and hence had survival benefits (1), it is losing popularity as patients detected by mass screening were in less advanced stages. Although gastric cancer equipments and examination methods, skill-up seminars for introduction of mass screening program, improvement of standardization of surgical resections. Consequently, 5-year survival of gastric cancers in Japan has been demonstrated by the decreasing screening rate which was now less than 10% of the target population (Figure 1). Therefore more efficient screening methods such as direct endoscopic screening or combination of serological tests and endoscopy have been introduced in recent years (2). Gastric cancer screening by either of these methods are more efficient in detecting gastric cancers in early stages with more genetic alterations accumulated (Figure 7-A and 7-B).

Gastric cancer is the second leading cause of cancer death in Japan. Throughout these 40 years, annual gastric cancer deaths totaling about 50,000 have been recorded. Therefore, nation-wide efforts have been made for early detection and treatment of GC including efficient, high-level of secondary screening system, gastric cancer prevention of gastric cancer. The author thanks The Hong Kong Society of Gastroenterology for their generous sponsorship. and last but not least, friends from the pharmaceutical industry for their generous support.

The next newsletter will be published in June 2013.

Best wishes for a merry Christmas and a happy new year.

**Early Detection and Treatment of Gastric Cancer**

Gastric cancer is the second leading cause of cancer death in Japan. Throughout these 40 years, annual gastric cancer deaths totaling about 50,000 have been recorded. Therefore, nation-wide efforts have been made for early detection and treatment of GC including introduction of mass screening program, improvement of equipments and examination methods, skill-up seminars for training physicians and radiologists to detect early lesions, and standardization of surgical resections. Although gastric cancer patients detected by mass screening were in less advanced stages and hence had survival benefits (1), it is losing popularity as...
much higher than those of the developed Western countries (Figure 3) (http://ganjoho.ncc.go.jp/public/statistics/backnumber/2009 en.html).

Then, how should we train gastrointestinal endoscopists to acquire diagnostic capability to efficiently detect early cancerous lesions, in other words to increase the quality of endoscopic examinations?

Some of the important points for high quality endoscopic examinations include preparation of patients before endoscopy (use of mucolytic and spasmylocytic agents), control of air insufflation, washing of the mucosal surface, a standardized observation procedure to cover the entire mucosa, taking biopsies from suspicious lesions, recording of the images with review, and repeated trainings to pick up subtle changes in the mucosa (9) (Table 2). Special attention should be paid when examining high risk groups: those with positive family history of gastric cancer, smokers, and elderly males. Endoscopists should be trained to detect mucosal atrophy and intestinal metaplasia during examinations, since these mucosal changes imply high risk conditions for gastric cancer (10). In recent years, high resolution endoscopy systems equipped with magnification and electronic image enhancement device (such as narrow band imaging: NBI and flexible spectral imaging color enhancement: FICE) are used for routine examinations, facilitating identification of the high-risk mucosa and early detection of cancers (11, 12) (Figure 4). With such endoscopy systems, fine images of altered mucosal and vascular patterns that can be distinct from the surrounding mucosa are utilized for discriminating malignant lesions from benign ones without taking biopsies (13 - 15) (Figure 5).

If gastric cancer extension is limited to the mucosa and fulfills certain criteria (16) (Table 3), they are amenable to endoscopic resection such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Various tools and devices for ESD have been developed to perform en-block resection of large-sized lesions. Although technically demanding and time-consuming, quality of life of the patients should be better maintained because it can preserve the entire stomach. Recently, it has been reported that long-term survival data after endoscopic resection of early mucosal cancers were excellent irrespective of the inclusion criteria (so-called “guideline criteria” and “expanded-criteria”) (17, 18). However, considering data from our institution showing a few cases that were revealed to have lymph node metastasis despite of satisfying “expanded criteria” (19), further accumulation of the cases with submucosal invasion (sm1) or with ulcerative (UL plus) lesions is required before recommendation of such criteria.

After ESD, a close follow-up should be recommended to the patients because of high-risk of metachronous cancer development. Furthermore, eradication therapy should be offered to them with positive *Helicobacter pylori* (HP) status to reduce metachronous and heterotopic recurrence, as recent Japanese multicenter data reported (20) (Figure 6). In contrast to the seminal study by Wong et al. showing cancer preventive effects of eradication therapy was limited to the subjects without precancerous conditions (21), this study could demonstrate cancer preventive effect of eradication therapy in subjects comprised of harboring advanced atrophy and intestinal metaplasia in most cases. One of the reasons for this difference between the two studies might be explained by more accurate exclusion of minute cancer foci in the Japanese study, because meticulous search for the presence of metachronous cancer foci are routine for post-ESD surveillance.

If cancer foci are excluded in the very early stages, eradication of HP may reduce growth-promoting and/or mutagenic factors in the stomach (22), which may halt or retard tumor growth, resulting in positive effects. However, when the intervention occur in the later stages only a small effects might be obtained by eradication because tumor growth becomes more autonomous with more genetic alterations accumulated (Figure 7-A and 7-B). Theoretically in considering effect of eradication therapy, we might postulate two points of no return, one where you may not be able to revert to the normal gastric mucosa (such as intestinal metaplasia), and another where you cannot halt growth of the tumor. Indeed, occurrence of gastric cancer after a long period after eradication therapy for benign conditions has been reported (23). Gastric cancers detected after eradication therapy might have been missed at the time of eradication due to diminutive sizes, or might arise later because the gastric environment still does not improve because of advanced atrophy and/or genetic alterations already engraved in the genome increase the risk of malignant transformation. Accordingly, it is critical in the future trials in attempting to demonstrate positive cancer preventive effects of eradication therapy to enroll subjects after detailed, high level of endoscopic examinations to exclude tiny gastric cancer foci. Furthermore, eradication therapy should be given before precancerous mucosal changes occur for better primary prevention of gastric cancer.

In the near future, insurance coverage of eradication therapy for chronic HP gastritis is expected in Japan, which will accelerate the reduction of gastric cancers in Japan because eradication therapy can be provided to people without atrophy. Together with more efficient, high-level of secondary screening system, gastric cancer eventually becomes a disease of the past.

**Acknowledgment**

The author thanks The Hong Kong Society of Gastroenterology for the nomination of honorary fellowship. The author also thanks colleagues in gastroenterology division, department of medicine, Jichi Medical University for their daily work on endoscopic diagnosis and treatment. Special thanks are Drs. Hiroyuki Osawa and Hironori Yamamoto for their expert diagnostic and therapeutic skills.

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**References**


Table 1. Role of general outpatient clinics in detecting early gastric cancer in Japan
Data obtained from reference 7.

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic Patients (N=714)</th>
<th>Symptomatic Patients (N=512)</th>
<th>Total (N=1226)</th>
</tr>
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<tbody>
<tr>
<td>Outpatient Clinics</td>
<td>320 (44.8%)</td>
<td>468 (91.4%)</td>
<td>788 (64.3%)</td>
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<tr>
<td>Private Health Assessment Clinics</td>
<td>306 (42.9%)</td>
<td>39 (7.6%)</td>
<td>345 (28.1%)</td>
</tr>
<tr>
<td>Mass Screening Programs</td>
<td>88 (12.3%)</td>
<td>5 (1.0%)</td>
<td>93 (7.6%)</td>
</tr>
</tbody>
</table>

Table 2. Factors to improve diagnostic performance

<table>
<thead>
<tr>
<th></th>
<th>Preparation</th>
<th>Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>Use of mucolytic agents</td>
<td>Proper sedation</td>
</tr>
<tr>
<td></td>
<td>Use of anti-spasmyotic agents</td>
<td></td>
</tr>
<tr>
<td>Equipment</td>
<td>High-resolution (definition) system Magnification capability Spectral Imaging (NBI*, FICE**)</td>
<td>High resolution TV monitoring</td>
</tr>
<tr>
<td>Operators</td>
<td>Awareness on high-risk conditions Training for identification of early neoplastic changes</td>
<td>Systematic order of examination Observation of entire mucosa Removal of adherent mucus (by careful washing) Control of air insufflation Biopsy from suspicious lesions (gastric ulcer scar, discoloration) Review recorded images</td>
</tr>
</tbody>
</table>

*NBI: Narrow band imaging
**FICE: Flexible spectral imaging colour enhancement

Table 3. Indications of endoscopic resection for early gastric cancer

<table>
<thead>
<tr>
<th></th>
<th>“Guideline* Criteria”</th>
<th>“Expanded Criteria”</th>
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</thead>
<tbody>
<tr>
<td>Macroscopic Appearance</td>
<td>Intramucosal cancer (m)</td>
<td>Intramucosal cancer (m)</td>
</tr>
<tr>
<td>Size</td>
<td>≤20mm</td>
<td>m: no limitation (elevated type) sm1≤30mm#</td>
</tr>
<tr>
<td>Histology</td>
<td>Differentiated type</td>
<td>Differentiated type</td>
</tr>
<tr>
<td>Ulcer/Ulcer Fibrosis (UL)</td>
<td>No</td>
<td>Yes if ≤30mm#</td>
</tr>
</tbody>
</table>

*JSGC guideline 2004
# The criteria still require further validation.
Figure 1. Time trend of cancer screening rate in Japan
Data obtained from the Health Statistics of the Japanese Ministry of Health Labor and Welfare

![Graph showing cancer screening rates](image)

Figure 2. Diagnostic performance of EGD examinations for gastric cancers in the West.
Data obtained from reference 7. Red arrow indicates 5 year point after diagnosis.
As shown in this figure, only one fourths of the patients with stage 1 cancers could survive longer than 5 years, indicating the majority were not categorized as early gastric cancer, because the 5 year survivals of early gastric cancer in the West are about 90 %, similar to Japan.

![Graph showing diagnostic performance](image)

Figure 3. Comparison of 5 year survival rates of the gastrointestinal cancers.

![Graph showing survival rates](image)

Figure 4. Features of the high-risk gastric mucosa observed with magnification endoscopy
Left: Absence of regular arrangement of collecting venules (RAC) and dilated pit pattern indicate chronic gastritis due to *Helicobacter pylori* infection.
Right: Light blue crest lines (LBC) indicate the presence of intestinal metaplasia.
Figures are obtained from reference 9.

![Features of high-risk gastric mucosa](image)

Figure 5. Small foci of cancer
Images with NBI with magnification (Left) and with FICE with magnification (Right)
Note abnormal tortuous vessels and distorted pit patterns of the cancer foci.

![Small foci of cancer](image)

Figure 6. Effect of *Helicobacter pylori* eradication on the subsequent development of gastric cancers
Data obtained from reference 17.

![Graph showing effect of *Helicobacter pylori* eradication](image)

*Data from 1995–99*
Autoantibody tests for gastrointestinal and hepatobiliary diseases

A number of gastrointestinal and hepatobiliary diseases are characterised by the presence of autoantibodies. Specific autoantibody testing has been developed to provide the basis of biochemical and immunological diagnoses of these inflammatory diseases.

Inflammatory bowel disease (IBD) comprises mainly ulcerative colitis (UC) and Crohn’s disease (CD). The majority of UC patients (over 70%) exhibit a positive test for anti-neutrophil cytoplasmic antibody (ANCA). Positive ANCA and negative anti-Saccharomyces cerevisiae (SAC) antibody/pancreatic antigen (PA) results support the differential diagnosis of UC. Among others, lactoferrin is considered a common target of ANCA in UC. A novel indirect immunofluorescence (IIF) assay against anti-DNA-bound lactoferrin has been developed. Additionally, anti-goblet cell antibody which is present in about a quarter of patients with UC is a highly specific diagnostic marker. Local studies conducted in the author’s laboratory reported sensitivity levels of 60%, 42% and 45% against ANCA, anti-lactoferrin and anti-goblet cell antibodies by IIF in UC patients, respectively (unpublished data).

Diagnosis of CD can be based on the testing of anti-SAC. Combination with other serological markers (eg, anti-PA) can improve the diagnostic yield. A sensitivity of 33% was reported using IIF assay for anti-SAC immunoglobulin G (IgG) and/or IgA locally.

The detection of anti-mitochondria antibody aids the diagnosis of primary biliary cirrhosis (PBC). Some members of the 2-oxo acid dehydrogenase family (including BCOADC-E2, OGDC-E2 and PDC-E2) are PBC-specific. Immunoassays employing these synthetic peptides exhibit high specificity and sensitivity levels of over 95%.

Anti-smooth muscle antibody is frequently found in patients suffering from type I autoimmune hepatitis (AIH-I). The current standard approach to serological screening is by traditional IIF method on tissue sections to identify the G (glomerular) or T (tubular) staining patterns specific for AIH-I. The result can be further validated by testing for anti-F-actin.

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With recent scientific and technological advances, the diagnostic and therapeutic armamentarium for gastroesophageal reflux disease (GERD) has become more sophisticated.

Wireless pH monitoring and multichannel intraluminal impedance monitoring have emerged as useful diagnostic tools for patients who have atypical reflux symptoms, or those who do not respond to acid suppression therapy. With improved patient comfort during GERD testing, wireless pH monitoring enables prolonged monitoring (up to 96 hours) and ‘on-off proton-pump inhibitor (PPI) monitoring’. In patients with reflux symptoms but negative initial catheter-based pH findings, continuous wireless pH monitoring improved the diagnostic yield for GERD.1 Oesophageal impedance monitoring can complement pH monitoring in detecting weakly-acidic or non-acidic reflux episodes with normal pH-metry. A cohort study revealed that the addition of impedance to on-PPI pH monitoring resulted in an overall diagnostic gain of 16.7% attributed to weakly-acidic reflux (Figure 1).2

Management of postoperative recurrence of Crohn’s disease

Although Crohn’s disease (CD) is predominantly managed through pharmacological interventions, surgical resection remains an integral part of its management, particularly for the treatment of complications such as stenosis or abscess formation. Surgical intervention is often necessary for patients with prolonged disease duration, especially for those with ileocolonic disease.1,3 In addition, endoscopic relapse is frequently preceded by symptomatic relapse for a large proportion of patients within 3 years of post-resection. As the severity of early recurrent lesions in the neoterminal ileum is prognostic of the postoperative clinical course of CD, preventing lesion recurrences is a viable strategy to alter the natural disease course.4,5

The efficacy of several prophylactics against postoperative recurrence of CD have been established.3 Mesalamine therapy significantly reduces the risk of clinical (relative risk [RR] 0.76; 95% confidence interval [CI] 1.5–3.7; number needed to treat [NNT]=12) and severe endoscopic (RR 0.50; CI 0.29–0.84; NNT=8) recurrences, despite being weakly effective. Although, nitroimidazole antibiotics (eg, metronidazole, ornidazole) were more effective that mesalamine in reducing clinical (RR 0.23; 95% CI 0.09–0.57; NNT=4) and endoscopic (RR 0.44; 95% CI 0.26–0.74; NNT=4) recurrences, they were associated with a higher risk of serious adverse events (RR 2.39; 95% CI 1.5–3.7).6 Combination therapy with azathioprine and 6-mercaptopurine also significantly reduces risk of clinical (RR 0.59; 95% CI 0.38–0.92; NNT=7) and severe endoscopic recurrence (RR 0.64; 95% CI 0.44–0.92; NNT= 4) compared with placebo. Although combination therapy with azathioprine and 6-mercaptopurine was more effective in preventing any endoscopic recurrence compared with mesalamine alone, it was associated with a higher risk of serious adverse events.9

Patients treated with metronidazole and azathioprine achieved significantly better postoperative ileocolonoscopy scores at 3 and 12 months, with 22% of patients (vs 3.4%; p=0.03) having no detectable lesions at 1 year, compared with patients treated with metronidazole alone. A risk factor analysis of the same study cohort also failed to identify any significant association between the types and numbers of risk factors, and the degree of endoscopic recurrence.10

A recent pilot study conducted in 24 patients, which investigated the use of infliximab for preventing recurrence of CD following ileocolonic resection, showed an endoscopic recurrence rate of 9.1% (vs 84.6%; p<0.001) for infliximab-treated patients over those treated with placebo, with 81.8% of these patients having no detectable endoscopic lesions.11

Due to the associated treatment costs, infliximab should only be indicated for patients at high risk of early symptomatic recurrence following surgical resection. Risk factors include younger patients with recent disease onset, those receiving steroid therapy, those with prior surgical resection, as well as female smokers.
High-risk patients should receive prophylaxis with azathioprine and 6-mercaptopurine, with or without metronidazole, and be monitored with ileocolonoscopy every 6 months post-resection. Upon detection of severe lesions, anti-tumour necrosis factor therapy is indicated for achieving and maintaining clinical remission (Figure).

References

Figure. Algorithm for prophylaxis against Crohn’s disease recurrence after resection

Table 1. IEE for colorectal cancer screening

<table>
<thead>
<tr>
<th>Dye-based IEE (chromoendoscopy)</th>
<th>Equipment-based IEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indigo carmine</td>
<td>Narrow band imaging (NBI)</td>
</tr>
<tr>
<td>Crystal violet</td>
<td>Autofluorescence imaging (AFI)</td>
</tr>
<tr>
<td></td>
<td>Fujinon intelligence colour enhancement (FICE)</td>
</tr>
<tr>
<td></td>
<td>Pentax i-scan</td>
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</table>

Invasive colorectal cancer (CRC) is now a preventable disease, given the long progression from precancerous colorectal lesions to neoplasm and the availability of colonoscopy as a screening tool. Detection of early, subtle lesions and those with flat morphology remains a challenge with conventional white-light colonoscopy. Image-enhanced endoscopy (IEE) – endowed with high definition and magnifying scopes, as well as contrast enhancement by optical (dye-based) or electronic means (equipment-based) – has been developed to improve the sensitivity of colorectal screening (Table 1).
Current evidence supports a wide range of roles for IEE, including the detection, diagnosis, treatment and surveillance of colorectal neoplasias. Among other procedures, chromoendoscopy and NBI are the most extensively studied.

High-risk populations, including those with long-standing ulcerative colitis and hereditary non-polyposis CRC, may benefit from pan-chromoendoscopic screening as it results in a higher diagnostic yield compared with conventional colonoscopy.

In contrast, there are inconclusive data on whether NBI is superior to conventional colonoscopy. After considering the costs and benefits, conventional colonoscopy remains the gold standard for detection of colorectal polyps among the general population.

Compared with conventional colonoscopy, IEE has higher capacity to differentiate neoplastic from non-neoplastic lesions. A systematic review showed both NBI and chromoendoscopy have high sensitivity and specificity levels (nearly 90%).

Additionally, IEE can potentially improve the determination of colorectal neoplasm margins and the characterisation of surface structures, especially for depressed lesions. In the evaluation of invasion depth, chromoendoscopy has demonstrated up to 98% accuracy in the hands of experts, whereas the accuracy of NBI is yet to be determined.

IEE accentuates the contours of lesions, and may facilitate marking of the resection margins of early CRC neoplasms for endoscopic submucosal dissection. It also aids the detection of residual adenomatous tissues after endoscopic mucosal resection.

Moving forward, simplification and standardisation of the IEE-based classification system are necessary to increase the usability of these techniques.

References:

Pathophysiology and novel approaches to managing chronic constipation

Chronic constipation – clinically defined as unsatisfactory defaecation characterised by infrequent stools, difficult passage or both – can be subcategorised as those with normal transit, slow transit, defaecatory disorders, or slow transit with defaecatory disorders. These subcategorisations can be used to guide therapy choices.

Symptoms of normal transit constipation may significantly overlap with those of irritable bowel syndrome (IBS) and these patients may also have visceral hypersensitivity and variable alterations in colonic motor function. Slow transit constipation, more commonly reported in women than men, is caused by a decrease in high-amplitude propagating contractions (HAPC) with impaired phasic colonic motor activity, resulting in diminished gastrocolonic response and altered release of neurotransmitters. In contrast, defaecatory disorders are usually acquired behaviour where the patient experiences dyssynergia – the inability to coordinate pelvic floor muscles to effectively expel stool from the rectal vault during defaecation. As symptoms alone cannot be used to accurately diagnose dyssynergia, specialised diagnostic tests including defaecography, balloon expulsion test, colonic transit study, anorectal manometry and/or wireless capsule transit should be considered for patients with refractory chronic constipation.

Patients with chronic constipation should first be managed by increasing their dietary fibre intake (through food or bulking agents) followed by osmotic laxatives and then stimulant laxatives as appropriate to the patient. Anorectal biofeedback therapy should be considered in patients with pelvic floor dyssynergia.

Newer pharmacological treatments currently available in some parts of the world, or under development, include lubiprostone, prucalopride, methylnaltrexone, alvimopam and linaclotide.

Lubiprostone, a minimally-absorbed chloride channel type II activator currently available in the United States as well as Switzerland, significantly increases spontaneous bowel movements (SBM) within 24 hours of the first dose (56.7% vs 36.9%; p=0.0024) and within the 4-week period (p≤0.002) compared with placebo-treated patients. Softening of stools and reduction of straining scores during defaecation were also reported by patients (p<0.0001), with its effectiveness sustained for up to 48 weeks without significant adverse effects apart from nausea.

Prucalopride, a 5-HT4 receptor agonist currently available in Europe, is responsible for inducing gastrointestinal motility. Its efficacy in inducing SBM was demonstrated in randomised controlled trials. A recent meta-analysis revealed a response rate of 28.3% in prucalopride-treated patients compared with 13.3% in placebo-treated patients. No increased incidence of cardiovascular events were observed.

Peripheral opioid antagonists such as methylnaltrexone and alvimopam have been studied in patients with opioid-induced constipation and postoperative ileus. Methylnaltrexone induces SBM within 4 hours in 48% of patients compared with 15% of placebo-treated patients following subcutaneous administration, when maintained as a laxative regimen.

More recently, linaclotide, a minimally-absorbed guanylate cyclase C agonist currently under investigation, which induces chloride and fluid secretion through cyclic guanosine monophosphate production, was demonstrated in two clinical trials to be efficacious in relieving constipation by inducing SBM at doses of 133 µg (16% and 21.2%) and 266 µg (21.4% and 19.3%) once-daily, compared with placebo-treated patients (6% and 3%; p<0.001). Its dose-dependent relationship was established in the randomised withdrawal period.
References


Spontaneous bacterial peritonitis in Hong Kong - clinical features, prognosis and predictors of mortality: a single centre experience

Introduction

Ascites is common in cirrhotic patients and approximately 50% of cirrhotic patients developed ascites after 10 years of observation. Patients with liver cirrhosis are vulnerable to bacterial infections due to defects in various host defense mechanisms. Spontaneous bacterial peritonitis (SBP) is one of the severe complications which carries a poor prognosis with reported over 80% mortality in 1970s and 20-30% mortality in recent studies.

Spontaneous bacterial peritonitis, the spontaneous infection of the ascitic fluid, was defined as a positive culture and an elevated cirrhotic ascitic fluid neutrophil count >250/mm3 as determined by microscopy, without an evident of intra-abdominal, surgical treatable source of infection. Cases with elevated Polymorphic mononuclear cell (PMN) but negative culture are termed culture-negative neutrocytic ascites (CNNA). Patients with positive bacterial ascitic fluid culture before there is a neutrophil response are termed bacterascites. Spontaneous bacterial peritonitis and Culture negative neutrocytic ascites have similar presentation and outcome and are therefore treated in a similar manner.

Overgrowth and translocation of bacteria were considered as important steps in the pathogenic process. Patient with high Child Pugh score, a low ascitic fluid protein and a high serum bilirubin level are at a higher risk of developing Spontaneous bacterial peritonitis.

Spontaneous bacterial peritonitis has a prevalence of 1.5-3% in asymptomatic outpatients and around 10% in hospitalized patients. Clinical presentation is nonspecific. Spontaneous bacterial peritonitis may precipitate circulatory and renal dysfunction. Hepatorenal syndrome (HRS), a functional type of pre renal acute kidney injury which does not respond to volume repletion, occurs in approximately 30% of SBP and is associated with poor survival. Empirical treatment with 3rd generation cephalosporin was reported to be effective in approximately 90% cases, covering the most common organisms including E coli, Klebsiella and pneumococcus. The use of albumin was studied as an adjuvant measure to reduce mortality. One randomized, controlled study showed that treatment with cefotaxime with albumin significantly decreased the incidence of type 1 Hepatorenal syndrome and reduction of mortality from 29% to 10% compared to cefotaxime alone.

Despite effective treatment, the recurrence rate at 1 year is approximately 70%. Randomized placebo control trial has shown that secondary prophylaxis with norfloxacin reduced the probability of recurrence of SBP from 68% to 20% and the probability of SBP due to Gram negative bacteriaemia from 60% to 3%. Cirrhotic patients with acute gastrointestinal haemorrhage or low ascitic total protein content are also considered as high risk group. Bacterial infection occurs in 20-45% of patients with gastrointestinal bleeding. Its presence in variceal bleeding is associated with increased rebleeding risk, failure to control bleeding and hospital mortality. In one randomized control trial, norfloxacin in patients with ascitic fluid lower than 15g/dL without prior history of SBP could reduce the risk of SBP and improve survival.

The in-hospital mortality rates are currently reported to be 23-37%. Age, Child-Pugh score, blood urea nitrogen level, serum aminotransferase level and hospital acquired infection were reported as predictors of mortality. A recent meta-analysis identified renal dysfunction, immunosuppressive factors, lack of SBP resolution and hospital acquired SBP as predictors of mortality.

There is limited local data regarding the characteristics and outcome of SBP in Hong Kong. This retrospective study was designed to investigate on the clinical- laboratory features, in-hospital mortality rates and predictors of SBP.

Methods

This is a retrospective analysis of the adult patients who were admitted for confirmed spontaneous bacterial peritonitis in the Department of Medicine and Geriatrics in Tuen Mun Hospital, Hong Kong from January 2007 to December 2010.
Data were collected from the ascitic fluid cell count database from the Department of Pathology. There were a total of 889 of ascitic fluid cell count specimen sent over the 48 months study period from the Department of Medicine and 59 patients with 72 episodes of confirmed SBP was recorded. Spontaneous bacterial peritonitis was diagnosed based on the definition of polymorphonuclear ascitic fluid cell count of 250 cells/mm3 or more, with or without positive culture in the absence of clinical and radiological findings suggestive of secondary peritonitis. Nosocomial SBP was defined as either acquired after 48 hours or defined by a normal ascitic fluid count on entry to hospital that subsequently became positive during hospital stay.

The etiology and severity of cirrhosis were classified by staging according to Baveno IV consensus statement (stage I – no varices, stage II – varices with no ascites, stage III – ascites with or without oesophageal varices, stage IV – oesophageal variceal bleeding with or without ascites), Child-Pugh score and staging, the model of end-stage liver disease (MELD) score from the Mayo clinic.

The initial laboratory data, treatment regimen and the use of albumin usage were studied. Albumin usage for treatment of SBP was given at a dosage of 1.5g/kg on day 1 and 1.5g/kg on day 3. The presence of renal dysfunction was defined as a creatinine level greater than 1.5mg/dL (132.6μmol/L) without pre-existing renal disease and an increase in 50% in those with pre-existing renal disease. Patients who had taken oral quinolone for more than 1 month before the episode of SBP were allocated to the previous prophylaxis group. Hepatorenal syndrome was diagnosed according to the International ascitic club consensus statement. Type 1 HRS is defined as doubling of creatinine level to >2.5mg/dL (221μmol/L) or halving the creatinine clearance to <20ml/min within 2 weeks. Type 2 HRS is defined as a moderate renal failure with serum Creatinine increasing to 1.5mg/dL (132.6μmol/L) or a creatinine clearance of <40ml/min.

Exclusion criteria
Patients with secondary bacterial peritonitis, non cirrhotic related and peritoneal metastasis were excluded from the study.

Outcome measurement
The main outcome measures were mortality rates, recurrence of SBP and the predictors of mortality. The cause of death, ascitic fluid microbiology, use of albumin and the prescription rate of antibiotic prophylaxis on discharge were also recorded.

Statistical analysis
Each patient was only considered once during the first episode of spontaneous bacterial peritonitis. Cox proportional hazard analysis was performed to identify the independent predictors of mortality. Proportional hazard assumptions were checked by visual inspection of plots of the logarithm of cumulative hazards and stratified analysis. Variables with p value <0.01 from the Univariate analysis were then evaluated in the multivariate analysis. Estimations of risk were made using 95% confidence intervals and their associated p-value. Cumulative probabilities of survival after an episode of Spontaneous bacterial peritonitis are calculated using the Kaplan-Meir method. Curves were statistically compared using the log-rank test.

Results
Demographic and clinical characteristics of the patients
A total of 59 patients had 72 episodes of spontaneous bacterial peritonitis over the study period. Amongst them 10 patients had one episode of recurrence and 3 patients had second episode of recurrence.

The majority of patients were male (male to female ratio 3:1) and the mean age was 64 year old. Over two thirds were viral hepatitis (HBV 53%, HCV 13%) related cirrhosis and all of them were Child-Pugh class B and C. Five (9%) of them had history of variceal bleeding (stage IV) and fourteen (23.7%) had hepatocellular carcinoma on treatment. Three (5.1%) had history of SBP before the study period and all of them were already on antibiotic prophylaxis. All of the cases were community acquired rather than nosocomial. Thirty-four cases (56%) had the presence of co-morbidity and immunosuppressive factors. The common conditions were diabetes mellitus (27%), malignancy (22%), and chronic lung or heart diseases (8.4%).

The common presentations were fever (54%), abdominal pain and distension (73%), hepatic encephalopathy (17%) and upper gastrointestinal bleeding (15%). Septicaemic shock occurred in 9% of the cases.

Figure 1. Clinical Presentation of SBP in 59 patients

Table 1. Demographic and clinical characteristics of patients with SBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients(n=59)</th>
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<tbody>
<tr>
<td>Age (mean SD)</td>
<td>64 ± 12</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>46/13</td>
</tr>
<tr>
<td>Etiology – HBV (%)</td>
<td>53 %</td>
</tr>
<tr>
<td>HCV (%)</td>
<td>13 %</td>
</tr>
<tr>
<td>Alcoholic (%)</td>
<td>25 %</td>
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<tr>
<td>Others (%)</td>
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</tr>
<tr>
<td>Childs score (mean, SD)</td>
<td>10 ± 2</td>
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<tr>
<td>Childs stage (A/B/C)</td>
<td>0/26/33</td>
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<tr>
<td>MELD score (mean, SD)</td>
<td>18 ± 6</td>
</tr>
<tr>
<td>Stage of cirrhosis(II/III/IV)</td>
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</tr>
<tr>
<td>Presence of HCC (%)</td>
<td>14 (23.7%)</td>
</tr>
<tr>
<td>Presence of EV (%)</td>
<td>32 (54.2%)</td>
</tr>
<tr>
<td>History of SBP (%)</td>
<td>3 (5.1%)</td>
</tr>
<tr>
<td>Antibiotic prophylaxis</td>
<td>3</td>
</tr>
<tr>
<td>Community /Nosocomial</td>
<td>59/0</td>
</tr>
<tr>
<td>Presence of Co-morbildities</td>
<td>33 (56%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16</td>
</tr>
<tr>
<td>Malignancy</td>
<td>13</td>
</tr>
<tr>
<td>Chronic lung/heart disease</td>
<td>5</td>
</tr>
<tr>
<td>Fever (%)</td>
<td>32 (54%)</td>
</tr>
<tr>
<td>Abdominal distension/pain (%)</td>
<td>43 (73%)</td>
</tr>
<tr>
<td>Upper GI bleeding (%)</td>
<td>9 (15%)</td>
</tr>
<tr>
<td>Hepatic encephalopathy (%)</td>
<td>10 (17%)</td>
</tr>
<tr>
<td>Shock (%)</td>
<td>5 (9%)</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean +/- SD
Liver failure (30.7%) and sepsis (37.2%) were the major causes of mortality.

**Recurrence of Spontaneous bacterial peritonitis**
A total of 13 recurrence of SBP was recorded in the 48-month study period. Ten patients had recurrence of SBP. Three of the ten patients had second episode of recurrence. The antibiotic prophylaxis prescription rate was 70.7%. The cumulative 1 year recurrence rate of SBP in our patients was 30%.

**Table 4. Outcome and mortality rates of SBP**

<table>
<thead>
<tr>
<th>Condition</th>
<th>In-hospital mortality</th>
<th>Overall mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver failure</td>
<td>5/18 (27.7%)</td>
<td>13/43 (30.2%)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>7/18 (38.9%)</td>
<td>16/43 (37.2%)</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>4/18 (22.2%)</td>
<td>7/43 (16.3%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2/18 (11.1%)</td>
<td>6/43 (14%)</td>
</tr>
<tr>
<td>Others</td>
<td>1/43 (2.3%)</td>
<td></td>
</tr>
</tbody>
</table>

**In Hospital mortality (%) 18/59 (30.5%)**
- 30 day mortality: 35%
- 6 month mortality: 50%
- 1 year mortality: 70%

**Recurrence of SBP (%) 10/41 (24.3%)**
- 2nd Recurrence of SBP (%): 3/41 (7.3%)
- Cumulative 1 yr recurrence: 30%
- Antibiotic prophylaxis on discharge (%): 29/41 (70.7%)
- Under specialty team care: 72%

**Figure 2. Kaplan Meir curve of recurrence in SBP**
One-year cumulative recurrence rate of SBP is 30%.

**Table 2. Laboratory characteristic (including ascitic fluid) of patients with SBP**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>White cell count (10⁹/L)</td>
<td>8.8 ± 5</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>10.4 ± 2</td>
</tr>
<tr>
<td>Platelet (10⁹/L)</td>
<td>127 ± 101</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>134 ± 6</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>11 ± 10</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>136 ± 111</td>
</tr>
<tr>
<td>Bilirubin (umol/L)</td>
<td>83 ± 139</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>75 ± 145</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>24 ± 5</td>
</tr>
<tr>
<td>INR</td>
<td>1.5 ± 0.4</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>17 ± 4</td>
</tr>
<tr>
<td>Ascitic fluid cell count (per cubic mm)</td>
<td>2945 (276-34506)</td>
</tr>
<tr>
<td>(mean, range)</td>
<td></td>
</tr>
<tr>
<td>Ascitic fluid PMN count (per cubic mm) (mean, range)</td>
<td>2649 (280-34391)</td>
</tr>
<tr>
<td>Ascitic fluid protein (g/L)</td>
<td>10 ± 9</td>
</tr>
<tr>
<td>Ascitic fluid albumin (g/L)</td>
<td>13 ± 3</td>
</tr>
<tr>
<td>Ascitic fluid culture (%)</td>
<td>15 (25.4%)</td>
</tr>
<tr>
<td>Diagnosis – SBP</td>
<td>15 (25.4%)</td>
</tr>
<tr>
<td>CNNA</td>
<td>44 (74.6%)</td>
</tr>
<tr>
<td>Bacteriasites</td>
<td>0</td>
</tr>
<tr>
<td>Renal dysfunction*</td>
<td>15 (25.4%)</td>
</tr>
<tr>
<td>Albumin usage</td>
<td>6 (10.2%)</td>
</tr>
<tr>
<td>Antibiotic – Cephalosporin</td>
<td>55 (93.3%)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>49 (83.1%)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>5 (8.5%)</td>
</tr>
<tr>
<td>Sulperazon</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Quinolone - Levofloxacin</td>
<td>2 (3.4%)</td>
</tr>
<tr>
<td>Beta lactam – Meropenum</td>
<td>2 (3.4%)</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean ± SD.

*Renal dysfunction - defined as a creatinine level greater than 1.5mg/dL (132.6umol/L) without pre-existing renal disease and an increase in 50% in those with pre-existing renal disease.

**Ascitic fluid analysis and Treatment**
Positive ascitic fluid culture was identified in 25.4% of cases. Escherichia Coli was the most frequently isolated organism (53.3%) followed by Klebsiella pneumonia (20%), Staphylococcus aureus (13.3%) and Enterobacter (13.3%). There were two ciprofloxacin resistant strains from patients who were already on quinolone prophylaxis. They were sensitive and responded to cefotaxime treatment. Fifteen patients (25.4%) and forty four patients (74.6%) were diagnosed as SBP and CNNA.

Albumin infusion was used in 10.2% of the patients and 25.4% patients had renal dysfunction associated with SBP.

**Table 3. Isolated bacteria in ascitic fluid**

<table>
<thead>
<tr>
<th>Ascitic fluid culture (%)</th>
<th>Positive culture n=15 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia Coli</td>
<td>8 (53.3%)</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>3 (20%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2 (13.3%)</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>2 (13.3%)</td>
</tr>
</tbody>
</table>

**Outcome**

Mortality of patients with Spontaneous bacterial peritonitis
The in-hospital mortality rate of SBP was 30.5% and sepsis accounted for 38.9%, followed by liver failure (30.5%), hepatorenal syndrome (22.2%) and malignancy (11.1%). The mortality rates of 30-day, 6-month and 1 year were 35%, 50% and 70% respectively.
Predictors of mortality
In the Cox proportional hazard univariate and multivariate analysis, 3 variables were found to be independent predictors of mortality. They were the presence of renal dysfunction (HR 5.215, p<0.001, 95% CI 2.216-12.274), co-morbidity and immunosuppressive factors (HR 2.619, p=0.008, 95% CI 1.29-5.317) and serum bilirubin (HR 1.005, p=0.009, 95% CI 1.001-1.008).

Renal dysfunction was the only independent predictor of in-hospital mortality (HR 10.9, p<0.001, 95% CI 3.0-39.949) and 1 year mortality (HR 5.06, p=0.002, 95% CI 1.828-13.997).

Table 5. Multivariate analysis of predictive factors of mortality in Spontaneous bacterial peritonitis

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic encephalopathy</td>
<td>1.911</td>
<td>0.77-4.743</td>
<td>0.163</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>5.215</td>
<td>2.216-12.274</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MELD score</td>
<td>0.998</td>
<td>0.972-1.074</td>
<td>0.952</td>
</tr>
<tr>
<td>Bilirubin(umol/L)</td>
<td>1.005</td>
<td>1.001-1.008</td>
<td>0.009</td>
</tr>
<tr>
<td>Presence of comorbidity and immunosuppressive factors</td>
<td>2.619</td>
<td>1.29-5.317</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Table 6. Predictive factors of In-hospital mortality and 1 year mortality

<table>
<thead>
<tr>
<th></th>
<th>In hospital mortality</th>
<th>1 year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value, multivariate</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>10.94(3.39-3.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MELD score</td>
<td>0.99(0.87-1.12)</td>
<td>0.994</td>
</tr>
<tr>
<td>Presence of comorbidity and immunosuppressive factors</td>
<td>2.16(0.96-4.87)</td>
<td>0.064</td>
</tr>
</tbody>
</table>

Figure 3. Kaplan Meier Survival curve of SBP

One year mortality is 70% and nearly half of the patients died within 6 months

Figure 4. Kaplan Meier survival curve and Log rank test for renal dysfunction.

Log rank (Mantel-Cox) 7.344 1 .007

Figure 5. Kaplan Meier survival curve and Log rank test for presence of comorbidity and immunosuppressive factors.

Log rank (Mantel-Cox) 29.059 1 .000
Predictors of recurrence in spontaneous bacterial peritonitis

Overall recurrence rate of SBP was 24.3%. Univariate analysis however did not reveal any predictor of recurrence in our study. History of SBP/antibiotic prophylaxis as a variable did not reach statistically significance (p=0.7).

Amongst the 41 patients who survived an episode of SBP, twelve were given on antibiotic prophylaxis, three of them (25%) developed recurrence.

Seven (24%) of the 29 cases that were on antibiotic prophylaxis developed recurrence.

Table 7. Recurrence rate in patients who survived an episode of SBP with or without antibiotic prophylaxis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of cases</th>
<th>Recurrence (%)</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis</td>
<td>29</td>
<td>7 (24.1%)</td>
<td>0.32</td>
</tr>
<tr>
<td>No antibiotic prophylaxis on discharge</td>
<td>12</td>
<td>3 (25%)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Discussion

Spontaneous bacterial peritonitis is a severe complication of cirrhosis associated with a high mortality rate. Our study recruited patients from a major hospital in Hong Kong covering over 1.1 million people and it provided important local data on the disease characteristic. The in-hospital mortality amongst patients with SBP was 30.5% and the 1 month, 6 month and 1 year all cause mortality rate were 35%, 50% and 70%.

Epidemiology of SBP

The study showed a male predominance with male:female ratio 3:1 consistent with western studies. The mean age was 64 years old. Over half of our cases are Hepatitis B-related cirrhosis, which is in contrast to the western studies where the etiology of cirrhosis are hepatitis C and alcohol-related. A recent Korean cohort of SBP also included 70% patients with hepatitis B-related cirrhosis

Diagnosis of SBP

The clinical presentations of the patients with SBP were nonspecific and since SBP could be asymptomatic, all patients with cirrhosis and ascites in hospital should undergo paracentesis to rule out SBP. Positive culture of microorganism was isolated from one fourth of cases. Over 80% were Gram negative organism, including Escherichia Coli and Klebsiella. Gram positive organism only accounted for 13%. Antibiotic resistance is a major issue concerning long term prophylaxis usage. Cefotaxime resistance was reported to be 17-28%. Two quinolone resistant strains were identified in our cases which were associated with prior ciprofloxacin prophylaxis. All were sensitive to cefotaxime and therefore cefotaxime remained an effective first line antibiotic in our locality.

Treatment of SBP

Empirical treatment of third generation cephalosporin is effective against the most common organism in a recent series (82% sensitive). Cefotaxime (2g intravenously every 8 hours) has been shown to result in excellent ascitic fluid levels and it has been recommended by AASLD and EASL. Ofloxacin (400mg twice per day) was reported in a randomized control trial to be as effective as cefotaxime in the treatment of uncomplicated SBP. A 5-day therapy is as effective as a 10-day treatment. A more cost effective strategy would be intravenous ciprofloxacin followed by oral administration, or intravenous amoxicillin/clavulanic acid intravenously then orally, when compared to cefotaxime. Levofloxacine remained a good alternative to cefotaxime, against gram positive bacteria and to those with penicillin allergy.

Use of albumin in SBP

In our unit, intravenous albumin was not commonly used for the treatment of spontaneous bacterial peritonitis. The relatively small number of patients given albumin limits the power in the statistical analysis on prognosis and outcomes of SBP.

One randomized control trial in 1999 demonstrated that in SBP patients treated with cefotaxime, the use of albumin (1.5g/kg body weight at diagnosis, followed by 1g/kg on day 3) significantly reduced mortality from 29% to 10% compared with cefotaxime alone. Treatment was particularly effective in patients with serum baseline bilirubin >68umol/L (4mg/dl) or serum Creatinine >88umol/L (1mg/dl). In this study with 126 patients treated with cefotaxime or cefotaxime plus albumin, plasma renin activity was increased in patients treated with cefotaxime and decreased in patients treated with cefotaxime and albumin, indicating that albumin prevents the deterioration of effective blood volume induced by SBP. Guidelines suggested that the use of albumin in SBP reduces the incidence of Hepatorenal syndrome and mortality. It is unclear whether it is useful in patients with baseline bilirubin <68mmol/L and Creatinine 88umol/L, as the incidence of type 1 HRS was low (7% without albumin and 0% with albumin).

Antibiotic prophylaxis in SBP

Secondary prophylaxis with antibiotic is a class I recommendation and has been proven to reduce recurrence, improve survival and cost-effective. In our study 70.7% (29/41) of the cases were prescribed antibiotic prophylaxis (ciprofloxacin) on discharge after an episode of SBP. Three of the 12 cases had recurrence of SBP within 6 months. A retrospective study on SBP antibiotic prophylaxis underscore in the States classified 29 SBP cases into preventable SBP (SBP occurring where prophylaxis was indicated but was not administered), non preventable SBP (SBP occurring despite proper adherence of guidelines), and inevitable SBP (SBP occurring in the absence of a documented indication for prophylaxis). Eighteen of the 29 (62%) were preventable and the most overlooked indication were GI haemorrhage(8.4%) when only one third of the patients who survived SBP received long term outpatient prophylaxis after discharge. Our centre has comparatively better prescription rate and further studies to identify reason for non adherence and develop intervention to increase utilization are needed. Improving patient’s compliance to treatment and prophylaxis is crucial in the management of SBP.

Mortality of SBP

Our study showed the in hospital mortality rate was 30.5%. The majority died of sepsis and liver failure. Hepatorenal syndrome accounted for 22.2% of the cases. This study showed that patients with renal dysfunction, presence of co-morbidity and immunosuppressive factors, and high serum bilirubin levels carried poor prognosis. MELD score, in contrast to other series, did not achieve a statistically significance in our cases when place in the multivariate model. This may be due to the limitation of sample size. Furthermore two patients who survived the SBP had undergone liver transplantation and now remained in stable condition. This may contribute to the findings of very high MELD score with better outcome in survival analysis. The findings also highlight the importance of evaluation for liver transplantation.
The estimated mortality of the four stages of cirrhosis (stage I – no varices, stage II – varices with no ascites, stage III – ascites with or without oesophageal varices, stage IV – oesophageal variceal bleeding with or without ascites) were 1%, 3.4%, 20% and 57% respectively. A new Stage V, decompensated cirrhosis with sepsis, was proposed and high mortality was reported (1-year mortality of 63%). In our study, we also reported high mortality rate at 1 year (70%) which was consistent with other study 18.

Renal dysfunction, defined as a creatinine level greater than 1.5mg/dL (132.6μmol/L) without pre existing renal disease and an increase in 50% in those with pre existing renal disease, was present in 25.4% and carried a hazard ratio of 5.25. Patients admitted with SBP with renal dysfunction were 5 times more likely to die than patients with normal renal function. Further analysis demonstrated renal dysfunction was the only independent predictor of in-hospital mortality and 1-year mortality. Bilirubin, as an indicator of liver function, was also found to be an independent prognostic factor. Patients with co-morbidity and immunosuppressive factors (hazard ratio 2.69) are believed to have poor organ reserve and impaired bodily defense system against infection.

Renal dysfunction is by far the most frequently reported predictor of mortality in the literature 9. Parameters of liver dysfunction and renal dysfunction were both powerful predictors of decompensated cirrhosis. Serum creatinine is one of the three variables in the MELD score and pre-transplant Creatinine is also the most important predictor of survival post liver transplant. Patients with cirrhosis are prone to intravascular volume depletion secondary to bleeding, diuretic use and lactulose induced diarrhea. They are more often exposed to nephrotoxic agents such as non steroidal inflammatory drugs, contrast agent and aminoglycoside, to which they are particularly susceptible.

Circulatory dysfunction is common in patients with cirrhosis and portal hypertension. There is hyper-dynamic circulation, progressive vasodilatation and relatively intravascular under-filling, resulting in the increased sympathetic system and renin-angiotensin system to main hemodynamic stability. Renal perfusion may be maintained in the early stage by the increased production of nitric oxide and prostaglandins. Arterial pressure falls as the systemic vasodilatation progresses and this result in decreased renal perfusion and finally overwhelming renal constriction and fall in GFR. Hepatorenal syndrome is the extreme expression of circulatory dysfunction. Various precipitating factors of HRS were identified and bacterial infection in particular SBP is the most important predictor.

Immunosuppressive factors and the presence of concurrent medical illness were present in 57.6% of our case. One Spanish study reported immunosuppression was independent of mortality in patients with SBP 19. Less virulent bacteria were identified in SBP compared with pyelonephritis, suggesting cirrhotic patients already have weakened immune defense allowing microorganism to cause infection.

In our study, all the cases were community acquired. Nosocomial infection has been identified as a predictor of mortality and associated with a poorer outcome. A respective cohort of 236 cases in Korea over a 7 year period included 126 cases of nosocomial and 110 cases of community acquired SBP showed higher 30-day mortality rate in nosocomial SBP compared to community acquired SBP (58.7% vs. 37.3%, p=0.001). There were significantly more gram negative bacteria in nosocomial SBP which were resistant to third-generation cephalosporin (41% vs 10%, p=0.001) and quinolone (50% vs. 30.9%, p=0.003) compared to community acquired SBP 16.

Prognosis after an episode of SBP is poor. In our study, only 7 out of 10 patients survived during the hospitalization and only 3 out of 10 survived at 1 year. Twenty four percent of the patients have recurrence of SBP despite the use of antibiotic prophylaxis and 1 year recurrence rate was 30%. Therefore, patients who recovered from an episode of SBP should be considered for liver transplantation. The survival rate of the potential transplant candidate surviving an episode of SBP at 3 months, 1 yr and 2 yr were reported to be 94, 46 and 30%, demonstrating the important role of transplantation for these patients 17. Spontaneous bacterial peritonitis does not affect the survival of patients after liver transplant 18.

Several limitations of the study require further discussion. Although the database covered all the patients admitted with paracentesis, it only included the confirmed cases of SBP and there might be cases being treated empirically as SBP when paracentesis was technically difficult to perform or refused by the patient. It is also limited by the retrospective analysis. For example, it was not possible to completely ascertain paracentesis to be performed on admission and there were difficulties in assessing the severity of ascites and hepatic encephalopathy. The use of antiviral treatment in hepatitis B cirrhosis was not recorded. Finally the statistical analysis of recurrence and the use of albumin on mortality were limited by the sample size. Further prospective study on the recurrence of SBP and the characteristic and reason for non compliance and patients’ knowledge and attitude to SBP may improve the outcome of these patients.

In conclusion, the demographics and clinical characteristic in patients with SBP in Hong Kong are similar to western population. Spontaneous bacterial peritonitis is associated with significant mortality, especially in patients with renal dysfunction, high bilirubin level and presence of co morbidity and immunosuppressive factors. Renal dysfunction was the only independent predictor of in-hospital mortality and 1-year mortality. Only one third of patients survived in 1 year. All patients surviving an episode of SBP should be evaluated for liver transplant. Cefotaxime can be offered as an empirical treatment and ciprofloxacin is an acceptable choice of prophylaxis in our locality.

References


22. The symposium was attended by 150 delegates including 42 local medical professionals.

<table>
<thead>
<tr>
<th>Topics</th>
<th>Speakers</th>
</tr>
</thead>
</table>
| 1. Understanding the Brain-esophagus Connection – Psychiatric Comorbidities in GERD | Dr. Arthur Dun-Ping Mak  
Associate Consultant, Department of Psychiatry  
Prince of Wales Hospital  
N.T., Hong Kong |
| 2. PPI Non-responders: What Can a Gastroenterologist Do Before Referring Them to Psychiatrist? | Prof. Justin Che-Yuen Wu  
Institute of Digestive Disease  
Department of Medicine & Therapeutics  
Assistant Dean (Clinical), Faculty of Medicine,  
The Chinese University of Hong Kong |
| 3. Treating Mixed Anxiety and Depression in the Real World Setting | Prof. Roger McIntyre  
Associate Professor of Psychiatry & Pharmacology Head,  
Mood Disorders Psychopharmacology Unit,  
University Health Network, University of Toronto, Canada |

The symposium was attended by 150 delegates including gastroenterologists and psychiatrists. The following Q&A session was actively participated.

<table>
<thead>
<tr>
<th>Topics</th>
<th>Speakers</th>
</tr>
</thead>
</table>
| 1. Management of Peptic Ulcer: Hong Kong Experience | Prof. Benjamin Wong  
Honorary Clinical Professor, Department of Medicine,  
The University of Hong Kong |
| 2. Bleeding Peptic Ulcer: What is the Best Therapy? | Prof. Colin Howden  
Professor, Division of Gastroenterology & Hepatology  
Department of Medicine, Feinberg School of Medicine,  
Northwestern University, Chicago, IL, USA |

The symposium was attended by 150 delegates including 42 local medical professionals.
Joint Scientific Symposium

Date: 20 August 2012

Venue: The Langham Hotel, Tsim Sha Tsui

Co-organized by:
The Hong Kong Society of Gastroenterology
The Hong Kong Society of Gastrointestinal Motility

Chairpersons:
Dr. Annie O.O. Chan
Director
Gastroenterology & Hepatology Centre
Hong Kong Sanatorium & Hospital

Prof. Justin C.Y. Wu
Assistant Dean (Clinical)
Faculty of Medicine
The Chinese University of Hong Kong

Sponsor: Invida (Hong Kong) Ltd.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS: from pathophysiology to treatment</td>
<td>Prof. Guy Boeckxstaens&lt;br&gt;Professor, Department of Gastroenterology, University of Leuven, Belgium</td>
</tr>
</tbody>
</table>

The symposium was attended by 68 medical professionals.

14th Joint Annual Scientific Symposium

Date: 15 September 2012

Venue: Langham Place Hotel, Mongkok<br>Kowloon, Hong Kong

Co-organized by:
The Hong Kong Society of Gastroenterology<br>Hong Kong Society of Digestive Endoscopy<br>Hong Kong Society for Coloproctology<br>The Hong Kong Association for the Study of Liver Diseases<br>The Hong Kong Society of Gastrointestinal Motility<br>Hong Kong IBD Society

Organizing Chairman:
Dr. Wai-Cheung Lao

Sponsors: AstraZeneca Hong Kong Limited<br>Bristol-Myers Squibb Pharma (HK) Ltd.<br>GlaxoSmithKline Limited<br>LF Asia<br>Novartis Pharmaceuticals (HK) Ltd.<br>Pfizer Corporation Hong Kong Ltd.<br>Olympus Hong Kong and China Limited<br>Takeda Pharmaceuticals (Hong Kong) Limited

Dr. Wai-Cheung Lao welcomed the delegates and thanked all co-organizing societies and sponsors for their support and contributions to the fourteenth Joint Annual Scientific Meeting.

There were 9 lectures covering hot topics in gastroenterology, hepatology, endoscopy and motility delivered by renowned speakers.

<table>
<thead>
<tr>
<th>Topics</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symposium A: GI motility disorders&lt;br&gt;Chairs: Prof. Justin C.Y. Wu (CUHK) / Dr. Wan-Chee Sze (Private)</td>
<td>Prof. Ronnie Fass (USA)</td>
</tr>
<tr>
<td>Investigations &amp; Treatment of GERD</td>
<td>Prof. Ronnie Fass (USA)</td>
</tr>
<tr>
<td>Updates in investigation and treatment of chronic constipation</td>
<td>Dr. Annie O.O. Chan (HKSH)</td>
</tr>
<tr>
<td>Esophageal Motility</td>
<td>Prof. Ronnie Fass (USA)</td>
</tr>
<tr>
<td>Symposium B: Advances in endoscopic technology&lt;br&gt;Chairs: Prof. Philip W.Y. Chiu (CUHK) / Dr. Ching-Kong Loo (KWH)</td>
<td>Prof. Mitsuhiro Fujishiro (Japan)</td>
</tr>
<tr>
<td>Endoscopic diagnosis of early GI cancer</td>
<td>Prof. Mitsuhiro Fujishiro (Japan)</td>
</tr>
<tr>
<td>Per Oral Endoscopic Myotomy</td>
<td>Prof. Philip W.Y. Chiu (CUHK)</td>
</tr>
<tr>
<td>Endoscopic treatment of early GI cancer</td>
<td>Prof. Mitsuhiro Fujishiro (Japan)</td>
</tr>
<tr>
<td>Symposium C: Cancer prevention and treatment&lt;br&gt;Chairs: Dr. William S.C. Meng (OLMH) / Dr. Francis T.W. Li (PYNEH)</td>
<td>Dr. Siew Chien Ng (CUHK)</td>
</tr>
<tr>
<td>Cancer Prevention and Surveillance in Ulcerative Colitis</td>
<td>Dr. Siew Chien Ng (CUHK)</td>
</tr>
<tr>
<td>Adjuvant Therapy for Colorectal Cancer</td>
<td>Dr. Wai-Man Sze (Private Clinical Oncologist)</td>
</tr>
<tr>
<td>Prevention of hepatocellular carcinoma in patients with chronic hepatitis B</td>
<td>Dr. Grace L.H. Wong (CUHK)</td>
</tr>
</tbody>
</table>

The Meeting was attended by 292 medical professionals. Panel discussions were actively participated. Souvenirs were presented to the speakers and sponsors in appreciation of their contributions.
Scientific Symposium

Date: 18 September 2012

Venue: B2, Forum Room I, Regal Hong Kong Hotel, H.K.

Sponsor: DiagCor Bioscience Incorporation Limited

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| New technology in colorectal cancer screening | Dr. med. Jürgen Beck  
M.B.B.S. (Universities of Berlin)  
M.D. (University of Heidelberg)  
Senior Vice President Medical Affairs of  
Epigenomics AG                  |

The symposium was attended by 53 medical professionals.

Joint Scientific Symposium

Date: 25 September 2012

Co-organized by:  
The Hong Kong Society of Gastroenterology  
The Hong Kong Society of Gastrointestinal Motility

Venue: Kowloon Hotel, Hong Kong

Chairman: Prof. Justin C.Y. Wu  
Assistant Dean (Clinical), Faculty of Medicine  
Director, S.H. Ho Centre for Digestive Health, Institute of Digestive Disease  
The Chinese University of Hong Kong

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<th>Topic</th>
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| From better to BEST: Do GERD patients need a DIFFERENT PPI? | Prof. David A. Peura  
Emeritus Professor of Medicine, University of Virginia School of Medicine  
Professor of Medicine, University of Virginia Health Sciences Center, USA |

The symposium was attended by 54 medical professionals.

Joint Scientific Symposium

Date: 6 November 2012

Co-organized by:  
The Hong Kong Society of Gastroenterology  
The Hong Kong Society of Gastrointestinal Motility

Venue: Langham Place Hotel, Mongkok, Kowloon, Hong Kong

Chairman: Prof. Justin C.Y. Wu  
Assistant Dean (Clinical), Faculty of Medicine  
Director, S.H. Ho Centre for Digestive Health, Institute of Digestive Disease  
The Chinese University of Hong Kong

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| 1. Update of GERD in Asia                                             | Prof. Joseph J.Y. Sung  
Mok Hing Yiu Professor of Medicine  
President and Vice Chancellor  
The Chinese University of Hong Kong            |
| 2. Striving for Excellence – How new GERD treatment goes above and beyond the clock | Prof. Ronnie Fass  
Director of the Division of Gastroenterology & Hepatology, MetroHealth Medical Centre, Cleveland, Ohio, USA |

The symposium was attended by 112 medical professionals including 91 local doctors.
Major Meetings

11-13 December 2012
23rd International Workshop on Therapeutic Endoscopy
Location: Prince of Wales Hospital, Shatin, N.T., Hong Kong
Website: www.hksge.org

12-13 December 2012
11th Asia Congress of Endoscopic and Laparoscopic Surgery (ELSA 2012)
Organizers: Endoscopic and Laparoscopic Surgeons of Asia (ELSA), King Saud University (KUD) and Saudi Laparoscopic Society (SLS)
Location: Riyadh, KSA
Website: www.elsa2012riyadh.com

13-15 December 2012
2012 Advances in Inflammatory Bowel Diseases
Organizer: Crohn’s & Colitis Foundation of America
Website: www.advancesinibd.com

17-18 December 2012
Amsterdam Live Endoscopy 2012
Endorsed by: European Society of Gastrointestinal Endoscopy
Location: Amsterdam, The Netherlands
Website: www.amsterdamendoscopy.com

14-15 January 2013
6th Paris Hepatitis Conference
Organized by: Prof. Patrick Marcellin
Location: Paris, France
Website: www.aphc.info/home.php

17-19 January 2013
AGA-ASGE Clinical Congress of Gastroenterology and Hepatology
Organizer: American Gastroenterology Association
Location: San Diego, CA, USA
Website: www.gastro.org/education-meetings/live-meetings/
clinical-congress

24-25 January 2013
Falk Workshop: Targeted Therapies in Hepatology
Organizer: Falk Foundation
Location: Hannover, Germany
Website: www.drfalkpharma.de/veranstaltungen

27-29 January 2013
14th International Colorectal Forum – Verbier
Organizer: The Association of Colospectrology of Great Britain and Ireland
Location: Verbier, Switzerland
Website: www.icfc-colorectal.com

31 January – 2 February 2013
15th Düsseldorf International Endoscopy Symposium
Endorsed by: World Endoscopy Organization
European Society of Gastrointestinal Endoscopy
American Society of Gastrointestinal Endoscopy
German Society of Digestive and Metabolic Diseases
Location: Düsseldorf, Germany
Website: www.endo-duesseldorf.com

14-16 February 2013
8th Congress of ECCO on Inflammatory Bowel Diseases (IBD)
Organized by: European Crohn’s and Colitis Organisation
Location: Vienna, Austria
Website: www.ecco-ibd.eu/ecco13.html

21-24 February 2013
3rd PSG Congress
Organizer: Pakistan Society of Gastroenterology and GI Endoscopy
Location: Lahore, Pakistan
Website: www.psg.org.pk/

1-4 March 2013
Canadian Digestive Diseases Week (CDDW 2013) &
and the Annual CASL Winter Meeting
Organizer: Canadian Association of Gastroenterology
Location: Victoria, British Columbia, Canada
Website: www.cag-acg.org/program-and-registration

7-8 March 2013
6th Sydney International Endoscopy Symposium
Location: Sydney, NSW, Australia
Website: www.sies.org.au/

7-10 March 2013
23rd Conference of the Asian Pacific Association for the Study of the Liver (APASL 2013):
Transforming Science to Clinical Practice
Organizer: Asian Pacific Association for the Study of the Liver
Location: Singapore
Website: www.apaconf2013.com

13-15 March 2013
2013 Joint Annual Convention
2013 Philippine Digestive Health Week
Location: Manila, Philippines
Website: www.pgsa.org/article.php?id=37

14 March 2013
32nd Annual General Meeting cum Scientific Meeting of
The Hong Kong Society of Gastroenterology
Organizer: The Hong Kong Society of Gastroenterology
Location: Langham Place Hotel, Mongkok, Kowloon, Hong Kong
Program: see page 21

27-30 March 2013
4th Biennial Congress of Asian-Pacific
Hepato-Pancreatic-Biliary Association
Hosted by: Asian-Pacific Hepato-Pancreatic-Biliary Association
Location: Shanghai, China
Website: www.aphpb2013shanghai.org

April 12-14, 2013
10th International Symposium on Functional Gastrointestinal Disorders
Sponsors: International Foundation for Functional Gastrointestinal Disorders (IFFGD)
Milwaukee, Wisconsin and University of Wisconsin School of Medicine and Public Health
Office of Continuing Professional Development in Medicine and Public Health
Location: Milwaukee, Wisconsin, USA
Website: www.iffgd.org/site/news-events/events/
professional-symposia/10th-symposium

19-20 April 2013
Falk Symposium 187: Overcoming Challenges in IBD Management
Organizer: Falk Foundation
Location: Barcelona, Spain
Website: www.drfalkpharma.de/veranstaltungen

19-20 April 2013
ESEGE/ESDO Symposium: Upper GI endoscopy and neoplasia
Organized by: European Society of Gastrointestinal Endoscopy (ESEGE) and European Society of Digestive Oncology (ESDO)
Location: Lisbon, Portugal
Website: www.quality-in-endoscopy.org/symposium

24-28 April 2013
The International Liver Congress 2013 & 48th annual meeting of
The European Association for the Study of the Liver
Organized by: European Association for the Study of the Liver (EASL)
Location: Amsterdam, The Netherlands
Website: www.easl.eu/_the-international-liver-congress/
general-information

1-3 May 2013
International Surgical Congress
Organizer: Association of Surgeons of Great Britain and Ireland
Location: Glasgow, United Kingdom
Website: www.augbs.org.uk/glasgow2013/CFID=1058&CToken=E1E5C35E-334F-4882-8609193F35D15851

12-15 May 2013
20th European Congress on Obesity (ECO 2013)
Organized by: The European Association for the Study of Obesity
Location: Liverpool, United Kingdom
Website: www.easos.org/eco2012/

18-21 May 2013
Digestive Disease Week 2013 (DDW)
Organizer: American Society for Gastrointestinal Endoscopy
Location: Orlando, FL, USA
Website: www.ddw.org

7-8 June 2013
Falk Symposium 188: Inflammatory Bowel Diseases: Microbiota versus the Barrier
Organizer: Falk Foundation
Location: Stuttgart, Germany
Website: www.drfalkpharma.de/veranstaltungen

19-22 June 2013
10th International Gastric Cancer Congress (IGCC 2013)
Location: Verona, Italy
Website: www.10gcc.com

28-29 June 2013
3rd International Symposium on Complications in GI Endoscopy
Location: Hannover, Germany
Website: www.complications-in-endoscopy.com

21-24 September 2013
Gastro 2013 APDW/WCOG Shanghai
Co-organized through a collaboration of the Asian Pacific Digestive Week Federation (APDF), Chinese Society of Digestive Diseases (CSDD), World Endoscopy Organization (WEO) and the World Gastroenterology Organisaton (WGO)
Location: Shanghai, China
Website: www.gastro2013.org

(More information is available from www.hksge.org/events)