Abstracts of Dissertations
June 2006 Exit Assessment Exercise

REVIEW OF ACUTE CHOLANGITIS IN CARITAS MEDICAL CENTRE 2002-2004

Dr. Hung Cheng Fang, Department of Medicine & Geriatrics, Caritas Medical Centre (June 2006 Advanced Internal Medicine Exit Assessment Exercise)

Background Acute cholangitis varies in severity. The mild form usually responded with antibiotics with low mortality whereas the severe form is a life threatening condition with high mortality requiring emergency biliary decompression. Endoscopic drainage has improved the outcome in recent decades even in the elderly. Most of the studies were conducted more than 10 years ago and came from tertiary centers.

Objectives To review the situation in a local hospital with an aging population and identify factors associated with the need for emergency ERCP and mortality.

Methods Two hundred and twenty-five patients being admitted for the first episode of acute cholangitis in a community hospital during the period of 2002 to 2004 were reviewed retrospectively. The clinical features, laboratory results, imaging findings, intervention procedures and outcomes were analyzed.

Results The mean age ± SD was 78 ± 11 years. Forty-nine percent of patients were ≧ 80 years of age. Patients presented with abdominal pain in 55.1%, fever and chill in 49.3%, jaundice in 22.2%, confusion in 7.6% and shock in 9.3%. Thirty-one percent of patients had septicaemia. E. coli and Klebsiella were the two most commonly identified organisms from the blood and bile cultures. 195 (87.4%) patients required ERCP of which 35.4% were emergency. 13.1% patients required intensive care or high dependency unit care. Mean duration of intravenous antimicrobial therapy was 8 ± 4 days. Median length of hospitalization was 8 (7-13) days. The overall mortality rate was 4%; 2.6%, 12.5% and 14.3% in patients treated with ERCP, antibiotic alone and operation respectively. Elderly of age ≧ 80 years had a similar outcomes comparing with the younger patients (mortality rates 4.5 vs. 3.5% p=0.683 and post-ERCP complication rates of 6.4% and 13.9% (p=00062), but a longer duration of hospitalization (mean ± SD, 10 ± 8 days vs. 8 ± 6 days p=0.014). Systolic blood pressure < 90 mmHg predicted the need for emergency ERCP whereas prothrombin time >14s, white cell count (x10^9/L) >15 and urea (mmol/L) >10.7 predicted mortality.

Conclusions The overall mortality rate of 4% is comparable with the published results. Advanced age is not a poor prognostic factor in our review. Elderly with acute cholangitis deserves more aggressive treatment.

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CAN HEPATOCELLULAR CARCINOMA SCREENING IMPROVE PATIENT SURVIVAL?

Dr Siu Fung Yee, Department of Medicine & Geriatrics, Caritas Medical Centre (June 2006 Advanced Internal Medicine Exit Assessment Exercise)

Background Heptocellular Carcinoma (HCC) is a major health problem in Hong Kong. Individuals with chronic hepatitis B and other chronic liver diseases are at risk of developing hepatocellular carcinoma. Screening of HCC in high-risk patients by serum alpha fetal protein (AFP) and ultrasonography (USG) of liver may improve survival outcome.

Objectives To evaluate for any survival benefit in HCC patients diagnosed by a screening program with regular 4 to 6 monthly AFP and USG liver in high-risk patients.

Methods This is a retrospective study done in a district hospital, Caritas Medical Centre. A total of 156 HCC patients diagnosed between 1995 and 2000 were reviewed, and were followed up until 31st December 2005. Those who defaulted follow up with uncertain survival status (n=13) were excluded. They were categorized into 3 groups: group 1 had HCC diagnosed by *screening* (n=35), group 2 presented with *symptomatic* HCC (n=67) and group 3 with *incidental* finding of HCC (n=41).The screening candidates included chronic hepatitis B virus (HBV) infected men aged 45 or above, HBV carriers with family history of HCC in first degree relatives and liver cirrhosis patients.

Results In this retrospective study, 143 patients were recruited, with male predominance (74.1 %) and mean age of 68.8 +/- 10.6 years old. We found that when comparing the symptomatic HCC patients with those diagnosed by screening, the later had smaller tumor size, lower AFP levels, less portal vein infiltration and metastases. Moreover, more patients in the screening group proceeded to treatment for the HCC including surgery, Transcatheter Arterial Chemoembolisation (TACE) and Percutaneous Ethanol Injection (PEI). The 5-year survival rate is best in the *screening group* (28.6%), followed by in those whom HCC was diagnosed incidentally (9.8 %) and worse in the *symptomatic group* (3%). The overall survival till 31st December 2005 was 25.8 months (IQR 9.7-68.8) in the *screening group*, compared with 2.75 months (IQR 1-9.5) in the *symptomatic group*, and 18 months (IQR 7.38-34.6) in *incidental finding group*, with $p<0.001$.

Conclusions Surveillance of HCC by regular 4-6 monthly USG and AFP in high risk patients is effective in identifying potentially treatable and smaller tumors, and demonstrated survival benefit.

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HAILEY-HAILEY DISEASE (FAMILIAL BENIGN CHRONIC PEMPHIGUS)IN HONG KONG CHINESE - A REVIEW OF CASES IN THE SOCIAL HYGIENE SERVICE WITH A STUDY ON MUTATION ANALYSIS AND THE QUALITY OF LIFE

Dr. Cheng Tin Sik, Social Hygiene Service, Department of Health (June 2006 Dermatology and Venereology Exit Assessment Exercise)

Hailey-Hailey disease is a rare genodermatosis affecting mainly the flexures. As local data was lacking, this study aimed to review the clinical data, perform mutation analysis and study the quality of life of Chinese patients with HHD in Hong Kong. Seventeen patients from thirteen families were recruited into this study. Fifteen patients (88%) had a family history. The patients were usually symptom free until the fourth decade. The mean age of onset was 36.59+/-12.9 years and the disease

usually involved the groin and neck at onset. However, the diagnosis was usually not established early. The diagnosis was not made until 11.8+/- 10.8 years after onset of disease. In many patients, the lesions were symptomatic. Itching was the major symptom in fifteen patients (88%). Limitation of physical activities was noted in 13 patients (76%). The sites of predilection were found to be axilla, neck, groin, perineum, natal cleft, elbow and knee flexures. Most patients noted aggravation of the disease by sweating (94%), heat (88%) and friction (88%). The disease usually ran a wax and wane course. Seasonal variation was the rule with more than half of the patients (59%) noted exacerbation in summers. Eight patients (47%) had one to three attacks a year. About 30% of the patients experienced skin infection. Most of our patients were given topical steroids in combination with topical antifungal and/or antibacterial medications. Additional systemic treatment was needed in three patients to control the disease. Nearly two-thirds of the patients (64%) found the medications to be helpful, though the disease would not go into remission in most of the patients. The disease usually became better after a period of time and three-quarters of the patients noted that there was improvement as time went by. The histopathological findings in most of the patients showed typical features of the HHD, namely intraepidermal acantholysis with suprabasilar cleavage plane and dilapidated brick wall appearance. Mutation analysis identified mutations in *ATP2C1* gene in many of the patients. Three known mutations were found and seven novel mutations were discovered. No 'hot-spot' mutation was found. Allelic heterogeneity was demonstrated. No relationship existed for the genotypic-phenotypic correlation. This study contributed to the further understanding and unraveling of the molecular basis of the disease. As regards the quality of life, the impact of the disease on this aspect was relatively benign though the patients were symptomatic at times.

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A STUDY OF THE PREVALENCE OF ARTERIAL STIFFNESS IN CHINESE TYPE 2 DIABETIC SUBJECTS

Dr. Cheung Wai Shing, Department of Medicine & Geriatrics, Our Lady of Maryknoll Hospital (May 2006 Endocrinology, Diabetes and Metabolism Exit Assessment Exercise)

Objective To assess the prevalence of increased arterial stiffness in Chinese type 2 diabetic patients with the measurement of brachial-ankle PWV (baPWV), and correlate baPWV with various cardiovascular risk factors.
Design: This cross-sectional study was carried out from 1 April 2005 to 31 Dec 2005 to investigate these relationships.

Methods 200 Chinese type 2 diabetic patients were recruited. The prevalence of increased arterial stiffness was 92 % as reflected by an increase in baPWV. baPWV correlated positively with age ($r= 0.415$, $p<0.01$), smoking status ($r= 0.141$, $p=0.046$), waist circumference ($r= 0.15$, $p = 0.03$), waist-to hip ratio ($r= 0.254$, $p<0.001$), duration of DM ($r=0.224$, $p<0.001$) systolic ($r=0.507$, $P< 0.001$) and diastolic blood pressure ($r =0.245$, $p<0.001$), pulse pressure ($r= 0.45$, $p< 0.001$), triglyceride level ($r =0.159$, $p=0.025$), the presence of metabolic syndrome ($r=0.152$, $p=0.032$) and the severity of erectile dysfunction among male patients ($r=0.246$, $p=0.037$). It also correlated negatively with HDL-c level ($r=-0.252$, $p<0.001$) and the use of antihypertensives ($r=-0.94$, $p<0.001$). In multiple regression analysis, only systolic blood pressure (standardized coefficient $=0.413$, $p<0.001$) and age (standardized coefficient $B=0.257$, $p<0.001$) were the independent predictors for baPWV, with a R

square of 0.366.

Conclusion The prevalence of abnormal baPWV was high in this cohort, and was not reflected entirely by the conventional cardiovascular risk factors and the level of macrovascular disease in these subjects. Measurement of baPWV can serve as an additional screening and monitoring tool for atherosclerosis.

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CTLA-4 GENE A-G POLYMORPHISM IN GRAVES' DISEASE

Dr. Hui Pui Sze Grace, Department of Medicine and Geriatrics, United Christian Hospital (May 2006 Endocrinology, Metabolism and Diabetes Exit Assessment Exercise)

Background Graves' disease is a common autoimmue disease. Studies suggested evidence of genetic susceptibility. Recently, cytotoxic T lymphocyte antigen 4 (CTLA-4) located on chromosome 2q33 has been shown to be associated with T cell regulation. Several recent reports also reviewed the association of CTLA-4 exon 1 polymorphism (49 A/G) with Graves' disease in different ethnic groups. The CTLA-4 exon 1 polymorphism (49 A/G) is also found associated with disease severity, risk of relapse, occurrence of ophthalmopathy, and association with other autoimmue disorders (especially Type 1 Diabetes Mellitus).

Aim The aim of the study was to see if CTLA-4 exon 1 polymorphism (49 A/G) is associated with Graves' disease in Hong Kong Chinese adult patient.

Patient and Methods Two hundred and sixteen patients (154 females and 58 males) with Graves' disease were recruited in the out-patient bases, comparing with 226 racially matched control subjects with no history of thyroid disease or any other autoimmue disease. Genomic DNA was extracted from the blood samples. The polymorphism at position 49 A/G was analyzed by polymerase chain reaction, restriction fragment length polymorphism and DNA sequencing.

Results There was no difference between the genotype distribution and the allele frequency when comparing the disease group with the control group. Though there was slight increase in frequency of G allele in male patient when compared with the control, it was not statistically significant. The clinical characteristics of the GD patient with genotype A/A, A/G and G/G were also of no difference.

Conclusion Graves' disease is a condition with both genetic and environmental contribution. CTLA-4 A/G polymorphism in the exon 1 position 49 has failed to show an association with Graves' disease in this study. Further study is suggested to delineate the association of CTLA-4 gene polymorphism and other non-genetic cause with Graves' disease in this locality.

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MANAGEMENT OF CONN'S SYNDROME

Dr Lau Wing Yan, Department of Medicine and Therapeutics, Prince of Wales Hospital (May 2006 Endocrinology, Diabetes and Metabolism Exit Assessment Exercise)

Primary hyperaldosteronism is increasingly recognized as an important cause of

secondary hypertension and cardiovascular morbidity. The treatment of primary hyperaldosteronism can reduce morbidity and mortality associated with hypertension, hypokalaemia and cardiovascular damage. Twenty-eight patients receiving unilateral laparoscopic adrenalectomy for primary hyperaldosteronism from 2000 to 2003 were evaluated for the factors associated with resolution of hypertension. All patients were found to have hypokalaemia at the time of diagnosis. The mean age of the patients was 45.7 years (± 8.1 years). The diagnosis of aldosterone-producing adenoma was made in twenty patients (71%) using the combination of postural test and CT scanning. Percutaneous venous sampling of the adrenal vein was performed in six patients (21%). There was no operative mortality. Sixteen patients (57%) had resolution of hypertension while twelve patients (43%) remained hypertensive. Hypokalaemia was resolved in twenty-seven patients (96%). Resolution of hypertension was independently associated with younger age at the time of diagnosis (p = 0.01), hypertension less than 5 years (p = 0.04) and positive response to spironolactone before operation (p = 0.04).

Apart from laparoscopic adrenalectomy, other minimally invasive treatments have been described for the treatment of Conn's adenoma. CT guided radiofrequency ablation has been used to treat primary and metastatic adrenal cortical carcinoma. Radiofrequency ablation (RFA) of Conn's adenoma was performed in a separate study to evaluate the effectiveness and follow-up results in terms of resolution of hypertension and hyperaldosteronism. Among eleven patients who underwent radiofrequency ablation, the plasma aldosterone levels fell to within normal range in ten patients (91%). Normalization of blood pressure was seen in nine patients (81%). The mean follow-up period was 10 months (range 4-16 months). One patient suffered from hypertensive crisis during the procedure and one patient developed peri-nephric haematoma after RFA. Overall, RFA is a safe and effective treatment for Conn's adenoma although long term outcome remains unanswered.

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PRIMARY HYPERPARATHYROIDISM: EFFECT OF PARATHYROIDECTOMY ON REGIONAL BONE MINERAL DENSITY IN CHINESE PATIENTS

Dr Liu Chi Ki, Department of Medicine, Tseung Kwan O Hospital (May 2006 Endocrinology, Diabetes & Metabolism Exit Assessment Exercise)

Objective Changes in bone mineral density (BMD) were observed as early as six months after parathyroidectomy (PTX) in Caucasian patients with primary hyperparathyroidism (PHPT). However, there has been no data available on BMD changes in PHPT patients with PTX in Chinese patients. The present study was designed to investigate short-term BMD changes at both trabecular and cortical sites in Chinese PHPT patients with PTX.

Design Retrospective study of clinical records

Setting University teaching hospital, Hong Kong

Subjects 44 patients who are diagnosed to have PHPT and who have undergone PTX at Queen Mary Hospital during the period of July 1995 to April 2005.

Main outcome measures Demographic data of patients; measurement of BMD pre- and 1-year post PTX at the forearm (proximal, middle and distal), at the hip (total,

femoral neck, intertrochanteric and trochanteric regions), and at the lumbar spine (L1-4) by dual-energy X-ray absorptiometry systems; measurement of serum levels of calcium, phosphate, alkaline phosphatase and parathyroid hormone (PTH) pre- and post- PTX; pre-operational 24 hour urine calcium and weight of excised parathyroid adenoma.

Results All patients were cured of the disease as evidenced by normalisation of biochemical parameters. Changes in regional bone mineral density were observed for one year in 44 Chinese patients (31 postmenopausal women, five premenopausal women and eight men; aged 62±1.7, range 34-81 years) after successful surgery for PHPT. At the lumbar spine, the site with the most cancellous bone, bone density was significantly increased from the preoperative value one year after PTX (4.60±0.8% above baseline; $p<0.01$). The total hip, containing more cortical bone than the lumbar spine, also showed a substantial rise in bone density after PTX. The change, being a 3.96±0.9% increased ($p<0.01$), was less prominent than that seen at the lumbar spine. The percentage rise of BMD of the femoral neck, intertrochanteric and trochanteric regions were 2.15±0.94%; $p<0.05$, 4.04±1.1%; $p<0.01$ and 5.5±1.1%; $p<0.01$ respectively. The distal third of the forearm, which contains more cortical bone than the hip or the lumbar spine, did not show a significant change in BMD after PTX. Similar trend of BMD changes was observed in postmenopausal women, premenopausal women and men. There was no correlation between the 1-year percent change in BMD at any site and the baseline serum calcium, PTH, ALP, urine calcium and adenoma weight. The 1-year percent changes in BMD at lumbar spine, total hip and forearm were significantly and negatively correlated with their respective baseline Z-score. In addition, the 1-year percent change in hip BMD was also significantly and negatively correlated with Z-score of lumbar and forearm BMD.

Conclusions This study showed that there was a modest but significant rise in BMD mainly in cancellous bone even at one year after PTX. The preoperative Z-score may be useful to predict the degree of BMD gain after PTX irrespective of age and sex.

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EFFICACY OF A FIXED DOSE OF RADIOACTIVE IODINE FOR THE TREATMENT OF HYPERTHYROIDISM – ONE YEAR OUTCOME IN A REGIONAL HOSPITAL IN HONG KONG

Dr Yau See Yun Joyce, Department of Medicine, Yan Chai Hospital (May 2006 Endocrinology, Diabetes and Metabolism Exit Assessment Exercise)

Background Radioactive iodine (131-I) has been one of the promising definitive treatments for hyperthyroidism. However, there is controversy on the optimal treatment dose of radioactive iodine and the adoption of calculated or fixed dose of 131-I. Also, anti-thyroid drugs (ATD) are known to be radio protective. But controversies exist between the effect of different ATD and of the varying time of stopping ATD before 131-I. There is at present no universal consensus or standardization on the treatment regimen of 131-I for the treatment of hyperthyroidism. Different centers formulate the protocol of their own. The Nuclear Medicine Department of Princess Margaret Hospital had adopted a standard protocol since September 1999; ATD was stopped two to three weeks prior to 131-I and a fixed dose of either 6mCi, 8mCi or 10mCi 131-I was given to patients. To evaluate the efficacy of this protocol, we reviewed the one year treatment outcome of the patients who received 131-I therapy in our hospital between September 1999 to September 2004.

Design This is a retrospective review on the patients who received first dose of 131-I for the treatment of hyperthyroidism in Princess Margaret Hospital between the year of September 1999 and September 2004.

Objective The primary objective is to assess the thyroid status one year after treatment with radioactive iodine. The secondary objective is to identify any risk factor associated with treatment failure.

Patients and Methods One hundred and thirteen patients received first dose of 131-I for the treatment of hyperthyroidism between the years of September 1999 and September 2004 in Princess Margaret Hospital. Medical records of the eligible patients are retrieved and data collected. The thyroid status at one year was recorded. Relapse or treatment failure was defined as clinical and biochemical evidence of hyperthyroidism which required second RAI or continuation of anti-thyroid drugs at one year. The timing of relapses and the need for second RAI was recorded. Age, gender, duration of hyperthyroidism, clinical evidence of ophthalmopathy, use of pretreatment anti-thyroid drug, duration of anti-thyroid drug before radioactive iodine, size of goiter, anti-thyroid antibodies titer, 24-hour 131-I uptake, dose of radioactive iodine 131 were measured as pretreatment variables. Thyroid function test including thyroid stimulating hormone (TSH), free thyroxine hormone (free T4), and total thyroxine hormone if applicable were also recorded.

Statistical analysis The baseline characteristics of patients with and without relapse were compared using Chi-square test for qualitative variables or by independent sample t-test for quantitative variables. Multivariate analyses of the baseline characteristics were reassessed using logistic regression. Survival analysis using Kaplan-Meier curves was used to estimate the time to relapse.

Results At one year, 42 patients (37.2%) had relapse, of which 69% received second 131-I. The median time to relapse after first 131-I was 4 months. The remaining 71 patients (62.7%) were successfully treated, 46 patients (40.7%) became euthyroid, 25 patients (22.1%) permanently hypothyroid at 1 year. Basal free T4 level (P=0.001) and goiter size (P=0.02) were significantly associated with a relapse rate after a single dose of 131-I. There was a trend of larger goiter size towards higher rate of relapse (OR 1.646, 95% CI 0.81 to 3.33, P=0.166). Multivariate logistic regression analysis showed free T4 level was the only factor significantly associated with relapse rate (P=0.029).
Survival analysis showed that patients pretreated with propylthiouracil had a higher rate of relapse during the first year after radioactive iodine than patients pretreated with carbimazole (P [log rank]=0.038). However, the relapsed rate different was not significant when combined with other pretreatment variables (P=0.416).

Conclusion Single fixed dose of radioactive iodine is simple, safe and effective in curing hyperthyroidism. High basal free T4 concentration and large goiter size are association with higher chance of relapse.

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USEFULNESS OF NON-INVASIVE VASCULAR MEASUREMENT TECHNIQUES FOR EVALUATION OF PERIPHERAL VASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND THEIR RELATIONSHIP WITH DIABETIC COMPLICATIONS- A CROSS

SECTIONAL STUDY IN A REGIONAL HOSPITAL IN HONG KONG

Dr. Yu Kin Chap, Department of Medicine & Geriatrics, Kwong Wah Hospital (May 2006 Endocrinology, Diabetes and Metabolism Exit Assessment Exercise)

Background The prevalence of Peripheral Arterial Disease (PAD) in Asian diabetic subjects has not been extensively studied by the use of non-invasive vascular measurement techniques such as ankle brachial index (ABI) and toe brachial index (TBI). Moreover, the usefulness of brachial ankle pulse wave velocity (BaPWV), a non-invasive measure of arterial stiffness, as a surrogate marker for diabetic macrovascular and microvascular complications in diabetic patients is unclear. In this study, we determined the prevalence of PAD and the use of BaPWV in a group of Asian diabetic patients, and assessed their relations with various cardiovascular risk factors and diabetic complications.

Material and Methods Two hundred and fifty three consecutive type 2 diabetic patients who attended the annual diabetic complication screening in a diabetes centre were recruited from November 2003 to October 2004 to participate in a one-stop non-invasive vascular study. Blood pressure (BP), ankle brachial index (ABI) and brachial ankle pulse wave velocity (BaPWV) were measured simultaneously with the use of a volume-plethymographic apparatus while toe brachial index (TBI) was measured with photoplethysmographic (PPG)-based sensor and digital cuff. Demographic data, anthropometric measurements, blood test, urine test, ECG, data on retinal and foot screening were obtained according to standard protocol.

Results We found a prevalence of PAD of 4.4% by an ABI criterion < 0.9 in our subjects. The additional use of TBI measurements in case of suspected tunica media calcification (ABI>1.3 and TBI<0.64) did not significantly improve the sensitivity in diagnosing PAD. Overall, diabetic patients with PAD were older, had a longer duration of diabetes, had a higher systolic blood pressure and were more likely to have nephropathy. BaPWV was found to be significantly associated with age, hypertension and its severity, duration of diabetes mellitus, serum creatinine, microvascular complications including retinopathy and nephropathy, and macrovascular complications including coronary heart diseases and cerebrovascular diseases. However, only age, duration of diabetes mellitus and systolic blood pressure were found to contribute to the degree of arterial stiffness independently, when using multivariate logistic regression analysis.

Conclusion We found a rather low prevalence of PAD in our type 2 diabetic patients using an ABI of less than 0.9 as the definition of PAD. Most of our diabetic patients with PAD were asymptomatic. TBI measurement did not significantly improve the diagnostic accuracy, possibly due to the low prevalence of tunica media calcification. BaPWV was found to correlate with traditional vascular risk factors, diabetic macrovascular and microvascular complications. It may be recommended in routine practice as a cardiovascular marker if its usefulness is further confirmed in longitudinal studies.

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ULCERATIVE COLITIS IN HONG KONG CHINESE – A REGIONAL HOSPITAL BASED STUDY

Dr Li Wing Heng Simon, Department of Medicine, Pamela Youde Nethersole Eastern Hospital (June 2006 Gastroenterology and Hepatology Exit Assessment Exercise)

Background Ulcerative colitis (UC) is a chronic inflammatory colorectal disorder of unknown aetiology and has been previously considered to be an uncommon clinical entity in the West Asian Pacific region. However, latest evidence suggest increased incidence among local communities. Local data about the disease is scanty.

Objective This study was carried out to assess the demographics and clinical characteristics of UC in our local Chinese population.

Methods Case records of all Chinese UC patients, including paediatric patients, actively attended follow-up in Pamela Youde Nethersole Eastern Hospital from November 1993 to June 2005 were retrospectively reviewed. Relevant data were retrieved and analyzed.

Results A total of 107 patients including one paediatric case were eligible for study. A slight male predominance of 1.09:1 was noted. The mean age at diagnosis was 43.0 $\pm$ 14.3 years (range: 5.0-83.0). The mean duration of follow-up was 52.2 $\pm$ 50.2 months (range: 1.0-288.0). The number of new cases per annum increased with time. The median duration between symptom onset and the diagnosis of UC was 21.2 months (range: 1.0-180.0). The major symptoms at presentation were per-rectal bleeding (96.2%) and diarrhoea (80.4%). Patients were presented mostly with mild disease activity (62.6%). Distal colitis (56%) was the most common mode of presentation. Sixty-eight (63.6%) patients experienced prolonged remission after initial episode. Proximal extension of the colitis occurred in 8 patients (7.5%). Extra-colonic manifestations were rare (3.7%). Familial aggregation of inflammatory bowel disease was absent. Colectomy was required in 3 patients (2.8%).

Conclusions Incidence of UC in Hong Kong seems to be increased in recent years. Family aggregation of inflammatory bowel disease is absent in local Chinese UC patients. Compared with the Western counterparts, our Chinese UC patients tend to have milder disease activity with predominant distal colonic involvement at presentation, lower colectomy rate, less relapsing and remitting course, less proximal extension of colitis and uncommon extra-intestinal manifestation.

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NONALCOHOLIC FATTY LIVER IN HONG KONG CHINESE

Dr Wong Wai Sun, Department of Medicine and Therapeutics, Prince of Wales Hospital (June 2006 Gastroenterology and Hepatology Exit Assessment Exercise)

Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases, and may result in cirrhosis and hepatocellular carcinoma. Data in Asia are scarce. In this report, we present four studies on Hong Kong Chinese with biopsy-proven NAFLD. Eighty-six percent of the patients had necroinflammation and 26% had fibrosis. Over a median follow-up of 6 years, nearly half of the patients had progression in fibrosis. Liver enzymes like alanine aminotransferase had poor correlation with disease stage, and might even normalize in advanced disease. NAFLD was strongly associated with diabetes and obesity. In particular, isolated post-challenge hyperglycemia (raised 2-hour plasma glucose but normal fasting glucose during oral glucose tolerance test) was common in NAFLD patients and was associated with steatohepatitis. A quarter of the diabetic NAFLD patients had normal fasting glucose. Hypoadiponectinemia was associated with NAFLD independent of other metabolic risk factors, while patients with nonalcoholic

steatohepatitis had raised tumor necrosis factor-alfa level. These adipokines may have pivotal role in the pathogenesis of NAFLD.

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A SURVEY ON THE UTILIZATION OF GASTROPROTECTIVE AGENTS AMONG USERS OF ASPIRIN AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS COMPLICATED BY UPPER GASTROINTESTINAL BLEEDING IN A REGIONAL HOSPITAL IN HONG KONG

Dr Wu Ping Ying Brian, Department of Medicine, Tseung Kwan O Hospital (June 2006 Gastroenterology and Hepatology Exit Assessment Exercise)

Introduction Nonsteroidal anti-inflammatory drugs (NSAIDs) including low-dose aspirin are an important cause of ulcer bleeding. Underutilization of gastroprotective agents (GPAs) among users with high ulcer risk is common in western countries.

Aims We aimed to study: (1) what proportion of patients with NSAID- or aspirin-related ulcer bleeding was eligible for receiving prophylaxis with GPAs according to the Hospital Authority's guidelines; and (2) what proportion of these high-risk patients had been prescribed with a GPA prior to ulcer bleeding.

Methods A survey conducted at a regional hospital. Consecutive patients with ulcer bleeding confirmed by endoscopy were screened. A standardized questionnaire was used to identify risk factors for NSAID-related ulcer bleeding and the use of GPAs before the bleeding. We confirmed patients' information by obtaining a collateral history from family members, tracing prescriptions from primary care doctors and hospital prescription database, and identifying over-the-counter drugs.

Results Between 2000 and 2004, 6401 consecutive cases of upper gastrointestinal bleeding were admitted. Of whom, 3268 had confirmed ulcer bleeding, 1647 cases (50.4%) were associated with NSAID and/or aspirin use. Among patients with NSAID- or aspirin-related ulcer bleed, 19.9% had past history of peptic ulcer, 45.4% was 75 or above, 40% had major comorbidities, and about 4% of used concomitant corticosteroids, warfarin or multiple NSAIDs, respectively. Overall, 1221 NSAID or aspirin users (74.1%) met the criteria of receiving GPAs for ulcer prevention. Only 6.6% of these high-risk users were prescribed with prophylactic GPAs prior to ulcer bleeding.

Conclusion The majority of patients with NSAID- or aspirin- related ulcer bleeding in this survey fulfilled the criteria of receiving prophylactic GPAs. Less than 7% of eligible patients received proper treatment prior to ulcer bleeding.

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OUTCOME OF INOPERABLE HEPATOCELLULAR CARCINOMA PATIENTS RECEIVING TRANSARTERIAL CHEMOEMBOLIZATION: RETROSPECTIVE ANALYSIS IN A REGIONAL HOSPITAL

Dr Yip Wai Man, Department of Medicine & Geriatrics, Tuen Mun Hospital (June 2006 Gastroenterology and Hepatology Exit Assessment Exercise)

Hepatocellular carcinoma (HCC) is a common cancer worldwide causing substantial

mortality. Although surgical resection is a form of curative treatment in HCC, only a minority of patients is suitable for this treatment and the postoperative recurrence remains high. Transarterial chemoembolization (TACE) is a treatment option for inoperable HCC and it was proven by randomized control trials that TACE can prolong survival in selected patients.

Objective The aim of this study is to evaluate the survival and the prognostic factors in patients with advanced HCC treated by TACE.

Methods Seventy four patients with inoperable HCC diagnosed from January 1998 to December 2003 were analyzed retrospectively in this study. Only patients with unresectable HCC or who refused operation were included. Patients with advanced cirrhosis, extrahepatic metastasis or previously treated HCC were excluded. Multiple host, tumor and treatment variables were analyzed in order to evaluate the predictive factors of favorable response to treatment and better survival. A critical appraisal on this topic will be presented.

Results The median survival of the study patients was 213.5 days. The cumulative survival rates at 1 year, 2 year and 3 year were 28.4%, 12.2% and 6.8% respectively. By multivariate analysis, superselective cannulation performed in TACE (hazard ratio: 0.47, 95% CI: 0.23-0.95, p=0.034), embolization with gelfoam (hazard ratio: 0.30, 95% CI: 0.11-0.80, p=0.017), treatment interval more than 45 days (hazard ratio: 0.33, 95% CI: 0.15-0.72, p=0.006), Child-Pugh grade B (hazard ratio: 5.62, 95% CI: 2.11-14.97, p=0.001), and pre-treatment serum αFP level (hazard ratio: 2.93, 95% CI: 1.50-5.73, p=0.002) were independent predictors of favorable survival.

Conclusions Survival of patients with inoperable HCC is still grave despite treatment. This study provided information in predicting the survival of patients with inoperable hepatocellular carcinoma treated by transarterial chemoembolization.

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ACUTE MYELOID LEUKEMIA IN THE ELDERLY

Dr Mak Wai Man, Vivien, Department of Medicine & Geriatrics, Princess Margaret Hospital (May 2006 Haematology and Haematological Oncology Exit Assessment Exercise)

Background Acute myeloid leukemia is a prevalent disease of the elderly. Aggressive chemotherapy is generally offered to patients in early 60 years of age. Palliative treatment is advocated in patients aged over 75 in most studies. The benefit of aggressive treatment for those between 66 and 75 is controversial. This retrospective study was conducted to analyze the impact of anthracycline-based chemotherapy on elderly patients over the age of 60 with particular attention to the controversial group.

Methods One hundred and ninety-two patients aged over 60 years with newly diagnosed AML (excluding patients with acute promyelocytic leukemia and therapy related AML) were treated in three centers in Hong Kong over 11 years. The aggressive treatment group received an anthracycline-based chemotherapy (daunorubicin, idarubicin or mitoxantrone) while the other group received antimetabolite-based chemotherapy (low-dose cytarabine, thioguanine, 6-mercaptopurine or hydroxyurea). The overall survival was compared between the two groups. Other disease related or host related factors were analyzed with respect

to overall survival.

Results The median age was 72 (range 60-99). A complete remission rate of 60% and an overall median survival of 8.5 months were achieved in the anthracycline-based group. The median total disease free survival was 7 months and the overall relapse rate was 82.5%. Anthracycline-based chemotherapy brought a median survival of 7 months to the age group 66-75. In the multivariate analysis of the entire group, anthracycline-based chemotherapy (p=0.007) and age as a continuous variable (p=0.033) significantly affected the overall survival. The former was a significant determining factor in overall survival in the age group 60-65 (p=0.000). The effect of anthracycline-based chemotherapy on overall survival tapered in the age group 66-75 (p=0.036) and was confounded by poor renal function (p=0.039).

Conclusions Patients aged older than 66 but younger than 75 should not be excluded from intensive chemotherapy. Decision should be based on prognostic factors that include comorbidity, performance status, disease related factors in particular cytogenetics.

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INFECTIVE ENDOCARDITIS : A FIVE-YEAR EXPERIENCE IN A LOCAL REGIONAL HOSPITAL IN HONG KONG

Dr Ng Yuk Yung, Department of Medicine and Geriatrics, Tuen Mun Hospital (June 2006 Infectious Disease Exit Assessment Exercise)

Background Infective endocarditis is an important disease with significant morbidity and mortality. The scenario of this disease in Hong Kong is not clearly revealed. A retrospective observational study is thus performed to fill this gap.

Patients and methods Over a five-year period at a regional hospital in Hong Kong, eighty-seven patients with a diagnosis of infective endocarditis were identified by retrospective record review. Clinical and epidemiological data was retrieved and analyzed. Risk factors associated with poor clinical outcome were assessed.

Results The annual incidence of infective endocarditis in this regional hospital was 0.1 per 1,000 population. The male to female ratio was 3 to 1; overall mean age was 44 years (43 years for men and 46 years for women). Intravenous drug abuse was the commonest predisposing factor in our locality (45%). Rheumatic heart disease was the commonest underlying heart disease (14%). Only 3% of patients had prosthetic heart disease. Duration from symptoms to diagnosis was short at a median of seven days. Fever (86%) and heart murmur (38%) were the commonest clinical findings. Blood culture was positive in 73 patients (84%). *Staphylococcus aureus (* 37%) and *viridans streptococcus* (17%) were the commonest organisms identified in blood culture. 16% of cases were culture-negative. Vegetations were present in 76% of cases. Complications of infective endocarditis included heart failure (22%), lung abscess or embolism (12%), shock (10%), cerebral embolism (9%), acute renal failure (7%), disseminated intravascular coagulation (6%) and splenic abscess (1%). All patients received antibiotic treatments and 10% required surgical intervention. In-hospital mortality was 20%. Congestive heart failure and shock were the independent predictors of death.

Conclusions Intravenous drug abuse is a common non-cardiac predisposing factor

to infective endocarditis. *Staphylococcus aureus* is commonly identified in our patients with infective endocarditis. Early diagnosis in susceptible population remains the key to successful treatment.

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RETROSPECTIVE STUDY OF THE CLINICAL PROFILES & OUTCOMES OF PATIENTS WITH COMPLICATED PARAPNEUMONIC EFFUSION OR EMPYEMA THORACIS IN A LOCAL REGIONAL HOSPITAL

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Background Complicated parapneumonic effusion is a significant complication of pneumonia. There is ongoing debate regarding the best strategy to manage complicated parapneumonic effusion particularly regarding the role of antibiotic choice, drainage, intrapleural fibrinolysis and surgical intervention.

Objectives To evaluate the outcomes of patients with complicated parapneumonic effusion with respect to different modalities of treatment.

Methods A retrospective review was conducted on 63 patients with diagnoses of empyema thoracis or complicated parapneumonic effusion admitted between January 2003 to June 2005. Patients were recruited if pus was aspirated on pleural tap or pleural fluid results indicated complicated parapneumonic effusion. The clinical presentation and outcomes of this group of patients were analyzed and the risk factors associated with length of hospital stay, need for surgery and mortality were explored.

Results The mean age of recruited patients was 64 ±16 year with a male to female ratio of 45:18. The pleural fluid culture positivity rate was 68.3%. Among culture-positive specimens, 52.7 % were Gram positive pathogens. Overall, *Streptococcus milleri (19.3%), Bacteroides (14%), Klebsiella pneumoniae (12.3%), Peptostreptococcus (7.0%), Escherichia.coli (7.0%)* were commonly isolated organisms. There were 13 deaths (20.6%) noted in this review. Lack of drainage with intrapleural fibrinolytic (p=0.007) and discordant initial antibiotic usage (p=0.002) were independenty associated with higher mortality. Decrease in surgery-free survival was independently associated with discordant initial antibiotic usage. Prolonged hospital stay was associated with high APACHE II (p=0.039) and female gender (p=0.002).

Conclusions Discordant initial antibiotic usage was associated with poor mortality and surgery-free survival. Early drainage with intrapleural fibrinolytic appeared to be associated with improved mortality. A randomized controlled trial of early intrapleural fibrinolytics in complicated effusion or empyema thoracis is warranted.

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THE EFFECT OF BODY MASS INDEX ON RECURRENCE AND SURVIVAL IN EARLY BREAST CANCER

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Breast cancer is the most common cancer amongst women. In the United States, it is the second leading cause of cancer mortality, behind lung cancer. The lifetime risk

of breast cancer is reported to be 1 in 8. Incidence has been rising since 1980, though the rate of increase has slowed in the 1990s.[1] The estimated number of new cases in the US in 2006 is expected to top 210,000.[2] In Hong Kong, the annual incidence of breast cancer was 60 per 100,000 according to the Hong Kong Cancer Registry in 2002. It is the third most common cause of cancer death in female, behind lung and colon cancer.

Through relentless research and clinical trials, significant advances have occurred in management of breast cancer. In terms of screening, by identification of the at-risk age group and other risk factors (positive family history, BRCA 1 or 2 gene mutation, prolonged oestrogen exposure), specific recommendations have been made on regular imaging by ultrasound and/or mammography for early detection, and thereby reduction of mortality. The American Cancer Society [3] recommends regular mammography every one to two years in women aged 40 years or older. Regular screening is reported to reduce mortality by 24% in women aged between 40 and 74, with the benefit more pronounced in those older than 50 years. Hereditary cause of breast cancer accounts for 5-10% of cases and of these, the most common gene mutations are BRCA 1 and 2. Women with an inherited BRCA 1 or 2 mutations are reported to have an 80% chance of developing breast cancer during their lifetime and at a younger age than those without. [4] Patients with a strong family history, especially with BRCA1 and 2 mutations should begin screening from age 30, or 5 years earlier than the earliest age at which their family member was diagnosed with breast cancer.

From a treatment perspective, the identification of new prognostic factors has modified treatment strategy. These adverse features include young age at diagnosis (<35), comorbidities, tumour size greater than 2cm, tumour histologic grading of 3 by Richardson and Bloom scale, histologic type (ductal, lobular, mixed, metaplastic), positive axillary lymph nodes involving 4 or more, negative oestrogen and progesterone receptor status, high cell proliferative index, evidence of lymphovascular invasion and HER2 over-expression. Tailored treatment would then integrate various management principles to improve outcome, such as dose-dense chemotherapy, the use of taxanes, addition of trastuzumab, loco-regional radiotherapy and hormonal therapy. The National Comprehensive Cancer Network[5] has just released new treatment guidelines for breast cancer in 2006, which recommend the consideration of HER2 and hormonal receptor status as key factors for the choice of adjuvant therapy; nodal status and tumour size have become secondary in weighting. Subsequent to discussions at American Society of Clinical Oncology (ASCO), St Galen and San Antonio conferences in 2005, the role of trastuzumab was substantiated in the adjuvant treatment of tumours with HER2 over-expression unless they are less than 1cm and well-differentiated.[6-9] The evidence for use of taxanes in the adjuvant setting was confirmed by 2 recent reports at the 28th Annual San Antonio Breast Cancer Symposium, both showing improved disease-free survival.[10,11] The disease-free survival (DFS) and overall survival (OS) are similar between weekly or 3-weekly paclitaxel or docetaxel after adriamycin/cyclophosphamide, but paclitaxel appeared better tolerated.[12] At the same meeting, dose-dense therapy with taxanes was confirmed to be superior to the conventional 3-weekly regimen, especially in oestrogen receptor negative and node positive patients.[13] There are differing opinions on adjuvant hormonal therapy. Whilst aromatase inhibitors (AI) are gaining popularity from the results of BIG 1-98, MA-17, ABCSG8, ARNO 95 and ITA trials, tamoxifen remains widely used in the first line adjuvant setting in hormone-receptor-positive, post-menopausal women.[14-19] The consensus is that there is a role for AI in the adjuvant setting but the exact sequence, timing and duration are yet to be defined.

In addition to genetics and tumour features, there are a number of “modifiable” risk factors, namely postmenopausal obesity, hormone replacement therapy, alcohol, smoking and physical inactivity. Of these, obesity has generated much enthusiasm in recent years, especially its prognostic role in breast cancer.

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COSTS AND BENEFITS OF DOSE-DENSE CHEMOTHERAPY SCHEDULING IN HONG KONG CHINESE PATIENTS WITH PRIMARY BREAST CANCER

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Cytotoxic chemotherapy has established benefits in terms of reducing the risk of relapse and death of women with resectable breast cancer treated in the adjuvant (post-operative) or neoadjuvant (pre-operative) settings. In 2003, Citron et al pioneered “dose-dense chemotherapy” by delivering standard-dose chemotherapy with shorter intervals between cycles as part of a randomized trial. This form of chemotherapy delivery - with the routine support of prophylactic granulocyte-colony stimulating factor (G-CSF) - was reported to improve the survival outcomes in the treated cohort. Hence, this study quickly became a milestone of the twenty-first century oncology literature.

However, subsequent to this, the costs and benefits of dose-dense chemotherapy have been subjected to more critical scrutiny. The aim of the present study is to assess the cost and utility of G-CSF in Chinese breast cancer patients receiving dose-dense as compared to conventional 3-weekly chemotherapy. This study aims to answer the question of whether routine use of G-CSF permits higher chemotherapy dose intensities, fewer treatment delays and/or less chemotherapy-related toxicities in this patient population. We also aim to assess the added expense from G-CSF and compare this extra cost with that accruing from febrile neutropenia, extra hospitalization or extra clinic visits attributable to the conventional regimen.

The data revealed that there was a difference in the mean dose intensity for the two arms ($p<0.01$), as well as a difference in the planned dose of doxorubicin and cyclophosphamide delivered (absolute increase 4%; $p=0.04$). There was a 28% reduction in chemotherapy delay for women receiving dose-dense chemotherapy ($p=0.01$). The use of G-CSF in dose-dense chemotherapy was shown to be well tolerated among Chinese breast cancer women with a decrease in chemotherapy-related toxicities such as nausea, vomiting, and stomatitis ($p<0.01$). G-CSF usage was associated with more arthralgia, but this was easily managed.

Concerning the extra costs, there was a net cost increase of HK$ 3,750 per dose-dense treatment cycle compared to conventional chemotherapy. This has to be weighed against the above benefits, as well as against the associated possibility that certain patient subsets (e.g. young, node-positive and ER negative) may benefit in terms of survival.

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OUTCOMES OF PATIENTS WITH DYSPHAGIA DETECTED BY VIDEOFLUOROSCOPIC SWALLOWING STUDY

Dr Chung Yiu Kwan Kenneth, Department of Rehabilitation, Kowloon Hospital (June 2006 Rehabilitation Exit Assessment Exercise)

Objective To evaluate the outcomes associated with patients with dysphagia detected by videofluoroscopic swallowing study (VFSS).

Design A retrospective study carried out from January 2005 to March 2006.

Subjects All patients (n=101) referred for VFSS assessment between January and June 2005 at Kowloon Hospital.

Main outcome measures Pneumonia and mortality according to public hospital information at 3 months, 6 months and 9 months after the VFSS were analyzed.

Results The overall pneumonia rate was 27.7% (n=28) at 3 months, 35.6% (n=36) at 6 months, and 41.6% (n=42) at 9 months. There was significantly more pneumonia in patients with tube feeding at: 3 months (oral vs tube, 19.7% vs 42.9%, p=0.013), 6 months (oral vs tube, 24.2% vs 57.1%, p=0.001), and 9 months (oral vs tube, 30.3% vs 62.9%, p=0.02). There was significantly more pneumonia in patients who were discharged to nursing homes at 6 months (home vs institution, 18.6% vs 40%, p=0.025), and at 9 months (home vs institution, 20.9% vs 50%, p=0.004). The overall mortality rate was 14.9% (n=15) at 3 months, 20.8% (n=21) at 6 months, and 24.8% (n=25) at 9 months. Patients on tube feeding had a higher mortality at: 3 months (oral vs tube, 6% vs 31.4%, p=0.002), 6 months (oral vs tube, 12.1% vs 37.1%, p=0.005), and 9 months (oral vs tube, 18.2% vs 37.1%, p=0.036). Patients who were discharged to nursing homes also had a higher mortality at 3 months (home vs institution, 0% vs 14%, p=0.014). In patients with VFSS showing aspiration, there was a non-significant higher pneumonia rate. Aspirators who were put on tube feeding had significantly more pneumonia at 9 months (oral vs tube, 35.3% vs 68.2%, p=0.041) and more deaths at 3 months (oral vs tube, 0% vs 22.7%, p=0.046). In stroke patients with VFSS showing aspiration, there was also a non-significant higher pneumonia and mortality rate. Stroke aspirators on tube feeding also had more pneumonia at 9 months (oral vs tube, 38.5% vs 84.6%, p=0.041) and more deaths at 3 months (oral vs tube, 0% vs 30.8%, p=0.048).

Conclusions Dysphagia is associated with significant morbidity and mortality. In patients with VFSS showing aspiration, there was a trend of higher pneumonia rate. There may be some prognostic value in VFSS detected aspirators. Aspirators who were put on tube feeding had more pneumonia and deaths comparing with oral feeding. In general, patients on tube feeding had a higher pneumonia and mortality rate. Dysphagic patients, despite being on tube feeding, were associated with unfavorable outcomes. Patients who were discharged to nursing homes had a higher pneumonia and mortality rate. Being institutionalized could be a risk factor in itself.

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OUTCOME EVALUATION OF A MAINTENANCE PROGRAM FOR PULMONARY REHABILITATION IN AN ACUTE RESPIRATORY MEDICINE DEPARTMENT IN HONG KONG

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Background: Pulmonary rehabilitation programs have been shown to be effective in improving exercise capacity, ability to carry out activities of daily living and better quality of life. While such programs have been shown to produce short-term effects, these improvements may not be sustained for longer than 6 months to 18 months in various studies and the benefits of maintenance programs are variable.

Objective: This paper will study the effect of a hospital-based semi-structured maintenance pulmonary rehabilitation program (PRMP) in a group of obstructive airway disease patients who attended outpatient sessions over 1 year in comparison to a group with usual treatment (control group) both after completing the standard 6 week intensive program.

Method: Outcomes in exercise tolerance (6 minute walk test), symptom scores (UCSD Shortness of Breath Questionnaire) and quality of life (Chronic Respiratory Questionnaire) and knowledge and practice of rehabilitation skills as at 6 months and 1 year are measured. Hospital admissions at one and 2 years after the initial 6 week program will be compared and mortality after the initial year will be examined. Factors that increase the likelihood of a positive outcome being maintained over the 1 year will also be analyzed enabling patient selection for future programs.

Results: Despite negative overall outcome in exercise tolerance, quality of life and rehabilitation skills scores, PRMP resulted in the maintenance of the dyspnea score at 12 months and decreased hospital admissions from the first to second year of follow up. Mortality was comparable for both groups. A frequency of at least 21 sessions per year is required to maintain most of the benefits gained in the initial program. Better quality of life outcomes were achieved in male patients, patients older than 70 years old, patients with low baseline CRQ scores and patients with low baseline exercise tolerance. This suggests that future maintenance pulmonary rehabilitation programs should not exclude such patients with low baseline scores.

Conclusion: This maintenance pulmonary rehabilitation program showed that a semi-structured set-up did not result in persistent beneficial effects at 1 year except in dyspnea scores and hospital admissions at 2 years. Higher frequency of attendance was more likely to lead to a better outcome.

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