The Hong Kong Society of Gastroenterology

FEBRUARY 2011

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President Message

Message from Prof. Benjamin C.Y. Wong, President

Welcome all of you to the first issue of our newsletter in 2011.

The year of 2010 has been a successful year for The Hong Kong Society of Gastroenterology with a number of academic activities for the gastroenterology field and related disciplines.

On behalf of the Society, I wish to thank all who have contributed to this Newsletter: Professors Joseph J.Y. Sung, James Y.W. Lau, Alan Barkun and Dr. Tina T. T. Fan for their scientific summaries, Dr. Wai-Mo Hui and Prof. Justin C.Y. Wu for editing this Newsletter; and friends from the pharmaceutical industry for their generous sponsorship and efforts.

This year of 2011 marked the 30th anniversary of our Society. Time flies and it is an opportunity for us to look back and also plan for the future. We shall be organizing an anniversary dinner to be held on Friday, 9th December 2011. Please mark this date in your calendar. In addition, the Society will also publish a book to commensurate the event. If anyone is interested to help in the organization of the dinner, or the publication of the book, please do not hesitate to contact me or our secretariat.

I look forward to your participation in the anniversary dinner.

Wishing you a happy Year of the Rabbit, and pleasure reading.

President
Prof. Benjamin C.Y. WONG

Scientific Updates

Management of Upper GI Bleeding in the 21st Century

MANAGING GI BLEEDING ASSOCIATED WITH CARDIOPROPHYLAXIS

Professor Alan Barkun
Professor of Gastroenterology
Division of Gastroenterology, McGill University
Montreal, Canada

At a lunch symposium held in Hong Kong on 18th June 2010, distinguished gastroenterologist Professor Alan Barkun, Chairholder of the DG Kinnear Chair in Gastroenterology at McGill University, Montréal, Canada, presented an overview of the latest recommendations regarding the management of patients with non-variceal upper gastrointestinal bleeding (UGIB). A highlight of his talk was the use of proton pump inhibitors (PPIs) for the management of UGIB associated with cardioprophylaxis. The symposium was sponsored by AstraZeneca.

Since the 2002 British Society of Gastroenterology guidelines1 and the 2003 consensus guidelines on the management of non-variceal UGIB2, new data has emerged suggesting that improved outcomes can be obtained with better management of patients with UGIB. These data have been incorporated into the latest international consensus guidelines (published January 2010)3 for the management of patients with UGIB. A summary of the recommended management approach to UGIB is shown in Figure 1.
Early endoscopy and risk stratification for patients with non-variceal UGIB

Early endoscopy (within the first 24 hours) allows for safe and prompt discharge of patients classified as low risk, improves outcomes for patients classified as high risk, and reduces resource utilisation for patients classified as either low or high risk. Additionally, recent observational data suggest that early endoscopy decreases the need for surgery and may improve mortality. With regard to very early or urgent endoscopy (<24 hours following bleeding), studies to date do not suggest any additional benefits from such procedures.

The Rockall Score is a good risk-scoring system for identifying patients at high risk of re-bleeding and death following an episode of UGIB. It is based on five variables comprising clinical and endoscopic data, viz. age, co-morbidity, haemodynamic status, diagnosis on endoscopy, and major stigmata of recent haemorrhage. If patients have a score of 0–2, the risk of re-bleeding is negligible; with scores greater than 2, the risk of re-bleeding follows an almost linear relationship as the score increases.

The importance of risk stratification is not only to determine which patients are at high risk for negative outcomes, but also to identify the sub-group of patients who could be sent home directly from the emergency room, thereby avoiding unnecessary hospitalisations for these patients. Such patients typically represent 20–40% of all patients presenting with peptic ulcer bleeding.

Role of pre- and post-endoscopic PPI therapy

New data concerning the use of PPIs pre- and post-endoscopy in patients with UGIB continues to emerge. In a study investigating the effects of pre-emptive infusion of high-dose omeprazole before endoscopy in 638 patients with UGIB, no significant differences were found between the omeprazole group and the placebo group in the number of patients who had recurrent bleeding, who underwent emergency surgery, or who died within 30 days of presentation. Nonetheless, improvement was seen in secondary outcomes – the proportion of patients requiring endoscopic treatment was less in the omeprazole group than in the placebo group, and hospital stay was less than 3 days in 60.5% of patients in the omeprazole group compared with only 49.2% in the placebo group. Less endoscopic treatments were required in the omeprazole-treated patients because these patients had less actively bleeding ulcers and more clean-base ulcers than patients in the placebo group. This indicates that high-dose pre-endoscopic PPI has a down-staging effect on high-risk lesions. PPI use in this setting may best be guided by data from cost-effectiveness analyses that have identified the most cost-effective scenarios.

With respect to PPI therapy following endoscopy, a Cochrane meta-analysis and its update have shown that the use of high-dose adjuvant PPI decreases the risk of re-bleeding and surgical intervention, and improves mortality, in patients with peptic ulcer bleeding. This result in patients with high-risk stigmata, if successful endoscopic haemostasis has been performed, supports the concept that profound acid suppression should be viewed as adjuvant treatment to endoscopic management.
Scientific Updates

The efficacy of high-dose intravenous (IV) esomeprazole for the prevention of recurrent peptic ulcer bleeding has been confirmed in a recent multi-national, randomised, placebo-controlled trial.11 Following endoscopic haemostasis, patients were randomised to receive either esomeprazole IV 80 mg over 30 minutes followed by 8 mg/hour for 71.5 hours, or placebo IV for 30 minutes followed by placebo for 71.5 hours. Following this, all patients were given oral esomeprazole 40 mg daily for 27 days. Compared with placebo, esomeprazole was found to significantly reduce the risk of re-bleeding within 72 hours (risk reduction of 43%, p=0.026), and this clinical benefit was sustained for up to 30 days following PPI therapy. Improvements in secondary outcomes the trial was powered for were also noted.

Management of UGIB associated with anti-platelet therapy

In patients who develop UGIB while on anti-thrombotic cardio-protective therapy such as low-dose aspirin (acetylsalicylic acid, ASA), it is common practice for physicians to discontinue ASA until the ulcers have healed. However, a meta-analysis involving 50,279 patients showed that ASA non-adherence/withdrawal carries with it a three-fold increased risk of major adverse cardiac and cerebrovascular events.12,13 Other data from randomised controlled trials (RCTs) suggest that the cardiovascular benefits of early re-introduction of ASA or clopidogrel may outweigh the gastrointestinal risks.14,15 In a sentinel trial by Sung et al, the immediate re-introduction of ASA was associated with a two-fold (but statistically insignificant) increase in the risk of recurrent UGIB; however, ASA discontinuation caused a significantly increased 8-week mortality rate.14

In some cases, patients on ASA who develop UGIB are switched to clopidogrel alone. This is not advisable because, even as monotherapy, clopidogrel is associated with a high risk of re-bleeding. In fact, pooled data from two RCTs revealed that the risk of re-bleeding was significantly less when ASA was given with a PPI, compared with clopidogrel given alone (OR 0.06, 95%CI 0.01, 0.32).16,17 For high-risk patients on ASA then, secondary prophylaxis should be given in the form of long-term PPI therapy. For clopidogrel-related UGIB, PPIs may also be used for secondary prophylaxis; however, data is lacking, especially in the light of concerns regarding the interaction of PPIs with clopidogrel.

While it is true that PPIs may compete with clopidogrel for the cytochrome P450 isoenzyme CYP2C19, which is needed to convert the pro-drug clopidogrel into its active metabolite, the question is whether this has any clinically relevant impact. Some observational studies support a clopidogrel-PPI interaction,18,19 while others do not.20,21 However, data from a recent RCT (which was unfortunately prematurely terminated, but results thus far involving over 3,000 patients have been published) showed that there was no apparent cardiovascular interaction between clopidogrel and omeprazole – no significant differences were noted in terms of adjudicated cardiovascular events, myocardial infarction and re-vascularisation between the PPI and the placebo group.22 Two other reports – a meta-analysis of 23 studies23 and a retrospective cohort study24 – also suggest that the concurrent use of PPI with clopidogrel is not associated with an increase in adverse cardiovascular outcomes. The reasonable conclusion would therefore be that if there is any interaction between clopidogrel and PPIs, it is at worst a weak one, and should not deter the physician from prescribing a PPI with clopidogrel as the potential benefits outweigh the potential risks in patients at high-risk for gastrointestinal bleeding.

Conclusion

The updated consensus guidelines provide new insights into the more effective management of patients with UGIB. PPIs are useful for diminishing the risk of re-bleeding in patients with non-variceal UGIB, both acutely and in secondary prophylaxis. This is especially true for acute patients exhibiting high risk endoscopic stigma, and in follow-up for patients at high risk of recurrent bleeding while continuing to receive anti-platelet therapy for cardioprophylaxis.

References

7. Barkun AN. Data presented 18th June 2010, Hong Kong.
A scientific conference was held on 24th June 2010, where Professor Joseph Sung provided an update on the International Consensus on Management of Non Variceal Upper Gastro Intestinal Bleeding while Professor James Lau shared an insight on current developments that may impact the future management of severe ulcer bleeding. The symposium was sponsored by AstraZeneca.

**Asia Pacific Consensus on Management of Non-variceal Upper GI Bleeding: Re-evaluating the ICON-UGIB**

Within the earlier part of 2010, the International Consensus On Management of Non-variceal Upper Gastro-Intestinal Bleeding (ICON-UGIB) was published as a means to update existing guidelines as well as to unify the management practices of upper GI bleeding. Due to differences between the East and the West, members of the Asia Pacific region held a conference to re-evaluate the ICON-UGIB for Asia, taking into consideration discrepancies in areas such as disease pattern, the nature of the healthcare system, and the socio-economic condition of the population in Asia. 12 statements from the ICON-UGIB were drawn by the steering committee and circulated among the members for review and voting until an 80% or above agreement was reached. 5 areas of recommendation comprising of 12 statements in the ICON-UGIB were examined:

1) **Resuscitation, Risk assessment and Pre-endoscopic management**

Among several scoring systems being used in the literature, the Rockall system and Blatchford system has been very useful in recording clinical and laboratory data of upper GI bleeding (UGIB) patients and identifying those who may require endoscopic intervention.

**Statement 1**

A pre-endoscopic prognostic scale is useful to predict patients that require endoscopic intervention.

- **Level of acceptance**
  - Complete = 73.3%
  - With reservation = 26.6%
- **Grading level of evidence**
  - Moderate

2) **Endoscopic management**

ICON-UGIB recommends that early endoscopy should be given within 24 hours from the first presentation of UGIB. A review of the literature show that the number of recurrent bleeding, re-bleed, transfusion, mean days of hospital stay, the number of patients requiring surgery, or the rate of mortality is independent of when endoscopy is given within the 24 hour period. Thus it was concluded that as long as patients are given endoscopy within 24 hours, the protocol is generally acceptable.

**Statement 4**

Endoscopic intervention within 24 hours of onset of bleeding improves outcomes in high-risk patients.

- **Level of acceptance**
  - Complete = 73.3%
  - With reservation = 26.7%
- **Grading level of evidence**
  - High to moderate
In the area of pharmacological treatment used after endoscopic therapy, the benefits of using iv PPI were controversial as studies from Europe showed an increase in mortality following the use of PPI, whereas Asian studies showed the contrary. Aiming to resolve this controversy, a multi-center randomized, double-blind, placebo-controlled trial was conducted. Over 700 patients were randomized to a 72-hour iv infusion period with either esomeprazole or placebo after endoscopic treatment. Results were consistent in the risk reduction of bleeding of around 43-54% when patients were treated with iv esomeprazole compared to placebo. Most of the recurrent bleeding also took place in the first 3-4 days, supporting the use of esomeprazole for 3 days. Interestingly, the post-hoc analysis revealed that esomeprazole seems to work better in the presence of Helicobacter pylori (Hp) infections; those who were Hp positive (more common in Asia compared to Europe) showed a greater reduction in recurrent bleeding compared to those without Hp infection. Furthermore, studies from India show that oral PPI reduces the incidence of recurrent bleeding.

In the area of angiographic embolization, the Asian consensus group generally agrees that the method is an alternative option to surgery in patients who are not successfully treated with endoscopic therapy:

**4) Non-endoscopic, non-pharmacologic in-hospital management**

Angiographic embolization should be considered as an alternative to surgery in patients with failed endoscopic hemostatic therapy. In the area of angiographic embolization, the Asian consensus group generally agrees that the method is an alternative option to surgery in patients who are not successfully treated with endoscopic therapy:

**5) Post discharge, ASA, and NSAIDs**

Among arthritis patients with a history of ulcer bleeding who require NSAIDs:

- Both nonselective NSAID plus a proton-pump inhibitor and a COX-2 selective NSAID alone, reduce rebleeding but substantial risk remains.
  - Complete acceptance = 86.7%
  - With reservation = 13.3%
  - Grading level of evidence: High to moderate

- A COX-2 selective NSAID plus PPI offers the best available upper GI protection.
  - Complete acceptance = 86.7%
  - With reservation = 13.3%
  - Grading level of evidence: High to moderate

In the area of pharmacological treatment used after endoscopic therapy, the benefits of using iv PPI were controversial as studies from Europe showed an increase in mortality following the use of PPI, whereas Asian studies showed the contrary. Aiming to resolve this controversy, a multi-center randomized, double-blind, placebo-controlled trial was conducted. Over 700 patients were randomized to a 72-hour iv infusion period with either esomeprazole or placebo after endoscopic treatment. Results were consistent in the risk reduction of bleeding of around 43-54% when patients were treated with iv esomeprazole compared to placebo. Most of the recurrent bleeding also took place in the first 3-4 days, supporting the use of esomeprazole for 3 days. Interestingly, the post-hoc analysis revealed that esomeprazole seems to work better in the presence of Helicobacter pylori (Hp) infections; those who were Hp positive (more common in Asia compared to Europe) showed a greater reduction in recurrent bleeding compared to those without Hp infection. Furthermore, studies from India show that oral PPI reduces the incidence of recurrent bleeding.
Following the acute phase, we discussed the agenda of prevention of recurrent bleeding. Based on data showing that Hp eradication prevents aspirin but not NSAID-induced ulcers, NSAID users should be given PPI. Studies by Chan et al compared a COX-2 inhibitor with a combination of NSAID plus PPI and found the same level of recurrent bleeding and cumulative incidence of ulcer at 6 months.\(^{11,13}\) Subsequently, Chan tested the hypothesis that a combined treatment with COX-2 inhibitor and the PPI esomeprazole after the eradication of Hp would be a better treatment than COX-2 inhibitor alone for the prevention of recurrent ulcer bleeding.\(^{13}\) The results reflected this, as the combination of esomeprazole and COX-2 inhibitor almost completely eliminated recurrent bleeding.\(^{13}\)

Another issue that has brought uncertainty among physicians was whether aspirin should be continued after endoscopic therapy in patients who develop ulcer bleeding. A study comparing patients who continued low-dose aspirin therapy and patients who received placebo for 8 weeks showed a significantly higher mortality rate in the placebo group.\(^{14}\) From this data, the consensus group felt it necessary to resume aspirin as soon as possible.

Subsequently the group explored other options which may offer better GI protection. A comparison study found that clopidogrel does not offer greater safety compared to the combination of low-dose aspirin and esomeprazole in preventing UGIB.\(^{15}\) Both groups recorded the same rate of lower GI bleeding but aspirin and esomeprazole significantly lowered UGIB compared to clopidogrel.

Lastly, a review of literature produced data that showed increased risk of cardiovascular events and recurrent myocardial infarction when clopidogrel and a PPI were given concurrently as combination treatment. Initially thought to be due to drug interaction, randomized trials reveal that PPIs were not associated with an increased risk of cardiovascular events in patients treated with clopidogrel.\(^{16,17}\) Moreover, PPIs reduce Gl events in patients taking dual antiplatelet therapy.\(^{17}\) The consensus group agrees that PPI should not always be added as dual therapy, though its prophylactic use reduces the risk of Gl adverse events.

### Managing Severe PUB – Where do we go from here?

Since the publication of studies showing the inadequacies of epinephrine for inducing thrombosis within the artery, the additional need for a second therapy to reduce the risk of bleeding was clear. The choice between hemostasis clips and thermo-coagulation as second therapy may depend on practicality in performing the procedure in a specific case.

Recently, there has been renewed interest in novel endoscopic therapy, though some proposed treatments are not yet in clinical use and are still under review by the FDA. TC325 is a topical nano-powder first used in the military which is highly effective in achieving hemostasis for external wound bleeding. Displaying no significant adverse events, it is now being evaluated for the use in GI. Preliminary results of its clinical use show promise; of 15 patients with Forrest I bleeding from peptic ulcers, 14 achieved acute hemostasis and 13 of these patients had no re-bleeding. A similar topical agent is the ankaferd herb which produces instantaneous hemostasis upon contact with blood and serum. This product is also under review for GI use, the main concern being the potential to cause systemic thrombosis if it enters the circulation. Another novel treatment is the mechanical over-the-scope clip, also known as the bear claw. It works by targeting the lesion and applying a clip on the target tissue to stop the bleeding. Mechanical devices such as this in theory should produce the most definitive hemostasis.

Exploring the limits of endoscopic therapy in clinical practice, studies have investigated the impact of the size of the arteries on the success of endoscopic therapy. Data show fatal bleeding usually occurs from arteries up to 3.45mm in external diameters. Arteries which supply into the duodenal area are usually bigger than 2mm; these arteries may not be sealed consistently with endoscopic therapy. A review of past clinical studies have shown predicting factors of recurrent bleeding after endoscopic hemostasis treatment, one of which is high risk ulcers that will likely erode into the gastroduodenal and gastric arteries.\(^{18}\)
The comparison of transarterial embolization versus surgery for peptic ulcer bleeding after endoscopic treatment failure has been ongoing for some years. Looking at past cases, the outcome for both procedures are comparable although patients who undergo surgery tend to have a longer stay in the hospital while patients who undergo embolization are more likely to have recurrent bleeding, though this data was produced from retrospective analyses.

“Transarterial embolization is comparable to surgery in safety outcome.”

Q & A

1) Do we stop endoscopic therapy after the 2nd session?

There is no data to examine how many times we should attempt endoscopic therapy. In one previous study comparing surgery and 2nd endoscopic therapy, both options had advantages and disadvantages. The endoscopy group achieved 75% hemostasis but at the risk of perforation, while surgical patients had greater success in hemostasis but also had more peri-operative complications. Both options are viable but the choice depends on the type of patient.

2) In terms of bleeding, if the spurring is torrential, should we operate on the patient quickly if an experienced radiologist is lacking?

Stopping bleeding is the key focus, whether by surgery or angiographic embolization. From retrospective comparison studies, patients who underwent embolization had a better outcome, though recurrent rate of bleeding was high.

3) Are there any contraindications for TAE?

TAE may have some local complications. Contrast nephropathy can be entirely reversible. There were very few cases of transient deterioration of renal function and they could've been attributed to hypotension; ischemic complications were also not observed. As far as procedure is concerned, there have been improvements in our techniques and technology in performing TAE.

4) What are the mechanisms of TC325?

Due to company privacy, the exact mechanism is not disclosed, though we know it is an inert powder that swells up in the presence of water to form blood clots more easily. The procedure is not difficult; we place the probe near the artery and use a short burst of powder by pressing on the handle, then the powder will be released.

5) Are there any side effects of PPIs if used at a high dose for a long period of time?

Prolonged use of oral PPIs has been associated with osteoporosis, Clostridium difficile infection and pneumonia based on cohort studies and retrospective data. For patients with ulcer bleeding, there is no reason for prolong use unless they require NSAID and aspirin. When we consider the rarity of these associated events, the benefits certainly outweigh the risk.

6) What are your views (Sung) on giving PPI alone?

The COGENT study and the O’Donoghue study show that adding PPI to clopidogrel decreases GI side effects without significantly increasing CV complications. That being said, we must ensure we are giving PPIs only to patients who need it. Aspirin in combination with PPI is shown to be safer than clopidogrel given alone, therefore we should make our treatment choices by seeing if the patient needs 1 or 2 anti-platelet agents.

References

6. Chiu et al. DDW 2006
INTRODUCTION
Nonalcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases worldwide on the background of an increasing prevalence of obesity, type 2 diabetes mellitus and metabolic syndrome. The prevalence of NAFLD in many affluent industrialized regions of Asia is similar to Western countries. The prevalence of NAFLD in an outpatient-based study in Hong Kong was 16%. 1

NAFLD consists of a spectrum of liver disease, ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), to fibrosis and ultimately cirrhosis. 2 It may even progress to liver failure and hepatocellular carcinoma in some cases. Most Patients with simple steatosis run a benign non-progressive clinical course and have mortality comparable to the general population of similar age and gender. 3 However, NAFLD patients who have progressed to advanced fibrosis or cirrhosis have higher overall and liver-related mortality. 4

Assessment of liver fibrosis is important for determining the prognosis. Currently, liver biopsy remains the gold standard means to assess fibrosis. However, liver biopsy is an expensive and invasive procedure associated with sampling error and a number of complications.

Harrison et al had recently developed and validated a simple noninvasive scoring system (BARD score) to predict advanced liver fibrosis in Caucasian patients with NAFLD using readily available clinical data (body mass index, AST to ALT ratio and presence of diabetes mellitus). 5 A score of two to four was associated with advanced fibrosis (OR 17, 95% CI 9.2 to 31.9) and had a high negative predictive value of 96%. There are two major drawbacks from using these scoring systems in our locality. Firstly, most of them were derived from Caucasian population. Secondly, all the studies focused on the prediction of advanced fibrosis. Although this is important, the identification of earlier stage of fibrosis is equally significant, as it would allow us to concentrate therapy or intervention on this group of patients in order to prevent the development of liver cirrhosis.

The primary aim of this study was to assess the accuracy of the BARD score to predict advanced fibrosis (F3-4) and significant fibrosis (F2-4) in Chinese patients with biopsy proven NAFLD and to compare it with other noninvasive scoring systems including the AST to ALT ratio (AAR), APRI and NAFLD fibrosis score. The secondary aim of the study was to determine independent predictors of significant fibrosis in Chinese patients with NAFLD.

METHODS
Patients
Consecutive patients with histological proven NAFLD from Tseung Kwan O Hospital and Prince of Wales Hospital were included from a prospective database of previous studies 7,8 and one ongoing study. All patients were Chinese and age more than 18 who were referred to the hepatology clinics of both hospitals for work-up for abnormal liver function tests and or ultrasonographic evidence of steatosis during the period of July 2001 to December 2008. Male patients who consumed more than 30 grams per day of alcohol and female patients more than 20 grams per day were excluded. Other exclusion criteria were chronic viral hepatitis (hepatitis B and C viruses), primary biliary cirrhosis, autoimmune hepatitis, Wilson’s disease, α1-antitrypsin deficiency, biliary obstruction, drug induced liver injury or previous jejuno-ileal bypass surgery.

Clinical evaluation and laboratory tests
All patients underwent comprehensive clinical and anthropometric evaluations including drug and alcohol histories, blood pressure, height (m) and weight (kg). Body mass index (BMI) was calculated by using the formula: weight (in kg)/height (in m2) and waist circumferences were measured. Patients with BMI \( \geq 25 \) kg/m2 were considered to be obese. Male patients with waist circumference \( \geq 90 \) cm and female waist circumference \( \geq 80 \) cm were deemed to have central obesity. Hypertension was defined as a blood pressure of \( \geq 130/85 \) in the medical record or a history of taking antihypertensive medication.

Complete blood count, clotting screen, liver biochemistry including serum alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gammaglutamyl transferase (GGT), fasting glucose and lipid profile were obtained within one week of liver biopsy. Whereas other data including hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (anti-HCV), antinuclear antibody, antismooth muscle antibody, antimitochondrial antibody, serum ferritin, serum copper, ceruloplasmin and \( \alpha-1 \)-antitrypsin were taken within 6 months of liver biopsy. Patients with fasting plasma glucose below 7.0 mmol/L underwent a 75-g oral glucose tolerance test.
Metabolic syndrome was diagnosed according to the International Diabetes Federation (IDF) consensus statement: presence of central obesity (waist circumference ≥ 90 cm in men and ≥ 80 cm in women) plus 2 or more of the followings: (i) serum triglycerides > 1.7 mmol/ l; (ii) HDL-cholesterol < 1.03 mmol/ l in men and < 1.29 mmol/ l in women; (iii) blood pressure ≥ 130/85 mmHg or treated arterial hypertension; and (iv) fasting glucose ≥ 5.6 mmol/ l or treated type 2 diabetes mellitus.

**Clinical scoring systems**

BARD score was calculated as weighted sum: BMI ≥ 28 = 1 point + AAR of ≥ 0.8 = 2 points + DM = 1 point. The APRI was calculated as AST (IU/l) ÷ upper limit of normal for AST × 100 / platelet (×10^9/l).9 The NAFLD fibrosis score was calculated according to the following formula: \( -1.675 + 0.037 \times \text{age (years)} + 0.094 \times \text{BMI (kg/m}^2\) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio – 0.013 × platelet (×10^9/l) – 0.66 × albumin (g/dl).10

**Histological assessment**

All biopsy specimens were reviewed by one experienced pathologist from each hospital. The histological grading and staging of NAFLD followed the Brunt’s criteria.11 Macrophase steatosis was graded from 0 to 3, necroinflammatory activity was graded from 0 to 3, and fibrosis was staged from 0 to 4. Stage 0 = absence of fibrosis; stage 1 = perisinusoidal /pericellular fibrosis; stage 2 = perisinusoidal and portal/perportal fibrosis; stage 3 = septal or bridging fibrosis; and stage 4 = cirrhosis. Significant fibrosis was defined as stage 2 fibrosis or above while advanced fibrosis was defined as stage 3 or above.

**Data analysis and statistics**

Continuous variables were expressed in median (interquartile range) and categorical variables were expressed in number (percentage) and were tested for association with significant fibrosis using the Mann–Whitney U-test, chi-squared or Fisher’s exact tests, respectively. The overall accuracy of the BARD score in predicting significant and advanced fibrosis was calculated using the area under the receiver operating characteristics curve (AUC) and its 95 percent confidence intervals (CI). The specificity, sensitivity, positive predictive value and negative predictive value were calculated for BARD score ≥ 2. The AUC of NAFLD fibrosis score, AST/ALT ratio and APRI in predicting significant and advanced fibrosis were also calculated for comparison. The independent effect of significant variables on significant fibrosis was evaluated by multiple logistic regression analysis, using both forward and backward stepwise selection procedures. All statistical tests were two-sided. Statistical significance was taken as p < 0.05.

**Results**

A total of 199 patients with histological proven NAFLD was included in this study. Ninety six patients were recruited from Tseung Kwan O Hospital and 103 patients from Prince of Wales Hospital.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=199)</th>
<th>F0-2 (n=180)</th>
<th>F3-4 (n=19)</th>
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<td>Age</td>
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<td>47 (29-54)</td>
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<td>53%</td>
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<td>BMI (kg/m²)</td>
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<td>27.9 (25.4-30.9)</td>
<td>28 (25.4-30.5)</td>
<td>27.5 (24.7-31.8)</td>
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<td>93 (86-100)</td>
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<td>65%</td>
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<td>Fasting glucose (mmol/L)</td>
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<td>5.8 (5.2-6.8)</td>
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<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.3 (5.6-7.1)</td>
<td>6.2 (5.6-7.1)</td>
<td>6.4 (5.9-7.4)</td>
<td>0.452</td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>5.4 (4.6-6.2)</td>
<td>5.4 (4.7-6.3)</td>
<td>5 (4.5-8.8)</td>
<td>0.018</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>2.0 (1.4-2.8)</td>
<td>2.0 (1.4-2.9)</td>
<td>1.7 (1.4-2.6)</td>
<td>0.755</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/L)</td>
<td>1.2 (1.1-1.4)</td>
<td>1.3 (1.1-1.4)</td>
<td>1.2 (1.1-1.3)</td>
<td>0.196</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/L)</td>
<td>3.1 (2.4-3.9)</td>
<td>3.1 (2.5-3.9)</td>
<td>2.4 (2-3.4)</td>
<td>0.023</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45 (44-47)</td>
<td>45 (44-47)</td>
<td>44 (42-46)</td>
<td>0.268</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (μmol/L)</td>
<td>12 (8-15)</td>
<td>12 (8-15)</td>
<td>9 (7-14)</td>
<td>0.69</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>84 (69-106)</td>
<td>84 (69-106)</td>
<td>83 (68-107)</td>
<td>0.975</td>
<td></td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>69 (46-98)</td>
<td>66 (42-91)</td>
<td>97 (64-120)</td>
<td>0.019</td>
<td></td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>34.5 (26.8-54)</td>
<td>34 (26-53)</td>
<td>48 (33-91.8)</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>57 (37-90)</td>
<td>56 (37-88)</td>
<td>66 (35-113)</td>
<td>0.306</td>
<td></td>
</tr>
<tr>
<td>Platelet (x10^9/L)</td>
<td>268 (224-316)</td>
<td>269 (226-319)</td>
<td>234 (192-310)</td>
<td>0.189</td>
</tr>
</tbody>
</table>

The baseline characteristics were shown in Table 1. One hundred and fifteen patients (58%) had metabolic syndrome, and 130 (65%) patients had either IFG or DM. One hundred and sixty-seven (84%) patients were obese (BMI ≥ 25 kg/m²).

One hundred and forty one (71%) patients had abnormal ALT that is above the upper limit of normal while 62 (31%) patients had AST above the upper limit of normal. Only ten (5%) patients had AAR above 1 and 29 (14.6%) patients had AAR above 0.8 which was the cut off value used in BARD score.

Patients with advanced fibrosis were significantly older and had higher AST and ALT level as compared with patients without advanced fibrosis. There was significant higher proportion of patient having DM in advanced fibrosis group than in F0-2 fibrosis group (74% vs 47% P = 0.028). None of our patients had liver decompensation.
Table 2 Histological findings of Chinese patients with NAFLD (n = 199)

<table>
<thead>
<tr>
<th>Score</th>
<th>Steatosis score †</th>
<th>Inflammatory grade‡</th>
<th>Fibrosis stage §</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>4 (2%)</td>
<td>70 (35%)</td>
</tr>
<tr>
<td>1</td>
<td>76 (38%)</td>
<td>108 (54%)</td>
<td>79 (40%)</td>
</tr>
<tr>
<td>2</td>
<td>90 (45%)</td>
<td>63 (32%)</td>
<td>31 (15.5%)</td>
</tr>
<tr>
<td>3</td>
<td>33 (17%)</td>
<td>24 (12%)</td>
<td>11 (5.5%)</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>8 (4%)</td>
</tr>
</tbody>
</table>

† Steatosis score: 1, mild (<33% of hepatocytes involved); 2, moderate (33–66%); 3, severe (>66%).
‡ Inflammatory grade: 0, steatosis only; 1, mild; 2, moderate; 3, severe.
§ Fibrosis stage: 0, no fibrosis; 1, mild; 2, moderate; 3, severe; 4, cirrhosis.

Table 2 summarized the histological findings of all patients. One hundred and ninety five (98%) patients had NASH and only four (2%) patients had simple steatosis. The number of patients with stage 1, 2, 3 and 4 fibrosis was 79 (40%), 31 (15.5%), 11 (5.5%) and 8 (4%), respectively. Fifty (25%) patients had significant fibrosis and 19 (9.5%) patients had advanced fibrosis.

The performance of BARD score
Seventeen patients did not have AST level and were excluded from the analysis of the four scoring systems. Among the remaining 182 patients, 17 patients belonged to advanced fibrosis group and 165 patients belonged to stage F0-2 fibrosis group.

The BARD score had moderate correlation with the advanced fibrosis (R = 0.25, P = 0.001). Using BARD ≥ 2 to predict advanced fibrosis, the sensitivity, specificity, positive predictive value and negative predictive value were 23.5%, 87.9%, 16.7% and 91.8% respectively. The area under ROC curve of the BARD score was 0.57 (95% CI 0.43 - 0.72) for the prediction of stage 3 to 4 fibrosis (Table 3). For significant fibrosis, the sensitivity, specificity, positive predictive value and negative predictive value were 51.1%, 67.9%, 34.4% and 80.9% respectively. The area under ROC curve of the BARD score was 0.64 (95% CI 0.55-0.74) (Table 3).

Table 3 Area under ROC curves of BARD score, NAFLD Fibrosis Score, AST/ALT Ratio and APRI score to predict advanced and significant fibrosis

<table>
<thead>
<tr>
<th>Scoring systems</th>
<th>Area under ROC curve (95% CI) for advanced fibrosis</th>
<th>Area under ROC curve (95% CI) for significant fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARD score</td>
<td>0.57 (0.43, 0.72)</td>
<td>0.64 (0.55, 0.74)</td>
</tr>
<tr>
<td>NAFLD fibrosis score</td>
<td>0.61 (0.47, 0.76)</td>
<td>0.67 (0.58, 0.76)</td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>0.56 (0.41, 0.70)</td>
<td>0.65 (0.56, 0.75)</td>
</tr>
<tr>
<td>APRI</td>
<td>0.61 (0.47, 0.76)</td>
<td>0.62 (0.51, 0.72)</td>
</tr>
</tbody>
</table>

Performance of other non-invasive scoring systems:
The median AAR in patients with and without advanced fibrosis were 0.6 (0.4-0.8) and 0.5 (0.4-0.7), respectively (P = 0.435). The median APRI was 0.4 (0.2-0.7) in patients with advanced fibrosis and 0.3 (0.2-0.5) in patients without advanced fibrosis (P = 0.126). The median NAFLD fibrosis score in patients with advanced fibrosis was -1.7401 (-2.939 - -0.902) while patients without advanced fibrosis was -2.488 (-3.350 - -1.688) (P = 0.12). The area under ROC curve of these three scoring systems ranging from 0.56-0.61 in predicting advanced fibrosis and 0.62-0.67 in predicting significant fibrosis (Table 4). In general, the performance of NAFLD fibrosis score, AAR and APRI in predicting advanced fibrosis and significant fibrosis were similar to BARD score in this cohort.

Predictors for significant fibrosis
Univariate analysis showed that age ≥ 50 (P = 0.012), DM (P = 0.001), impaired fasting glucose (P = 0.012), metabolic syndrome (P = 0.009), AST ≥ 2 times upper limit of normal (ULN) (P = 0.037) and AAR ≥ 0.8 (P = 0.006) were associated with significant fibrosis. On multivariate analysis, only three of these parameters were significantly and independently correlated with significant fibrosis: AAR ≥ 0.8 with odd ratio 2.6 (95% CI 1.11 - 6.20, P = 0.029), DM with odd ratio 2.2 (95% CI 1.08 - 4.61, P = 0.031) and age ≥ 50 with odd ratio 2.2 (95% CI 1.08 - 4.46, P = 0.03).

DISCUSSION
Performance of BARD score and other non-invasive scoring systems
Harrison et al reported a simple non-invasive scoring system (BARD score) which could predict the presence of advanced liver fibrosis in NAFLD patients with high accuracy. The calculation of BARD score required only three simple variables: (1) presence of DM, (2) AAR ≥ 0.8 and (3) BMI ≥ 28. In our study, the performance of the BARD score in predicting advanced fibrosis in Chinese NAFLD patients was fair with an AUC of 0.57 (95% CI 0.43-0.72). The positive predictive value and sensitivity were poor (16.7% and 23.5% respectively). The negative predictive value and specificity were 91.8% and 87.9% respectively. This was in contrast to the original study where the performance was good with an AUC of 0.81 in Caucasian population.

Our results concurred with the study published by Wong and colleague to validate the NAFLD fibrosis score in Chinese NAFLD patients. The performance of the NAFLD fibrosis score in Chinese patients was inferior to Caucasians, with the AUC of the NAFLD fibrosis score of 0.64 (95% CI 0.49-0.79) for the prediction of advanced fibrosis. Using the low cutoff point proposed by Angulo and colleagues (less than −1.455), negative predictive value for advanced fibrosis was 91% while positive predictive value was only 21%. In contrast, the AUCs were 0.88 and 0.82 in the estimation and validation groups, respectively in Angulo et al’s cohort. The negative predictive value was 88-93% and positive predictive value was 82-90% depending on the different cut-off values used. The NAFLD fibrosis score performance in our study was similar to that reported by Wong et al with AUC 0.61 (95% CI 0.47-0.76) in predicting advanced fibrosis. The negative predictive value and positive predictive value were 81.1% and 6.9%, respectively.
There are several reasons which may account for the different performance of non-invasive scoring systems in different ethnic populations. Firstly, the prevalence of advanced fibrosis was lower in Chinese NAFLD patients when compared with Caucasian patients. The prevalence of advanced fibrosis in our cohort was 9.5% which was significantly less than 30% reported by Harrison et al. Secondly, all these scoring systems were derived from the Western Caucasian populations where the prevalence of severe obesity was higher (BMI ≥ 30, 31% vs 74%). Thirdly, the AST level in our cohort was lower than that was reported in Western countries. The median level of AST was 34.5 IU/l (26.8-54) in our patients and 48 IU/l (11-445) in Harrison et al’s cohort. Fourthly, the liver biopsy is a flawed gold standard, where significant in inter & intra observer variation may occur. Different fibrosis stage in the same patient with two samples from different liver lobes had been reported.

We also tried to compare the performance of BARD score with other non-invasive scoring systems namely AAR, APRI and NAFLD fibrosis score. The performances of the AAR, APRI and NAFLD fibrosis score were no better than BARD score with the AUC ranged from 0.56–0.61 for advanced fibrosis and 0.62–0.67 for significant fibrosis.

Independent predictors of significant fibrosis
We tried to identify the predictors for significant fibrosis (F2 or above) in our cohort. By multivariate analysis, 3 variables remained significantly and independently correlated with significant fibrosis: age ≥ 50, DM and AAR ≥ 0.8. These findings concurred with reports from previous studies which assessed non-invasive markers to predict liver fibrosis. Age at biopsy reflected the probable duration of exposure to the risks (for example, to obesity and/or insulin resistance). DM had been shown to be a strong predictor for more advanced disease both Asia and Western countries. An association between an elevated AAR and fibrosis had been recognized in non-NAFLD chronic liver disease and may reflect impaired AST clearance by sinusoidal cells in the liver. This finding supported AAR may be a useful clinical tool in predicting fibrosis, especially if it was incorporated into a predictive model.

Limitations of the study
Our study has several limitations. Firstly, most of patients were referred to our hepatology clinics for investigation for elevated ALT or ultrasonogram features of fatty liver. The patients we studied may not be representative of the whole spectrum of disease in the community. Secondly, our patients who agreed to have liver biopsy were relatively young which may account for the milder histology overall as more advanced disease is likely to occur at older age. Thirdly, we did not have sufficient data to evaluate the length of liver biopsy specimens, which may be a cause for incorrect histological diagnosis as previous studies had shown that inadequate biopsy length led to underestimation of fibrosis.

CONCLUSIONS
This large prospective study assessed the performance of BARD score in predicting liver fibrosis in Chinese NAFLD patients and compared it with other three scoring systems. We found these scoring systems performed poorly in local Chinese patients. The BARD score had only fair accuracy in predicting advanced and significant fibrosis in Chinese NAFLD patients. The BARD score was not better than other non-invasive scores like NAFLD fibrosis score, APRI and AAR in predicting both advanced and significant fibrosis, but it was easier to use as compared to NAFLD fibrosis score which involved numbers of parameters and cumbersome equation. We should keep in mind that these non-invasive tests for liver fibrosis cannot replace liver biopsy totally.

References
2. Yiu DS, Leung NW. Epidemiological study: nonalcoholic fatty liver disease in Hong Kong Chinese. Hepatology 2004;40 (Suppl. 1): S82A
12th Joint Annual Scientific Meeting

4 September 2010 (1:00 p.m. – 6:10 p.m.)
Ballroom, Level 7, Langham Place Hotel, Mongkok, Kowloon, Hong Kong

Co-organizers:
The Hong Kong Society of Gastroenterology
Hong Kong Society of Digestive Endoscopy
Hong Kong Society for Coloproctology
The Hong Kong Association for the Study of Liver Diseases
The Hong Kong Society of Gastrointestinal Motility

Organizing Chairperson: Dr. Annie O.O. Chan

Sponsors: AstraZeneca Hong Kong Limited & GlaxoSmithKline Limited

Dr. Annie Chan welcomed the delegates and thanked all co-organizing societies and sponsors for their support and contributions.

The twelfth Joint Annual Scientific Meeting was very successful attended by 329 local medical professionals. As a result of the hard work of the organizing committee, it was a substantial program with lectures on a variety of topics relating to gastroenterology, hepatology, endoscopy and motility delivered by eminent speakers: “Margins and planes of resection in colorectal cancer” and “Colorectal Cancer Screening” by Professor Philip Quirke from UK, “PET/CT in detection of peritoneal carcinomatosis from colonic malignancy” by Dr. Garrett C.L. Ho of the Hong Kong Sanatorium & Hospital, “Understanding HBV resistance to prevent treatment failure” and “HBsAg quantification: From research tool to standard diagnostic test” by Professor Hans Tillmann from USA, “Contrast-enhanced ultrasound (CEUS) of the liver” by Dr. Grace L.H. Wong of Prince of Wales Hospital, “Multi-discipline approach to the treatment of chronic constipation” by Dr. William C.S. Meng of Kwong Wah Hospital and Our Lady of Maryknoll Hospital, “Achalasia in Hong Kong” by Dr. In-Son Leong of Pamela Youde Nethersole Eastern Hospital, and “New Advances in Small Bowel Enteroscopy” by Dr. Larry H. Lai of The Chinese University of Hong Kong.

Their stimulating presentations have aroused interactive discussions after each session led by chairpersons, Drs. Chi-Wai Lau and Vincent K.S. Leung, Professor Henry L.Y. Chan and Dr. Tai-Nin Chau as well as Professor Justin C.Y. Wu and Dr. Annie O.O. Chan. Crystal trophies were presented to the speakers and sponsors as tokens of appreciation.
### Major Meetings

**30th Annual General Meeting & Scientific Meeting**  
**The Hong Kong Society of Gastroenterology**  
**10th March 2011 (Thursday)**

1. **6:15 – 7:00 p.m.**  
   Registration & Refreshments/Viewing of Industry Exhibits

2. **7:00 – 7:10 p.m.**  
   Presentation of Honorary Fellowship  
   by Prof. Benjamin C.Y. Wong

3. **7:10 – 7:40 p.m.**  
   Chairman: Prof. Justin C.Y. Wu  
   "The causes and prevention of gastric cancer"  
   Prof. Jaw-Town Lin  
   Dean of College of Medicine  
   I-Shou University  
   Kaohsiung, Taiwan

4. **7:40 – 7:45 p.m.**  
   Q & A

5. **7:45 – 8:20 p.m.**  
   Digestive Disease Case Discussion

   **Presenters:**  
   - Dr. Vincent K.S. Leung, Consultant  
   - Dept. of M&G, United Christian Hospital  
   - Dr. Kelvin C.W. Chow, Resident  
   - Dept. of M&G, United Christian Hospital

   **Panel Discussants:**  
   - Dr. Ivy S.C. Luk, Pathologist, St. Paul’s Hospital  
   - Dr. Tony Loke, Consultant Radiologist  
   - United Christian Hospital  
   - Dr. Yuk-Tong Lee  
   - Honorary Clinical Associate Professor  
   - The Chinese University of Hong Kong

6. **8:20 – 8:30 p.m.**  
   Q & A

7. **8:30 – 8:55 p.m.**  
   EGM / AGM / Viewing of Exhibits

8. **8:55 – 10:00 p.m.**  
   Dinner

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**Coming Soon**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
<th>Location</th>
<th>Organizing Body</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-20 February 2011</td>
<td>21st Conference of the Asian Pacific Association for the Study of the Liver (APASL)</td>
<td>Bangkok, Thailand</td>
<td>Website: <a href="http://www.apas2011bangkok.org">www.apas2011bangkok.org</a></td>
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<tr>
<td>24-26 February 2011</td>
<td>6th Congress of ECCO on Inflammatory Bowel Diseases</td>
<td>Dublin, Ireland</td>
<td>Website: <a href="http://www.ecco11.ecco-ibd.eu">www.ecco11.ecco-ibd.eu</a></td>
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<tr>
<td>6-7 April 2011</td>
<td>IBS - The Global Perspective</td>
<td>Milwaukee, WI, USA</td>
<td>Website: <a href="http://www.romecriteria.org/global_perspective/reg/">www.romecriteria.org/global_perspective/reg/</a></td>
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<td>15-16 April 2011</td>
<td>Falk Symposium 177: Endoscopy Live Berlin 2011</td>
<td>Berlin, Germany</td>
<td>Website: <a href="http://www.drfalkopharma.de/veranstaltungen">www.drfalkopharma.de/veranstaltungen</a></td>
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<tr>
<td>16-17 April 2011</td>
<td>International Gastric Cancer Congress (IGCC 2011) &quot;A Gate to the Future Gastric Cancer Treatment&quot;</td>
<td>Seoul, Korea</td>
<td>Hosted by: Korean Gastric Cancer Association</td>
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<tr>
<td>20-23 April 2011</td>
<td>9th International Gastric Cancer Congress (IGCC 2011)</td>
<td>Seoul, Korea</td>
<td>Location: Langham Place, Mongkok, Kowloon, Hong Kong</td>
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<tr>
<td>28-30 April 2011</td>
<td>7th International EPR Congress: &quot;Surgical Congress – Multidisciplinary Treatment of Colorectal Cancer&quot;</td>
<td>Vienna, Austria</td>
<td>Organized by European Federation for Colorectal Cancer</td>
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<tr>
<td>7-10 May 2011</td>
<td>Digestive Disease Week 2011 (DDW)</td>
<td>Chicago, IL, USA</td>
<td>Website: <a href="http://www.ddw.org">www.ddw.org</a></td>
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<tr>
<td>11-13 May 2011</td>
<td>21st Century Surgery</td>
<td>Bournemouth, United Kingdom</td>
<td>Website: <a href="http://www.asgbi.org.uk/en/international_surgical_congress/">www.asgbi.org.uk/en/international_surgical_congress/</a></td>
</tr>
<tr>
<td>3-6 June 2011</td>
<td>The 5th Shanghai - Hong Kong International Liver Congress (ILC 2011)</td>
<td>Shanghai, China</td>
<td>Location: <a href="http://www.livercongress.net/">www.livercongress.net/</a></td>
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<tr>
<td>11-12 June 2011</td>
<td>The International Digestive Disease (IDD) Forum 2011: &quot;Pioneering Research and Practice&quot;</td>
<td>Hong Kong</td>
<td>Organized by: Institute of Digestive Disease, The Chinese University of Hong Kong</td>
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<tr>
<td>22-25 June 2011</td>
<td>13th World Congress on Gastrointestinal Cancer</td>
<td>Barcelona, Spain</td>
<td>Website: <a href="http://www.worldgicancer.com">www.worldgicancer.com</a></td>
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<tr>
<td>3-7 July 2011</td>
<td>2011 Tripartite Colorectal Meeting</td>
<td>Cairns, Australia</td>
<td>Organized by: The Association of Coloproctology of Great Britain and Ireland</td>
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<td>10 September 2011</td>
<td>Tripartite Colorectal Meeting</td>
<td>Singapore</td>
<td>Website: <a href="http://www.tripartite2011.org/">www.tripartite2011.org/</a></td>
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<tr>
<td>1-4 October 2011</td>
<td>Asian Pacific Digestive Week (APDW 2011)</td>
<td>Barcelona, Spain</td>
<td>Hosted by: Gastroenterological Society of Singapore</td>
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<tr>
<td>1-4 October 2011</td>
<td>Asian Pacific Digestive Week (APDW 2011)</td>
<td>Singapore</td>
<td>Website: <a href="http://www.apdwcongress.org">www.apdwcongress.org</a></td>
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