urea levels were identified as the independent risk factors for mortality, while age, co-morbidities, functional status, social background, severity of hypothermia and different rewarming methods were not.

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EVALUATION OF REHABILITATION OUTCOMES IN ELDERLY PATIENTS WITH HIP FRACTURE IN A LOCAL REHABILITATION HOSPITAL

Dr Lam Pui Shan, Department of Rehabilitation & Extended Care, Wong Tai Sin Hospital (June 2010 Geriatric Medicine Exit Assessment Exercise)

Objectives This study aims to evaluate the rehabilitation outcomes in elderly patients with hip fractures and to determine the prognostic factors affecting the outcomes.

Design Retrospective study.

Methodology Patients aged 65 or above who were admitted to the TWGHs Wong Tai Sin Hospital musculoskeletal rehabilitation programme from 1st January 2006 to 30th June 2008 with a principal diagnosis of hip fracture were included. Demographic data, mobility status, functional levels, medical and surgical information were collected retrospectively from medical records. Outcome measures included mortality rate, ambulatory and functional levels. Mobility outcomes were assessed by the

Elderly Mobility Scale and the Modified Functional Ambulation Category. Functional outcome was assessed by the Modified Barthel Index. The risk factors associated with the adverse outcome were identified.

Results There were 147 subjects recruited in the study. The mean age was 81.54 +/- 7.34 (SD) and 72.8% were female. 57.8% developed peri-operative complications. The most common complications were acute retention of urine (23%), urinary tract infection (22.3%) and chest infection (20.3%). 1 year mortality rate was 10.8%. Male gender

(HR = 2.7; CI = 1.03-6.94) and age (HR = 1.07, CI = 1-1.15) were predictors of mortality. Patients with AMT score ≥ 7 were associated with higher gain in the Elderly Mobility Scale and the Modified Barthel Index. 15% of patients became institutionalized upon discharge. Being alone at daytime at home (OR = 4.58) and the use of walking aids before admission (OR = 6.30) were predictors for being institutionalized.

Conclusion Male gender, age, higher mental scores, availability of carer and premorbid ambulatory status were found to be predictors of ambulatory outcomes, mortality and institutionalization after hip fracture in elderly. The mortality rate was lower when compared with studies in other countries.

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RISK FACTORS FOR DELIRIUM IN ACUTE GERIATRIC INPATIENTS: A PROSPECTIVE STUDY

Dr Wong Yuet Lin Elaine, Department of Medicine & Geriatrics, United Christian Hospital (June 2010 Geriatric Medicine Exit Assessment Exercise)

Delirium is a commonly encountered problem in our daily geriatric practice. It is usually associated with prolonged hospital stay, poor function and cognitive status and mortality. Despite its commonness and poor outcome, it is frequently poorly understood and under-recognized. Identification of the predisposing and precipitating risk factors of delirium is the key for successful management of this geriatric syndrome. Numerous studies about the prevalence and risk factors for delirium have been done in the West but limited data is available in our locality.

A prospective study was performed in a regional hospital from 27 Oct 2009 to 7 November 2009. All consecutive admissions to acute geriatric ward were recruited. Recruited patients were screened by Confusion Assessment Method (CAM) within 36 hours to determine the occurrence of prevalent delirium. Risk factors were identified by review of medical records and interview with caregivers. A total of 161 patients acutely admitted to the geriatric ward were recruited. Prevalent delirium was found in 24% of patients. Multivariate logistic regression analysis was performed. Underlying cognitive impairment (OR 15.12, $p < 0.001$), electrolyte abnormalities (OR 8.83, $p = 0.003$) and infection (OR 7.69, $p = 0.006$) were found to be the independent risk factors for developing delirium.

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DIGOXIN TOXICITY AMONG ELDERLY PATIENTS IN HOSPITAL PRACTICE – A RETROSPECTIVE STUDY

Dr Yip Wai Man, Department of Medicine & Geriatrics, Princess Margaret Hospital (June 2010 Geriatric Medicine Exit Assessment Exercise)

Background The reported prevalence of digoxin toxicity is said to be declining in some overseas studies.^{1,2} However, there has been concern on the increased risk of exposure to digoxin toxicity among elderly patients. As there have been no local studies on digoxin toxicity, a retrospective review was conducted to clarify the present situation in a local hospital setting.

Objectives The main objectives are: (i) to estimate the prevalence of digoxin toxicity in the present clinical practice; (ii) to evaluate the clinical correlations of serum digoxin concentrations (SDCs) to digoxin toxicity and (iii) to evaluate the risk factors predisposing to digoxin toxicity.

Methods Retrospective evaluations through medical records were made on all in-patients aged over or equal to 60 years old admitted to all specialties of Princess Margaret Hospital (PMH) over two 3-month periods in 2008 and 2009 and in whom digoxin level was checked. Patients were grouped into definite, possible and not toxic, according to clinical presentations and course. Prevalence was calculated by the total number of patient episodes with definite clinical digoxin toxicity divided by the total number of patient episodes with SDCs checked within the study period. Demographical data included age, sex, place of accommodations, body weight, co-morbidities, drugs being taken, indications for digoxin, serum chemical values, clinical evidence of digoxin toxicity and pre-disposing risk factors were collected and analyzed.

Results A total 12013 patients aged over or equal to 60 years old were admitted for the study periods. The total patients' episodes taking digoxin was 883. There were 297 patients' episodes with SDCs checked. The prevalence of digoxin toxicity was 7.4% (22/297). The levels of SDCs were found significantly correlated with clinical toxicity. Risk factors of digoxin toxicity included: advanced age, those lived in institutions, low body weight, low serum albumin, poor renal function, hypokalaemia, loading dose of digoxin used, pneumonia, and thyroid diseases were found particularly significant.

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THE PROGNOSTIC SIGNIFICANCE OF TOTAL DOSE OF CISPLATIN ADMINISTERED DURING CONCURRENT CHEMORADIOTHERAPY IN PATIENTS WITH LOCOREGIONALLY ADVANCED NASOPHARYNGEAL CARCINOMA

Dr Loong Ho Fung Herbert, Department of Clinical Oncology, Prince of Wales Hospital (June 2010 Medical Oncology Exit Assessment Exercise)

Background Radical radiotherapy (RT) is the mainstay of treatment for nasopharyngeal carcinoma (NPC). However, in locoregionally advanced NPC, despite good local control after RT, distant recurrence remains the main cause of treatment failure. Concurrent chemoradiotherapy is superior to RT alone in the treatment of locoregionally advanced NPC in terms of survival. However, to date, there is no published data on the minimum dose of cisplatin that is required to achieve such a survival benefit.

Purpose

1. To evaluate the prognostic significance of the total dose of cisplatin administered during chemoradiotherapy on the survival of patients with locoregionally advanced NPC.
2. To evaluate any association between the total dose of cisplatin administered during

chemoradiotherapy and the rate of local and distant recurrence in patients with locoregionally advanced NPC.

Patients & Methods A single-centre retrospective analysis was carried out on 241 patients with American Joint Committee on Cancer (AJCC) (6th Edition 2002) Stage II to IVB NPC, who were treated with chemoradiotherapy at the Prince of Wales Hospital between May 1994 and August 2006. The cut-off date for data analysis was set at January 2010, and the median duration of follow-up was 56.5 months (range: 4.2 - 200.2 months). All patients received weekly intravenous cisplatin at 40mg/m²/week during a 6-7 week course of RT. Cisplatin was either delayed or omitted in patients who developed intolerable toxicities, but the dose of cisplatin remained unmodified. Patients were grouped according to the number of weekly cycles of cisplatin they had received during RT – less than 5 cycles, 5 or more cycles. Univariate analysis was performed using the Chi-square test to compare two groups in terms of survival outcomes including median overall survival (OS), progression-free survival (PFS) as well as local recurrence (LRR) and distant recurrence (DRR) rates. Survival and time to events were estimated using the Kaplan Meier method, and the curves were compared using the Log-rank test. Multivariate analysis was performed with covariates including overall stage, TNM stage, age and sex. A planned subgroup analysis based on overall, T and N-stages was performed.

Results Of the 241 patients included in this analysis, 77% were male (n=185) and 23% were female (n=56). The stage distribution at diagnosis was as follows: stage II (n=33), stage III (n=109), stage IV (n=99). The median number of cycles of cisplatin administered per patient was 5 cycles (range: 1 – 8 cycles). At a median follow-up 56.5 months, 38.6% (n=93) patients experienced disease relapse. There were 47 local recurrences and 65 distant recurrences. There was no statistically significant association between the number of cycles of cisplatin received per patient, and survival outcome (OS, PFS) and recurrence rates (DRR and LRR). In the sub-group analysis of patients with stage II and III NPC (n=142), both univariate and multivariate analysis showed that patients who received more than 5 cycles of concurrent cisplatin chemotherapy (i.e > 200mg/m²) had significantly improved OS than those who received 5 cycles or less (HR 0.46; 95% CI (0.24 – 0.89); p=0.02). Difference in PFS was significant in univariate but not in multivariate analysis. There was also a non-significant trend of longer time to distant recurrence in patients who received more than 5 cycles of chemotherapy (HR 0.55; 95% CI (0.28 – 1.11); p=0.098).

Conclusion The total dose of cisplatin received during concurrent chemoradiotherapy has prognostic significance in patients with Stage II and III NPC. Patients who received more than 5 cycles of weekly cisplatin during radical RT had significantly improved OS and also a trend towards longer time to development of distant recurrence. This finding has potential implication on clinical practice.

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A PROSPECTIVE STUDY ON THE SIGNIFICANCE OF QUALITY OF LIFE MEASUREMENT AND CLINICAL FACTORS IN PREDICTION OF SURVIVAL IN CHINESE PATIENTS WITH HEPATOCELLULAR CARCINOMA

Dr Li Leung, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (June 2010 Medical Oncology Exit Assessment Exercise)

Background Quality of life (QOL) assessment with EORTC QLQ-C30 questionnaire was reported to be prognostically significant in patients with hepatocellular carcinoma (HCC). The HCC-specific QOL EORTC QLQ-HCC18 may have a better reflection of QOL in HCC patients with chronic liver disease. The potential mechanisms of QOL being prognostic for survival were investigated. Various staging systems were developed in different populations, however, differences in etiological pattern and prognosis between Chinese and Caucasian HCC patients were noted. The objectives of this study were 1) to evaluate the prognostic significance of EORTC QLQ-HCC18 module, 2) to validate the prognostic value of EORTC QLQ-C30 module, 3) to assess correlation between QOL and the stage of HCC and severity of cirrhosis, and 4) to find the best HCC staging systems for Chinese HCC patients.

Methods Two hundred and three patients with newly diagnosed HCC were prospectively recruited. Treatment included surgery, loco-ablative therapies, transarterial therapies, chemotherapies, sorafenib and best supportive care as determined by clinicians. Patients' baseline QOL assessment, clinical factors, staging and treatment were analysed to identify independent factors for survival in Cox proportional hazards regression model. The correlations between QOL and stage of HCC and severity of cirrhosis were analysed by Wilcoxon rank-sum test.

Results Median overall survival of the 203 HCC patients (79% hepatitis B) was 8.1 months (95% CI 6.2-9.6 months). 1) In combined multivariate analysis, independent poor prognostic factors for survival among QLQ-HCC18 were worse scores in HCC18 fatigue domain (HR 1.146; $p=0.0042$) and nutrition domain (HR 1.137; $p=0.0244$). 2) of the QLQ-C30, no factor was identified as independent prognostic factor. 3) There were significant correlations between worse QOL scores in C30/HCC18 and advanced cirrhosis, as well as advanced stages in Chinese University Prognostic Index (CUPI), Okuda, the American Joint Committee on Cancer Tumor Node Metastasis (AJCC TNM), Cancer of the Liver Italian Program (CLIP). 4) In Chinese HCC patients, CUPI ($p=0.0037$) and Okuda (0.0019) were significantly superior among various staging systems.

Conclusions This study was the first to report the significant prognostic value of EORTC QLQ-HCC18 module in HCC patients. The combined multivariate analysis was unable to confirm previous report on EORTC QLQ-C30's prognostic significance. Worse QOL scores correlated significantly with advanced cirrhosis and advanced HCC stage. CUPI and Okuda had significantly better prognostic value in Chinese HCC patients.

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LONG TERM OUTCOME OF HBsAg+ RENAL TRANSPLANT RECIPIENTS WITH LAMIVUDINE RESISTANCE AND THE RESPONSE TO SALVAGE NUCLEOSIDE ANALOGUES

Dr Yap Yat Hin Desmond, Department of Medicine, Queen Mary Hospital (May 2010 Nephrology Exit Assessment Exercise)

Anti-viral treatment has improved the short-term outcome of kidney transplant recipients with chronic hepatitis B infection, but its long-term impact, especially in patients who have developed drug resistance, remained uncertain. We studied 63 HBsAg+ve patients who have undergone kidney transplantation since 1985, with 119.7±83.3 months of follow-up after transplantation. With lamivudine as initial treatment, 62% of patients developed drug resistance after 4 years. Lamivudine

resistance was associated with a higher incidence of chronic hepatitis, but exerted no significant impact on liver stiffness score or patient survival during follow-up. Salvage treatment with adefovir or entecavir was well tolerated, and resulted in a 3-log decrease in HBV DNA after 6 months and normalization of ALT in 50% of patients. HBsAg+ve patients who received kidney transplants prior to the availability of anti-viral treatment showed poor patient survival, with 20-year survival rate at 71%. The survival rate of HBsAg+ve patients transplanted in the recent era of anti-viral treatment was 81% at 10-year. Treatment of hepatitis B with nucleoside/nucleotide analogues resulted in significantly improved patient survival (83% vs 34% at 20-year, $p=0.006$). Although anti-viral treatment was associated with reduced mortality due to liver complications ($p=0.036$), liver-related deaths still accounted for 40% of mortalities in HBsAg+ve patients in the era of anti-viral therapies, and 22.2% of all deaths that occurred in patients who had received anti-viral treatment.

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THE STUDY OF THE PREVALENCE OF MTHFR C677T GENOTYPE VARIANT IN MIGRAINE AND THE EFFECTS OF HOMOCYSTEINE-LOWERING BY VITAMINS SUPPLEMENTATION ON THE DISEASE DISABILITY IN THE HONG KONG CHINESE PATIENTS

Dr Chan Chun Kong, Department of Medicine & Geriatrics, United Christian Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Migraine is a common and debilitating neurological problem worldwide. It was shown that migraine with aura is linked to MTHFR C677T polymorphism especially TT genotype. Carriers of this genotype showed reduced MTHFR enzymatic activity leading to hyperhomocysteinemia. The roles of MTHFR polymorphism and hyperhomocysteinemia in the pathogenesis of migraine remain controversial. Recent Caucasian studies showed encouraging result on improving migraine disability by vitamin supplementation.

Objectives We pilot to study the pattern of MTHFR C677T polymorphism and examine the homocysteine-lowering effect by vitamin supplementation on migraine disability, headache frequency and pain intensity in Chinese migraineurs.

Methods This is a single centered and prospective intervention study with one-way within subjects design. We prospectively examined and intervened 34 patients who were diagnosed of migraine according to the IHS classification. Baseline clinical assessment by history and questionnaires (MIDAS and HIT), biochemical analyses and genetic assays of MTHFR polymorphisms were performed at the first visit. 3-month trial of folic acid together with vitamin B6 and B12 supplementation was carried out. Serum homocysteine level, migraine disability and grading, headache frequency and pain intensity before and after treatment were compared.

Results 34 subjects were eligible for the study and 31 subjects completed the trial. The prevalence of MTHFR polymorphism in Hong Kong Chinese migraineurs (41% CC genotype, 47% CT genotype, 12% TT genotype) was different from that in our community dwelling population but was similar to the migraineurs in other Caucasian studies. TT genotype was more prevalent in migraine with aura than migraine without aura (17% vs 6%). Vitamins supplementation reduced the serum homocysteine level (median 10.1 to 7.9 $\mu\text{mol/L}$, $p<0.001$), MIDAS score (median 26 to 10, $p=0.001$) and HIT score (median 65 to 56, $p<0.001$). With reduction in the headache scores, there was a decrease in the headache disability grading in MIDAS and HIT. The treatment

effects were statistically significant in the CC genotype in terms of homocysteine lowering ($p=0.001$), MIDAS score reduction ($p=0.039$) and HIT score reduction ($p=0.001$) whereas the effects were not statistically significant in TT genotype in areas of homocysteine lowering ($p=0.068$), MIDAS score reduction ($p=0.068$) and HIT score reduction ($p=0.593$). Overall there was a trend of decline in headache frequency (mean frequency 11.5 to 10.0, $p=0.039$) and pain score (mean score 4.8 to 4.0, $p=0.061$). At the end of study, 45% subjects reported improvement in symptoms and preferred to continue the vitamin therapy.

Conclusions This is the first study providing data on the MTHFR C677T polymorphism in Chinese migraineurs. We provide evidence that vitamin may be another safe and effective alternative of prophylactic treatment. We found that TT genotype was more prevalent in migraine with aura, with higher grade of migraine severity and is less responsive to vitamin therapy. Aggressive treatment of this subgroup is recommended. Consideration of classifying and prognosticating migraine according to different MTHFR polymorphisms is warranted.

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THE ROLE OF ALA746THR VARIANT IN THE ATP 13A2 GENE AMONG CHINESE PARKINSON'S DISEASE PATIENTS

Dr Chan Yin Yan, Anne, Department of Medicine and Therapeutics, Prince of Wales Hospital (May 2010 Neurology Exit Assessment Exercise)

Background and Purpose To date, 15 loci have been identified to be associated with familial, young onset, and even sporadic late onset Parkinson's disease (PD). Recently, a study showed that a novel missense variant (Ala746Thr) in the ATP13A2 gene (PARK 9) maybe associated with early onset and / or familial PD among Chinese in Taiwan and Singapore.

In this study, we aimed to clarify the association between this particular missense variant (Ala746Thr) in ATP13A2 in both early onset PD (EOPD) and late onset PD (LOPD) among Chinese patients in Hong Kong.

Methods Genomic DNA was extracted from peripheral blood from PD patient with informed consent. Ala746Thr was genotyped by polymerase chain reaction (PCR) amplification. Primers CTCCAGGGACACTGTGGAAG and ATTGTACCTGTCGCCATGACGG were used.

We investigated its frequency among 69 EOPD (≤ 50 years old) and 192 LOPD in Hong Kong Chinese patients. We compared its frequency with that of 180 Chinese healthy controls.

Results The mean age of disease onset for EOPD was 43.2 years and the mean age of disease onset for LOPD was 61.6 years. We identified heterozygous mutation among 1 patient in the EOPD group (1.4%; odds ratio [OR] 2.63, 95%CI 0.16-42.68, $p=0.50$), 1 patient in the LOPD group (0.5%; OR 0.94, 95% CI 0.06-15.10, $p=0.96$) and also 1 patient among the healthy controls (0.6%).

Conclusions Ala746Thr is an uncommon polymorphism among Hong Kong Chinese PD patients and is unlikely to be associated with PD among EOPD and LOPD in our region.

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THE STUDY OF PREVALENCE OF NMO-IGG IN PATIENTS SUFFERING FROM RECURRENT OPTIC NEURITIS, TRANSVERSE MYELITIS AND OPTIC NEURITIS AND THEIR CHARACTERISTICS

Dr Lau Wing Yun, Department of Medicine & Geriatrics, Kwong Wah Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Neuromyelitis optica (Devic's disease) is an idiopathic, demyelinating disease of the central nervous system. It was previously regarded as a variant of multiple sclerosis (MS); however recent studies showed it is different from MS clinically, radiologically and pathologically. Patients with Asian ancestry are more predominantly affected. However there are only few studies regarding neuromyelitis optica (NMO) conducted in Hong Kong to characterize this particular population. The distinction between NMO and MS is crucial since treatment modality is different.

Methods This is a retrospective study of 14 patients suffered from optic neuritis and transverse myelitis in different local hospitals and with their NMO-IgG titer checked. We identified a total of 11 NMO patients and their data are used to compare with the MS groups. Another 4 patients with recurrent optic neuritis were identified and with NMO-IgG tested. Parameters of different patient groups are analyzed.

Results There are 8 patients and 6 patients with seropositive and seronegative result for NMO-IgG respectively. The seropositive group tends to have longer segment of cord involvement ($p=0.024$) and poorer functional outcome when compared to seronegative group. For the comparison between NMO and MS groups, the NMO group was noted to have more patients with long segment of cord involvement, more patients with MRI brain not satisfying MS Barkhof criteria and also poorer functional outcome. For the recurrent optic neuritis group, since the number of patients is too small and no conclusion can be drawn.

Conclusion NMO-IgG seropositive rate was up to more than 70% in NMO patients but none in the non-NMO group. Thus NMO-IgG is a useful marker for NMO. Long segment of spinal cord involvement is a very distinguishing feature of NMO when compared with MS patients. Results showed statistically significant differences between NMO and MS in many aspects and so NMO should be regarded as a separate disease entity

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GOOD COLLATERAL CIRCULATION PREDICTS BETTER OUTCOME IN PATIENTS WITH INTRACRANIAL LARGE ARTERY OCCLUSIVE DISEASE

Dr Lau Yuk Lun Alexander, Department of Medicine and Therapeutics, Prince of Wales Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Collateral circulation via circle of Willis (COW) and leptomeningeal anastomosis stabilizes cerebral perfusion. Its role in the prevalent intracranial large artery occlusive disease (ILAD) among Chinese has not been explored. This study aimed to assess stroke outcomes in these patients by examining the antegrade and collateral circulation status, and the stroke topography to elucidate its pathogenesis.

Methods This retrospective study recruited ischemic stroke patients who underwent MRI *and* digital subtraction angiography (DSA). Antegrade flow in DSA was

classified by the Thrombolysis in Cerebral Infarction (TICI) grading, and collateral flow by the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading. COW was assessed by MRA. Composite *circulation scores* were derived to incorporate antegrade, collateral, and COW status. Outcome measures included the National Institute of Health Stroke Scale (NIHSS) for index stroke severity, functional independence at 3-months, and recurrent stroke or transient ischemic attack (TIA) in 12-months. Stroke topography was classified into perforator, pial, borderzone, and territorial infarcts in the corresponding vascular territories using published templates.

Results In 79 patients analyzed, the majority (n=56, 71%) had MCA stenosis and mild stroke (median NIHSS 3). 44 (58%) patients had good antegrade flow (TICI grade 2b and 3), 66 (89%) patients had good collateral flow (ASITN/SIR grade 2-4), and 55 (70%) patients had complete COW; corresponding to 65 (88%) patients with good *circulation score*. Patients with good circulation score had less severe index stroke (NIHSS 3±2 versus 3±4, p=0.038), better stroke recovery with functional independence at 3-months (94% versus 6%, p=0.035), and less recurrent stroke or TIA in 12-months (91% versus 9%, p=0.073). Good *circulation score* (OR 13.9, 95% CI 1.37-142.4, p=0.026), and complete COW (OR 15.3, CI 2.50-93.83, p=0.003) predicted functional independence. In the stroke topography analysis, borderzone (n=41, 52%) and pial (n=28, 35%) infarcts were the commonest and corresponded to more severe stroke (NIHSS 3±3 versus 3±2, p=0.029, and 3.5±2 versus 3±2, p=0.028, respectively). High-grade (>70%) stenosis predicted multiple infarcts (OR 6.4, CI 1.20-34.30, p=0.03), and diabetes predicted pial infarcts (OR 4.9, CI 1.54-15.75, p=0.007).

Conclusion A composite circulation score incorporating the leptomeningeal collateral and COW status was found to have prognostic value in patients with symptomatic ILAD. Better prognosis can be anticipated in patients with good collateral compensation despite compromised antegrade flow. Pial, borderzone, and multiple infarcts are unfavorable stroke topography, suggesting that impaired washout of thromboemboli in hypoperfused region is important in the stroke pathogenesis.

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FACTORS AFFECTING STRATEGY FOR STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION IN A REGIONAL HOSPITAL OF HONG KONG

Dr. Lo Chi Hung, Department of Medicine & Geriatrics, United Christian Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Anticoagulation therapy is a well-proven strategy for stroke prevention in patients with atrial fibrillation (AF). However, underutilization is not uncommon, leaving avoidable stroke to occur.

Objective We aim at investigating the utilization rate of anticoagulation therapy for stroke prevention in patients with known history of AF, to identify the factors that have been responsible for the under-utilization of anticoagulation in patients with ischemic stroke with underlying AF, and to compare the outcome among patients with anticoagulation prophylaxis before stroke onset to those without.

Methods A single-centered 1-year prospective cohort study was conducted. Patients with known history of AF admitted for acute stroke were recruited for

analysis. The risk profile and the reason(s) for not taking anticoagulation prior to stroke onset were analyzed retrospectively. Comparison of demographic data between warfarin and non-warfarin users, and that between patient receiving and not receiving advice for anticoagulation was made using different parametric and non-parametric statistical tests.

Results 48 patients were recruited prospectively during the 1 year study period for final analysis. Ischemic stroke occurred in 46 patients (95.9%). 44 patients (91.7%) had CHADS2 score ≥ 2 . Only 6 of these patients (12.5%) were taking warfarin prior to index stroke episode. 13 patients (27.1%) suffered from paroxysmal AF with CHADS2 score ≥ 2 , none of them received anticoagulation therapy for stroke prevention before. 22 patients (50%) having moderate to high risk of stroke had never received any advice / discussion on the use of anticoagulant for stroke prevention from physicians prior to the index stroke episode. 7 out of 42 patients who have not received anticoagulation therapy died within 3 months of stroke, whereas all 6 patients taking warfarin survived. Female patients were more likely to receive anticoagulation therapy than male in this cohort. Patients with diabetes were less likely to receive advice / discussion on the use of anti-coagulation for stroke prevention.

Conclusion Underuse of anticoagulation therapy for stroke prevention in AF patients having moderate to high risk stroke risk is not uncommon, which might be contributed by physicians' underawareness of stroke prevention using anticoagulation therapy. The risk of stroke in patients with paroxysmal AF is probably underestimated. Further study is needed to clarify the effect of gender on the choice of treatment strategy for stroke prevention in patients with AF.

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INFECTIVE MENINGITIS AND ENCEPHALITIS – CASE REVIEW IN A REGIONAL HOSPITAL

Dr Ng Lai Han Betty, Integrated Medical Service, Ruttonjee Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Epidemiological pattern of infective meningitis and encephalitis has been well described in the literature and yet little is known about the relative frequency of different etiological agents in our community. Recent local studies showed that *Mycobacterium tuberculosis*¹⁰ and herpes simplex virus¹⁷⁶ was the most common causative agent in bacterial meningitis and viral encephalitis respectively. The epidemiological pattern in Hong Kong may be changing, given the rising number of immigrants, HIV cases and more widespread use of immunomodulatory agents. A retrospective study of the condition was conducted.

Method All patients aged 16 or above diagnosed to have infective meningitis and encephalitis in Ruttonjee and Tang Shiu Kin Hospitals (RTSKH) from September 1, 1998 to August 31, 2008 were identified. Demographic, clinical, laboratory and radiological data were recorded.

Results Data of 82 patients were analyzed. Presentation with the classical clinical triad of fever, nuchal rigidity and altered sensorium was uncommon. Delayed administration of antimicrobials was seen in 37.5 %, 34.6 %, 20%, 0% and 50 % of cases of acute bacterial meningitis, tuberculous meningitis, viral encephalitis, viral meningitis and fungal meningitis respectively. Failure to recognize neuroinfections,

difficulties in differentiation among various types of neuroinfections, advanced age, presence of comorbidities and complications were common factors contributing to morbidity and mortality. Corticosteroids were infrequently prescribed: Among the 71 patients whose outcome was known at 6 months, 54 were independent in self-care and 9 patients died.

Conclusion There was potential room for improvement in diagnosis for meningitis and encephalitis, particularly in the elderly. A high index of clinical suspicion, earlier lumbar puncture and more frequent use of corticosteroids for acute bacterial and tuberculous meningitis may help improve outcome.

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MAGNITUDE AND PROFILE OF POST STROKE CARDIOVASCULAR AUTONOMIC DYSFUNCTION: IT'S CORRELATION WITH STROKE LOCATION AND SEVERITY

Dr Tse Man Yu Mona, Department of Medicine, Queen Mary Hospital (May 2010 Neurology Exit Assessment Exercise)

Background and Purpose Cardiovascular autonomic dysfunction complicating acute stroke is well documented but with widely variable prevalence. Data on relevance of stroke location and severity on various adverse cardiac events are either conflicting or lacking especially regarding cardiac enzymes assay and vasomotor functions. We aimed to determine the prevalence of cardiovascular autonomic dysfunctions in acute stroke patients, to clarify their association with stroke location and severity, and to assess their predictive value.

Methods From June to Dec 2009, 50 first ever acute stroke patients admitted to Queen Mary Hospital with no history of ischaemic heart disease were recruited for assessment of cardiovascular dysfunctions which included cardiac enzymes assay, 24 hour holter monitoring, autonomic function test and sympathetic skin response (SSR).

Results Abnormal troponin I or CKMB level were seen in 10% and 22% of our patients, new onset paroxysmal atrial fibrillation (PAF) or atrial fibrillation (AF) was seen in 16% of the patients. Orthostatic hypotension (OH), abnormal sympathetic pressor response, impaired heart rate variability (HRV) and impaired SSR were seen in 30%, 11%, 32% and 62% of the patients respectively. The overall mortality rate was 8%. Insular cortex involvement particularly on the left was associated with raised troponin I level ($p=0.001$), various arrhythmias ($p=0.000$ to 0.029), impaired HRV ($p=0.032$ to 0.042) and all cause mortality ($p=0.029$), such association could not be completely explained by stroke severity. Vasomotor dysfunctions were associated with stroke severity ($p=0.000$ to 0.015) and Barthel Index (BI; $p=0.000$ to 0.021) but not with stroke location or laterality. Insular cortex involvement and non-sustained ventricular tachycardia (NSVT) were the predictors for mortality ($R^2=0.582$, $p=0.027$). Impaired SSR and presence of OH were weak predictors for dependence state and discharge destination ($R^2=0.214$ and 0.329 respectively) when functional scores were excluded from analysis.

Conclusion Post stroke cardiovascular autonomic dysfunctions are common in acute and subacute phase of stroke particularly with increased severity and/or insular cortex involvement. Vasomotor dysfunctions are particularly prevalent in patients with severe stroke and profound functional impairment. Our findings have important implications in acute and rehabilitation care of these groups of stroke patients.

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THE PREVALENCE OF MAJOR VASCULAR EVENTS FOLLOWING PRIMARY INTRACEREBRAL HAEMORRHAGE

Dr Yuen Mang Ho, Department of Medicine & Geriatrics, Tuen Mun Hospital (May 2010 Neurology Exit Assessment Exercise)

Background Survivors of primary intracerebral haemorrhage (ICH) are at risk of both recurrent ICH and future ischaemic events, such as ischaemic stroke and myocardial infarction (MI). The nature and outcomes of the next vascular events in these patients are unclear.

Objective To determine which vascular event being more prevalent after primary ICH and the outcomes and predictors for the corresponding events.

Methods Primary ICH is defined as intracerebral parenchymal haemorrhage without known underlying vascular anomalies, trauma or brain tumour. We evaluated 200 ICH survivors with first-ever primary ICH admitted to Tuen Mun Hospital from 2004 to 2005. Vascular events during the 5-year follow-up were analysed using Kaplan- Meier method and Cox regression for predictors of ICH recurrence, MI, ischaemic stroke and all vascular events.

Results Forty five vascular events were identified in the 200 patients during 5-year follow-up. The risks of ischaemic stroke, recurrent ICH and MI were 13%, 6.5% and 3% respectively. The composite ischaemic endpoint (ischaemic stroke and MI) was much more common than recurrent ICH at a ratio of 7:3. Few ICH survivors (15.4%) suffered from two or more ischaemic strokes. Patients with recurrent ICH had more death and poor functional outcome of modified Rankins Scale >3 when compared with those with composite ischaemic endpoint (77% vs. 56%). Age, prior use of aspirin before ICH and prior use of statin before ICH were identified as independent risk factors for subsequent vascular events. Aspirin use after ICH was not significantly associated with recurrent ICH during the study period ($p=0.936$).

Conclusion ICH survivors were at much higher risk of ischaemic events than recurrent ICH as their next major vascular events. Recurrent ICH caused more death or poor functional outcome. These provide clinicians more information to understand the prognoses of ICH survivors and to decide on treatments for secondary prevention.

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