



The Hong Kong Society of Gastroenterology

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President Message

Welcome to our June 2016 Newsletter!

It was my honour to take over as president from Dr. Wai-Cheung Lao. I would like to welcome the new Council and thank everyone in the Council for their valuable contributions to the Society in the past two years especially Dr. Lao for leading the Council.

The year of 2016 will see continuous efforts of our Society in organizing activities to promote the advancement of gastroenterology. On 31 March 2016, the Annual General Meeting cum Scientific Meeting was held during which honorary fellowship was bestowed upon Professor Suk-Kyun Yang, The Chief of Department of Gastroenterology, Asan Medical Center, Seoul, South Korea. The 18th Joint Annual Scientific Meeting will be held on 28 August 2016 at the Cordis Hotel at Langham Place, Mongkok.

I would like to thank Dr Wai-Fan Luk for organizing the Annual General Meeting cum Scientific Meeting on 31 March 2016, Professor Wai-Keung Leung for editing this Newsletter, Professor Suk-Kyun Yang, Professor Ernst J. Kuipers, Professor Ping-Hong Zhou, Dr. Thomas Ka-Luen Lui and Dr. Ka-Shing Cheung for their scientific updates in this Newsletter and last but not least, all the sponsors who rendered support and contributions to the Society.

As you may be aware, the Asian Pacific Digestive Week Congress will be held in Hong Kong on 23-26 September 2017. Your support will be imperative for a successful Congress.

The next newsletter will be published in December 2016.

I look forward to seeing you all at the 18th Joint Annual Scientific Meeting on 28 August 2016.

Professor Justin C. Y. Wu
President, The Hong Kong Society of Gastroenterology

Scientific Updates

Inflammatory bowel disease in Korea



Professor Suk-Kyun Yang, M.D.

Department of Gastroenterology
University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory bowel diseases (IBD) of unknown etiology. Knowledge of differing incidence rates and characteristics of IBD in different geographic areas or among races may provide insights into possible etiologic factors.

For the last few decades, we have noticed rapidly increasing incidence rates of IBD in various areas of Asia. According to a population-based study in the Songpa-Kangdong district of

Seoul, the incidence of UC in Korea began to increase in the late 1980s and that of CD in the mid to late 1990s. The absolute incidence rate of UC is higher than that of CD. However, the incidence ratio of UC to CD decreased from 6.8 in 1986-1990 to 2.3 in 2001-2005. The incidence rates of CD and UC in Hong Kong show temporal changes similar to those in Korea. Westernization in lifestyles including dietary habits as well as environmental changes caused by industrialization and urbanization are probably responsible for these changes in incidence. Only a few Asian studies to identify environmental risk factors have been published. Further studies on this issue are expected to improve our understanding of the pathogenesis of IBD.

The frequency of a positive first-degree family history of IBD in Korea increased from 1.3% in 2001 to 4.7% in 2013, while there was a 4.7-fold rise in the prevalence of IBD over the same time period. This finding suggests that the low rate of familial aggregation in Korean IBD patients is partly explained by the low prevalence of IBD in Korea. Genome-wide association studies from Korea and Japan and many other genetic studies in Asian populations revealed similarities and differences in IBD-associated genes between Asians and Caucasians. However, many of these Asian genetic studies included only a small number of patients and controls, which raises the issue of a false lack of association due to limited statistical power. Recently, a very large scale study including 96,486 Europeans and Asians was performed by a trans-ethnic IBD working group. This study confirmed genetic heterogeneity between East Asians and Europeans. For example, NOD2 is strongly associated with CD in Europeans, but shows no association in East Asians. Similarly, the IL23R SNP with the largest effect on risk of CD in Europeans is not associated with CD in East Asians. However, another variant of IL23R has some role in CD in East Asians. In contrast, TNFSF15 has much larger effects on CD risk in East Asians. TPMT gene mutation results in low enzyme activity, thereby causing bone marrow suppression during the thiopurine treatment. The overall frequency of variant TPMT genotypes in Korea, Japan and China is between 2% and 3%, which is lower than the 10% reported in Western countries. However, thiopurine-induced leukopenia is much more common in Korea, China, and Japan than in the West. These results suggest that the genetic basis of leukopenia in Asian populations remains poorly defined. Therefore, to identify genetic variations associated with thiopurine-induced leukopenia in Koreans, we performed an Immunochip-based 2-stage association study in 978 Korean patients with CD treated with thiopurines. We found that a nonsynonymous SNP in NUDT15 was strongly associated with thiopurine-induced early leukopenia. This association was replicated in IBD patients of European descent. We suggest the NUDT15 variant is more useful than TPMT variants in predicting thiopurine-induced early leukopenia in East Asians.

The long-term clinical course of Asian patients with IBD is not well-known. Recently, long-term prognoses of CD and UC and their temporal changes were reported in hospital-based cohort studies from Korea. These studies have demonstrated that

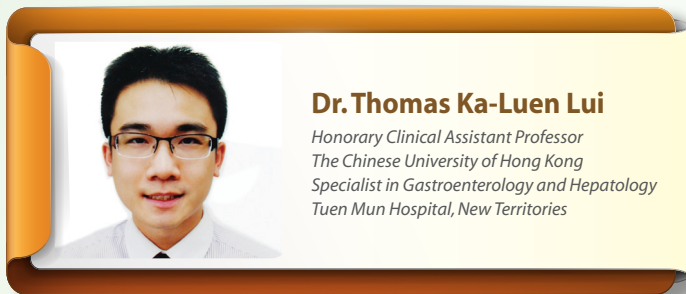
thiopurines and anti-TNF agents are being used more often and earlier in recent years than in the past in both UC and CD. The cumulative risk of intestinal resection in Korean patients with CD is 43.5% at 10 years, 70.0% at 20 years, and 76.1% at 30 years after diagnosis. These figures from our hospital-based study are similar to or slightly higher than those from Western population-based studies. The cumulative probability of intestinal resection is significantly lower in the most recent cohort than in the oldest cohort. The cumulative risk of colectomy in Korean patients with UC is 7.8% at 10 years, 14.2% at 20 years, and 21.3% at 30 years after diagnosis. Of note, the cumulative risk of colectomy in the inception cohort is just 4.4% at 20 years, which is significantly lower than that in the referred cohort. This rate is actually lower than that in Western population-based studies. Moreover, over the past 30 years, the cumulative probability of colectomy has decreased significantly. The 30-year cumulative probability of colorectal cancer was 3.8% for CD and 9.4% for UC.

Although several studies have claimed that the course of IBD, especially UC, is milder among Asians than among Caucasians, we need more data from various ethnic groups of Asia before drawing any firm conclusion.

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Colorectal endoscopic submucosal dissection



Dr. Thomas Ka-Luen Lui

Honorary Clinical Assistant Professor
The Chinese University of Hong Kong
Specialist in Gastroenterology and Hepatology
Tuen Mun Hospital, New Territories

Traditional surgical methods for the treatment of large colonic neoplasms, such as endoscopic piecemeal mucosal resection, are associated with increased rates of local recurrence and fibrosis, rendering it difficult to achieve complete eradication of the lesion.¹ Colorectal endoscopic submucosal dissection (ESD) is an advanced endoscopic procedure for the diagnosis and treatment of early colorectal lesions and is associated with high en-bloc resection and curability rates and low local recurrence rate.² ESD also enables accurate histopathological assessment of large colonic lesions and evaluation of pathological features known to be associated with risk of metastasis, such as tumor grading, vascular permeation/invasion, cribriform pattern and tumor budding, thereby helping to determine curability.³

Indications

Colorectal ESD is indicated for lesions that require en-bloc resection which are traditionally treated with piecemeal removal with snare (endoscopic mucosal resection), as well as those that are confined to the gastrointestinal tract and can be managed endoscopically. Patients with lesions with no massive submucosal invasion, no evidence of distant metastasis, and no invasive features in pathology assessment, are good for colonic ESD.

Good quality pre-ESD imaging-enhanced endoscopy (IEE) provides useful information on lesion histology; helps to assess feasibility of the ESD procedure; and is essential for proper case selection. IEE assessment provides accurate estimation of the depth of submucosal invasion, which has been shown to correlate with the risk of microscopic lymph node metastasis.⁴ However, IEE needs to be carried out by trained experts and is associated with inter-observer variability, rendering multiple investigations necessary.

Bleeding complications

A common problem associated with ESD is bleeding during the procedure, which blocks the endoscopic view and affects the dissection. Color dye (eg, indigo carmine) may be used for visualizing vessels as clear vessel identification is important when performing colonic ESD. Precoagulation can be considered to reduce the risk of bleeding during dissection, and use of the coagulation mode should be considered throughout the submucosal dissection process to reduce bleeding. Optimal control of bleeding is important as over-coagulation could result in delayed perforation while under-coagulation could lead to re-bleeding. Antiplatelet medications (eg, aspirin, clopidogrel,

warfarin) should be stopped before the procedure in patients with low thrombotic risk; aspirin may be continued in patients with high thrombotic risk. Prophylactic closure of the post-ESD wound is recommended in patients at high risk of bleeding.

Colorectal ESD technique

Novice clinicians should ideally perform their first colorectal ESD on rectal lesions as there is sufficient space in the rectum for easy manipulation of the endoscope. Moreover, the rectum has a thick muscle wall, which reduces the risk of perforation.

Proper selection of surgical tools and manipulation technique are important. A ball-tube type of knife is particularly useful when the direction of the knife needs to be perpendicular to the muscle layer; a knife with flushing function enables a clear endoscopic view and submucosal injection, helps to identify bleeding points, allows easy clearance of adhering tissue, and reduces the need for frequent changing of device.

The double layer clipping method is most commonly used for post-ESD wound closure, while the loop-clip technique may be considered for double-channel endoscopy. Endoscopic tissue shielding with polyglycolic acid sheets and fibrin glue may be used to delay perforation after duodenal or colonic ESD.⁵

Antibiotics should be administered to prevent post-ESD infection, which may cause delayed perforation. Early recognition of complications is important. Most perforations during colorectal ESD can be managed non-surgically if there is successful closure with hemoclips and absence of diffuse/localized peritonitis or high-grade fever.⁶

“ Preventing complications before colorectal ESD is preferable to managing complications during or after the procedure ”

Conclusion

Colorectal ESD is a technically demanding procedure that requires endoscopists to recognize and manage complications promptly to ensure patient safety. Preventing complications before colorectal ESD is preferable to managing complications during or after the procedure. Good-quality colorectal ESD may improve patient outcomes and prevent unnecessary surgery.

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Recent advances in endoscopic treatment of achalasia and oesophageal submucosal mass lesions



Professor Ping-Hong Zhou

Endoscopy Centre
Zhongshan Hospital
Fudan University
Shanghai, China

Peroral endoscopic myotomy (POEM) is a minimally invasive endoscopic technique that is of increasing importance in the treatment of achalasia.¹ The procedure incorporates natural orifice transluminal endoscopic surgery with myotomy, which is performed using the submucosal tunnel as an operating space.¹ POEM is suitable for all patients with achalasia and has also been successfully performed in other hypertensive motor disorders such as diffuse oesophageal spasm.¹ Sigmoid-type oesophagus, megaesophagus, recurrent or persistent symptoms after Heller myotomy, or previous POEM may make subsequent endoscopic tunnelling and myotomy more challenging, but do not prevent successful POEM.¹ Contraindications for POEM include severe cardiopulmonary disease or other serious disease associated with unacceptable surgical risk, pseudoachalasia, and failure to create a submucosal tunnel because of severe fibrosis and adhesion.¹ Severe oesophagitis and/or a very large ulcer in the lower oesophagus are also considered a relative contraindication.¹

The conventional POEM procedure involves four key steps: an initial mucosal incision is made on the anterior wall of the oesophagus (performed in the 2 o'clock position about 10 cm above the oesophagogastric junction); a submucosal tunnel is created distally using a technique similar to that used for endoscopic submucosal dissection; myotomy is performed with selective dissection of the circular muscle layer; the mucosal entry is closed with hemostatic clips.¹

There have been a number of attempts to simplify the procedure and a few modifications have been successfully introduced. These include the following: an incision is made on the posterior wall in the 5 to 6 o'clock position (this makes surgery more convenient and faster as knife control is easier when incising the posterior versus anterior wall of the oesophagus); a full-thickness myotomy is performed (a circular myotomy preserving the longitudinal outer oesophageal muscle layer is often difficult to achieve as the longitudinal muscles are very thin and incomplete myotomy with possible fibrotic healing is considered a major reason for postoperative recurrence); a "push and pull" myotomy technique is employed (the knife tip is used to lift the longitudinal muscle fibres up towards the oesophageal lumen and full-section muscle bundles are sectioned by continuous cutting using pushing movements of the scope); water-jet assisted POEM is used (a hybrid knife that combines high-pressure injection with electrical cutting is used to reduce the time taken to perform the procedure).^{1,2} (**Figure**)

Numerous clinical studies have reported encouraging outcomes following POEM, with treatment success rates ranging from 82% to 100% with few serious adverse events (rate <10%). However, more long-term comparative studies are still needed.^{3,4}

POEM can also be performed for special cases such as the sigmoid type of achalasia in which the oesophageal lumen is significantly dilated and tortuous.¹ The technique also appears to be a promising new treatment for pediatric achalasia.^{1,5,6}

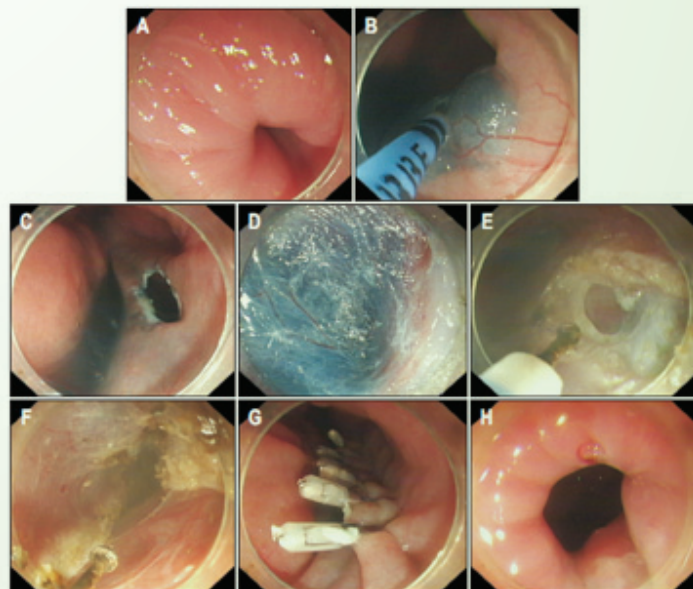
Common POEM complications include gas-related complications such as subcutaneous emphysema, pneumothorax, and pneumoperitoneum, pneumonitis, and mucosal injury.¹ Other rare but severe complications include delayed bleeding and gastrointestinal tract leakage due to early breakage of the clips used to close the tunnel entry.¹ Mucosal injury or perforation sometimes occurs, especially at the cardia, as a consequence of tissue adhesions and limited space.¹

The emergence of POEM marks a new branch of therapeutic endoscopy that involves a number of novel procedures utilizing the submucosal tunnel as an operating space. The future of flexible endoscopy is not only operating in the natural orifice but also within and outside the gastrointestinal wall.¹

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Figure. Water-jet assisted peroral endoscopic myotomy performed using modified techniques



A= Cardiac stricture; B=Submucosal injection in the 5- to 6-o'clock position using a water jet-assisted hybrid knife; C=Mucosal incision made on the posterior wall; D=Creation of the submucosal tunnel; E, F=Full-thickness myotomy; G=Closure of the mucosal entry point; H=Substantial reduction of lower esophageal sphincter tone after POEM.

H. pylori therapy circa 2015: Putting different options in perspective



Professor Ernst J. Kuipers

Professor of Medicine
Erasmus MC University Medical Center
Rotterdam, The Netherlands

Helicobacter pylori infection is the primary cause of different gastric conditions including chronic gastritis, peptic ulcer, gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma, rendering the eradication of *H. pylori* important in the prevention and management of gastric disease.

H. pylori eradication

H. pylori eradication is indicated in gastric cancer prevention and should be considered in patients with high-risk gastritis (eg, severe pan-gastritis, corpus-predominant gastritis, severe atrophy) as recommended by the Maastricht guidelines.¹ The Kyoto global consensus report on *H. pylori* gastritis also recommended that "depending on the epidemiological context, it is appropriate to search and screen for *H. pylori* gastritis at an age before development of atrophic gastritis and intestinal metaplasia" and suggested *H. pylori* eradication as the first-line treatment for *H. pylori*-infected dyspeptic patients.²

It is important to note that not all peptic ulcer disease is associated with *H. pylori* infection. For example, the concomitant use of nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 (COX-2) inhibitors or low-dose aspirin with selective serotonin reuptake inhibitors, steroids or aldosterone antagonists has been shown to significantly increase the risk of upper gastrointestinal bleeding and is one of the causes of idiopathic ulcer disease.³ Therefore, careful evaluation of the underlying cause of gastric disease is important for optimal treatment selection.

H. pylori eradication may improve various extra-gastric conditions. Unexplained iron-deficiency anaemia has been associated with *H. pylori* infection, and a meta-analysis of randomized controlled trials has suggested that treatment of *H. pylori* infection may be effective in improving anemia and iron status in patients with iron-deficiency anaemia.⁴ A systematic review also showed that *H. pylori* eradication improved platelet count in patients with immune thrombocytopenic purpura with an overall response of >50%.⁵

Overview of *H. pylori* therapies

Combination therapy is required in the treatment of *H. pylori* infection and is usually given as triple or quadruple therapies (Table). The standard triple therapy involves the concurrent use of a proton-pump inhibitor (PPI) with amoxicillin (1g bid) and clarithromycin (500 mg bid). High-dose PPI (eg, 2x40 mg bid) and prolonged treatment duration (10–14 days) have been shown to increase the eradication rate^{6,7} and the addition of probiotics such as lactobacilli has been suggested to improve eradication rate and reduce side effects.⁸

Due to the widespread occurrence of antibacterial resistance, quadruple therapies, either bismuth-based (eg, three antimicrobials or a PPI plus two antimicrobials) or non-bismuth-based (eg, a PPI with three antimicrobials), are becoming increasingly common as both primary and rescue treatments in the eradication of *H. pylori*.

Non-bismuth-based quadruple therapies are categorized as sequential, hybrid, or concomitant treatments depending on the dosing schedule. Similar overall eradication rates have been observed between hybrid and sequential therapies but the efficacy was highly dependent on geographical location.⁹ Data from an ongoing meta-analysis study showed that sequential quadruple therapy achieves higher eradication rates compared to standard triple therapy (although no differences were observed when the latter therapy was extended to 14 days).¹⁰

Table. Therapeutic agents used in *H. pylori* eradication

Drug class	Drug	Triple therapy	Quadruple therapy
		Dose	Dose
Acid suppression	proton pump inhibitor	20-40 mg bid	20-40 mg bid
Standard antimicrobials	bismuth compound	2 tablets bid	2 tablets bid
	amoxicillin	1 g bid	1 g bid
	metronidazole	500 mg bid	500 mg tid
	clarithromycin	500 mg bid	500 mg bid
	tetracycline		500 mg qid
Salvage antimicrobials	levofloxacin	300 mg bid	300 mg bid
	rifabutin	150 mg bid	
	furazolidone	100 mg bid	
	doxycycline		100 mg bid
	nitazoxanide		1 g bid

Adapted from Kuipers EJ & Blaser MJ. Cecil Textbook of Medicine 2015.

Bismuth is not readily available in many countries at present, but there is evidence to support bismuth-based quadruple therapies as effective treatment of *H. pylori* disease. Bismuth-based quadruple therapy with PPI and standard antibiotic combinations (ie, amoxicillin with clarithromycin or metronidazole) has been shown to be a highly effective first-line *H. pylori* treatment, achieving a cure rate of up to 97%.¹¹ In addition, bismuth-based quadruple therapy with PPI and levofloxacin was shown to be an effective and safe second-line *H. pylori* rescue treatment after failure of standard triple or non-bismuth quadruple therapy.¹²

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Relationship between hepatocellular carcinoma development and serum viral markers in patients with undetectable serum HBV DNA level while on nucleos(t)ide analogues (Summary of Thesis 2015)



Dr. Ka-Shing Cheung

Department of Medicine
The University of Hong Kong
Queen Mary Hospital
Hong Kong

Introduction

Hepatitis B virus (HBV) infection is one of the commonest infections worldwide with 248 million people being HBV carriers.¹ It is estimated that more than 1 million people die from HBV-related diseases every year.^{2,3} The major complications include cirrhosis which may lead to hepatic decompensation and hepatocellular carcinoma (HCC).⁴ There are various risk factors for the development of HCC. Serum HBV DNA is well recognized to play a major role.⁵ Subjects with low serum HBV DNA levels (< 2,000 IU/mL) have a lower risk of HCC development compared with those with high DNA levels ($\geq$ 2,000 IU/mL).^{5,6} However, patients with HBV DNA levels < 2,000 IU/mL are still at risk of developing HCC with an annual incidence rate of 0.06%.⁷

Recent studies have shown that HBsAg quantification (a cutoff value of $\geq$ 1,000 IU/mL) can predict HCC development in treatment-naïve subjects with serum HBV DNA levels < 2,000 IU/mL.^{8,9}

Linearized HBsAg (HQ-HBsAg) is measured by a novel assay, which detects both the outer epitope (determinant 'a') and the inner epitope (which is embedded inside the lipid bilayer of the viral envelope). It has a higher sensitivity of detection (lower limit of detection of 0.005 IU/mL) than conventional HBsAg assays (lower limit of detection of 0.05 IU/mL).^{10,11} There is strong correlation between HBsAg and HQ-HBsAg levels in hepatitis B e antigen (HBeAg)-negative infection.¹² However, the role of HQ-HBsAg in HCC development has yet been studied.

Hepatitis B core-related antigen (HBcrAg) is another novel viral marker which detects a common amino-acid sequence shared by HBeAg, hepatitis B core antigen and a 22-kDa precore protein.¹³ Production of the amino-acid sequence depends on the level of transcription and translation of the HBV precore/core gene.¹³ HBcrAg correlates well with serum HBV DNA, intrahepatic HBV DNA, covalently closed circular DNA (cccDNA), as well as histologic severity.¹⁴ It can predict HCC development in patients who are either treatment-naïve or taking nucleos(t)ide analogue (NA) therapy.¹⁵ In patients who have undergone treatment (resection or percutaneous ablation) for HCC, it also serves to predict HCC recurrence.¹⁶

However, there are currently no studies investigating whether quantification of conventional HBsAg, HQ-HBsAg and HBcrAg levels are useful in predicting HCC development in patients who have achieved undetectable serum HBV DNA levels on NA therapy. The number of chronic HBV carriers taking NA therapy has been growing, and with the use of more potent NA (entecavir and tenofovir), a majority of them are able to have profound viral suppression with HBV DNA levels below detection limit. However, antiviral therapy can only reduce but not eliminate the risk of HCC¹⁷ and the risk factors for predicting HCC in this special population have not been well defined.

The aim of this study is to determine whether there are associations between the levels of the two viral proteins, HBsAg (using conventional and the new HQ-HBsAg assays) and HBcrAg with the development of HCC in patients who have already achieved the best viral suppression with undetectable HBV DNA by NA therapy.

Patients and Methods

Patient recruitment

The study patient cohort was recruited from the Hepatology Clinic, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, from January 2007 to November 2014.

We recruited 76 HBV carriers who developed HCC despite achieving undetectable serum HBV DNA levels with NA therapy for more than one-year before the diagnosis of HCC. Other inclusion criteria included HBsAg positivity ≥ 6 months, age ≥ 18 years, follow-up at our clinic ≥ 1 year, no significant alcohol consumption (> 30 g per day for men and > 20 g per day for women), no concomitant HCV infection or other chronic liver diseases including autoimmune hepatitis, primary biliary cirrhosis, Wilson's disease and no past history of HCC.

One hundred and fifty-two chronic HBV carriers without HCC were recruited as controls. They were matched with the 76 HCC patients by age, gender, baseline HBeAg status, cirrhosis status, serum HBV DNA levels and duration of NA therapy in a 2:1 ratio.

Post-treatment serum HBsAg, HQ-HBsAg and HBcrAg levels (at the time of HCC diagnosis for the HCC group and at the time when the control group had the same matched duration of therapy as the HCC group) were analyzed and compared between the two groups. In addition, the pre-treatment (within 1 year before commencement of NA therapy) levels of HBcrAg and HBV DNA levels were determined in both groups.

The study protocol was approved by the Institutional Review Board, the University of Hong Kong and West Cluster of Hospital Authority, Hong Kong. The disposition of the patients recruited is illustrated in **Figure 1**.

Surveillance and diagnosis of HCC

Patients were followed up at least every 6 months with regular monitoring of HBeAg, anti-HBe, HBsAg, anti-HBs, platelet count, alanine aminotransferase (ALT), bilirubin, albumin, international normalized ratio (INR), alpha-fetoprotein (AFP) and serum HBV DNA levels. Patients requiring HCC surveillance as suggested by standard criteria¹⁸ were advised for ultrasonography of the liver at 6-month intervals.

The diagnosis of HCC was confirmed by histology or typical radiological features (arterial enhancement and venous wash-out by triphasic computed tomography [CT] scan or contrast magnetic resonance imaging [MRI]). Cirrhosis was defined by imaging (USG/CT/MRI showing small, nodular liver, or features of portal hypertension namely splenomegaly, varices and ascites), transient elastography by fibroscan with score > 11 kilopascals with inter-quartile range (IQR) to liver stiffness < 0.3 or clinical features including thrombocytopenia, coagulopathy, gastroesophageal varices, ascites and hepatic encephalopathy.

Treatment

The indications of prescribing NA therapy to patients include (1) evidence of active hepatitis (either histologically proven or with raised ALT) associated with high serum HBV DNA levels ($\geq 2,000$ IU/mL) or (2) evidence of cirrhosis with detectable serum HBV DNA.¹⁹

Quantification of HBV DNA, HBsAg, HQ-HBsAg, HBcrAg levels

Serum HBV DNA level was measured by the Cobas Taqman HBV Test (Roche Diagnostics, Branchburg, NJ, USA) with a lower limit of detection of 20 IU/mL. Serum HBsAg level was measured using Elecsys HBsAg II quant assay (Roche Diagnostics) with a lower limit of detection of 0.05 IU/mL. By using a chemiluminescent enzyme immunoassay (CLEIA) Lumipulse G1200 automated analyzer (Fujirebio Inc, Tokyo, Japan) as previously described,¹⁰ serum HQ-HBsAg level was quantified with a lower limit of detection of 0.005 IU/mL. Serum HBcrAg level was measured using the same CLEIA method as described previously,¹⁴ with a lower limit of detection of 1 kU/mL.

Sample size estimation

According to Tseng et al.,⁸ the crude hazard ratio of HCC development in HBV carriers with serum HBsAg level ≥ 1000 IU/mL was 3.2 compared with those with serum HBsAg level < 1000 IU/mL. With a power of 90%, alpha risk of 5% and a control: case ratio of two, the estimated sample sizes for the HCC group and control (non-HCC) group were 60 and 120 respectively.

Statistical analyses

All statistical analyses were performed using IBM SPSS version 19.0 (SPSS Inc, Chicago, Illinois). Continuous variables were expressed as median IQR. Serum viral marker results were expressed in logarithm for evaluation of correlation. The Mann-Whitney U-test was applied to compare continuous variables of the two groups. The Chi-square test or Fisher's exact test when appropriate, was applied for comparing categorical variables. Spearman's bivariate correlation was used to test the correlation between the clinical and laboratory parameters. For viral marker(s) that show statistically significant difference between the HCC and control groups, the receiver operating curve was created by plotting the true positive rate against the false positive rate at various values. The area under receiver operating curve (AUROC) was then calculated to measure the overall prediction accuracy. By maximizing the Youden's index (i.e. sensitivity + specificity - 1) from the AUROC analysis, optimal cut-off values for predicting HCC development were derived. The accuracy of using these cut-off values was then assessed by the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Factors with p-value < 0.10 were included in multivariate analysis. Statistical significance was defined by a two-sided p-value of < 0.05 .

Figure 1. Flow chart of disposition of patients

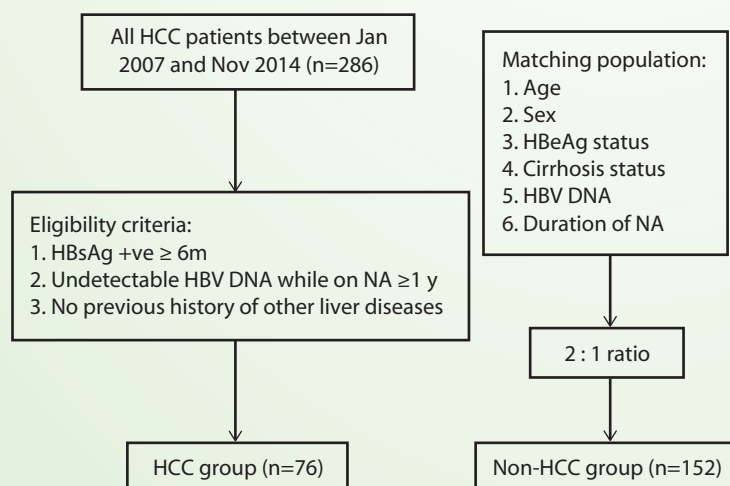


Table 1. Demographics of 228 HBV carriers

	HCC (n=76)	Non-HCC (n=152)	p value
Age [#] , years	61.3 (54.8-66.8)	60.7 (56.6-65.8)	0.918
Male [#] , n (%)	63 (82.9%)	126 (82.9%)	1.00
HBeAg-negative [#] , n (%)	73 (96.1%)	146 (96.1%)	1.00
Cirrhosis [#] , n (%)	44 (57.9%)	88 (57.9%)	1.00
Albumin, g/L	44 (41-46)	44 (42-46)	0.220
Bilirubin, umol/L	12 (8-17)	11 (8-15)	0.258
ALT, U/L	28 (20-38)	25 (20-31)	0.053
Platelet, x 10 ⁹ /L	159 (101-198)	165 (133-208)	0.044
INR	1.1 (1-1.1)	1.0 (1-1.1)	0.249
AFP, ng/mL	11 (5-28)	3 (2-4)	<0.001
Undetectable DNA [#] , n (%)	76 (100%)	152 (100%)	1.00
Duration of therapy [#] , years	3.5 (2.0-5.0)	3.6 (2.2-5.1)	0.555

Continuous variables expressed as median (interquartile range)

HBV hepatitis B virus, HCC hepatocellular carcinoma, ALT alanine aminotransferase, INR international normalised ratio, AFP alpha-fetal protein

[#] Matched variables

Results

Patient Characteristics

Table 1 depicts the demographics of the 228 patients (76 HCC patients; 152 controls). Age, gender, HBeAg status, cirrhosis status, serum HBV DNA level, and duration of therapy were well matched between the two groups. There were no significant differences in serum albumin, bilirubin, ALT, and INR levels. There was a small difference in the median platelet counts between HCC and control groups (156 x10⁹/L and 163 x10⁹/L, respectively, p=0.044). A significantly higher median AFP level was also noted in HCC than control group (11 and 3 ng/mL, respectively, p < 0.001). **Table 2** shows the demographics of patients stratified according to the cirrhosis status.

Eighty-three percent were males, 96.1% were HBeAg-negative and 57.9% had cirrhosis. The median age of the HCC group was comparable with that of control group (61.3 and 60.7 years, respectively, p=0.918). These two groups also had similar median duration of therapy (3.5 and 3.6 years, respectively, p=0.555). Seventy eight percent of the HCC group received either entecavir or tenofovir compared with 91.4% in the non-HCC group (**Table 3**).

Correlation between serum viral markers and age

There was a strong correlation between HBsAg and HQ-HBsAg levels (r=0.97, p <0.001). The correlations between HBsAg, HQ-HBsAg and HBcrAg levels were weak (r=0.32 and 0.33, respectively, p <0.001). All three viral markers had a weak inverse correlation with age (r=-0.19, -0.18, -0.22, respectively, all p < 0.05). Since HBsAg and HQ-HBsAg levels were highly correlated, only HQ-HBsAg levels will be included in the following analyses.

Comparison of post-treatment HQ-HBsAg and HBcrAg levels between HCC and control groups

The median HQ-HBsAg levels were 588 IU/mL (IQR: 152-1228 IU/mL) and 536 IU/mL (IQR: 198-1167 IU/mL) in the HCC and control groups respectively (p=0.766). HCC group had a significantly higher median HBcrAg level compared to the control group (10.2 and 1.7 kU/mL, respectively, p=0.005) (**Figure 2A**). Undetectable HBcrAg level was noted in 23.7% and 40.8% of the HCC group and control groups respectively (p=0.011).

Table 2. Demographics of 228 HBV carriers stratified according to cirrhosis status

	Cirrhosis-positive (n=132)			Cirrhosis-negative (n=96)		
	HCC (n= 44)	Non-HCC (n =88)	p value	HCC (n = 32)	Non-HCC (n=64)	p value
Age [#] , years	61.1 (56.8-67.8)	62.3 (58.4-65.6)	0.958	61.3 (50.4-66.7)	60.2 (51.0-67.4)	0.929
Male [#] , n (%)	39 (88.6%)	78 (88.6%)	1.00	24 (75.0%)	48 (75.0%)	1.00
HBsAg-ve [#] , n (%)	42 (95.5%)	84 (95.5%)	1.00	31 (96.9%)	62 (96.9%)	1.00
Albumin, g/L	42 (40-46)	44 (42-46)	0.119	45 (42-46)	45 (42-46)	0.842
Bilirubin, umol/L	12 (8-18)	12 (9-16)	0.860	12 (8-16)	10 (7-14)	0.115
ALT, U/L	33 (23-43)	25 (21-31)	0.007	25 (19-32)	24 (19-32)	0.904
Platelet, x 10 ⁹ /L	117 (187-168)	145 (116-182)	0.029	183 (157-216)	194 (170-234)	0.137
INR	1.1 (1.0-1.1)	1.1 (1.0-1.1)	0.841	1.1 (1.0-1.1)	1.0 (1.0-1.1)	0.100
AFP, ng/mL	10 (5-20)	3 (2-4)	0.001	15 (6-47)	3 (2-4)	0.001
Undetectable DNA [#] , n (%)	100%	100%	1.00	100%	100%	1.00
Duration of therapy [#] , years	3.2 (1.8-5.0)	3.4 (2.1-5.0)	0.652	3.6 (2.2-5.3)	3.8 (2.5-5.6)	0.611

Continuous variables expressed as median (interquartile range)

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; INR, international normalised ratio; AFP, alpha-fetal protein

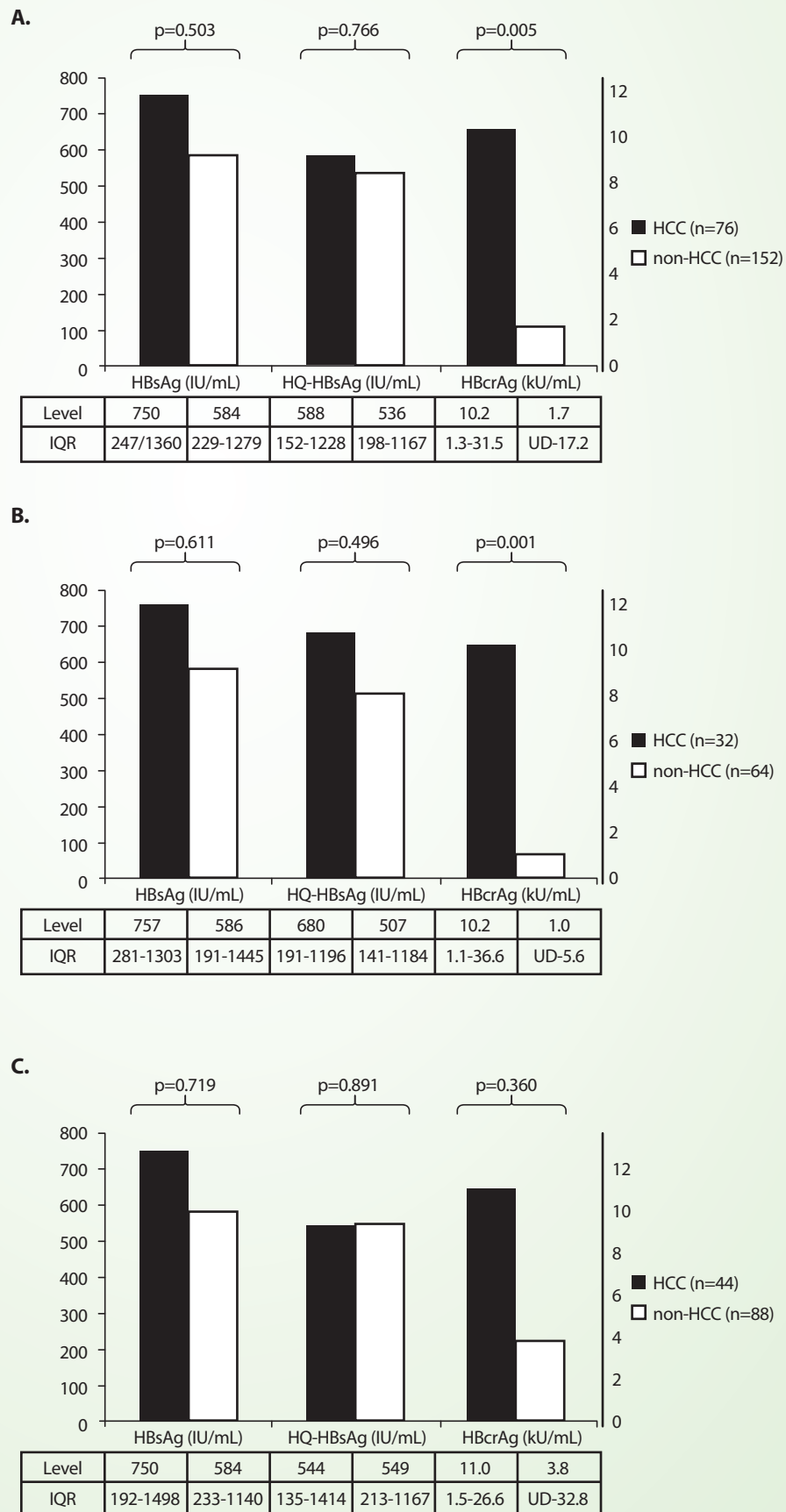
[#] Matched variables

Table 3. Different NA therapies in HCC and control groups

	HCC (n=76)	Non-HCC (n=152)
Entecavir	56 (73.7%)	132 (86.8%)
Lamivudine	9 (11.8%)	6 (3.9%)
Telbivudine	2 (2.6%)	1 (0.7%)
Adefovir	6 (7.9%)	6 (3.9%)
Tenofovir	3 (3.9%)	7 (4.6%)

NA, nucleos(t)ide analogue; HCC, hepatocellular carcinoma

Figure 2. Comparison of post-treatment viral marker levels between (A) HCC and control groups (whole cohort); (B) HCC and control groups (without cirrhosis); (C) HCC and control groups (with cirrhosis)



HCC, hepatocellular carcinoma; HBsAg, hepatitis B surface antigen; HQ-HBsAg, linearized hepatitis B surface antigen; HBcrAg, hepatitis B core-related antigen; IQR, interquartile range; UD, undetectable

Figure 2B and 2C show the comparison of the viral marker levels between the HCC and control groups according to the cirrhosis status. In the cirrhosis-negative group ($n=96$), the difference in the median HQ-HBsAg level was insignificant (680 and 507 IU/mL, respectively, $p=0.496$) while the median HBcrAg level remained significantly higher in the HCC group (10.2 and 1 kU/mL, respectively, $p=0.001$). In the cirrhosis-positive group ($n=132$), there was no significant difference in the median HQ-HBsAg level (544 and 549 IU/mL, respectively, $p=0.891$). Although there was higher median HBcrAg level in the HCC group compared with the control group (11.0 and 3.8 kU/mL, respectively), it was not statistically significant ($p=0.360$).

The role of post-treatment HBcrAg in predicting HCC development

Using HBcrAg to predict HCC in HBV carriers who achieved undetectable serum HBV DNA while on NA therapy, the AUROC was 0.61 (95% CI: 0.54-0.69) (**Figure 3A**). For the non-cirrhotic group, the AUROC became 0.70 (95% CI: 0.58-0.81) (**Figure 3B**). The sensitivities, specificities, PPV, and NPV by using HBcrAg as a predictive marker are depicted in **Table 4**. The optimal cutoff values were derived according to the maximal Youden's index. For the whole cohort, by using a cutoff value of ≥ 7.8 kU/mL, the sensitivity, specificity, PPV and NPV was 57.9%, 70.4%, 49.4%, and 77.0% respectively, and the odds ratio (OR) of HCC development was 3.27 (95% CI: 1.84-5.80). In the non-cirrhotic patients, a cutoff value of ≥ 7.9 kU/mL yielded a sensitivity of 62.5%, specificity of 78.1%, PPV of 58.8%, and NPV of 80.6%. The OR of HCC development in this group of patients was 5.95 (95% CI: 2.35-15.07).

Comparison of pre-treatment HBcrAg levels between the HCC and control groups

As post-treatment HBcrAg was the only viral marker found to be associated with HCC development, we proceeded to measure the pre-treatment HBcrAg level. The HBcrAg levels were measured in 58 HCC and 116 control patients in which pre-treatment stored samples were retrievable. The HCC group had a significantly higher median HBcrAg level compared to the control group (279.0 and 35.4 kU/mL, respectively, $p=0.005$).

Pre-treatment HBcrAg levels were then compared between the HCC and non-HCC groups according to the cirrhosis status. For cirrhosis-negative group ($n=78$), the difference in the median HBcrAg level remained significantly higher in HCC group (240.8 and 6.9 kU/mL, respectively, $p=0.030$). For cirrhosis-positive patients ($n=96$), there was no significant difference between the HCC and control groups (389.6 and 108.4 kU/mL, respectively, $p=0.071$). By using a cutoff value of ≥ 47.1 kU/mL (as derived from the maximal Youden's index), the AUROC was 0.63 (95% CI: 0.54-0.72) and the OR of HCC development was 3.29 (95% CI: 1.66-6.52).

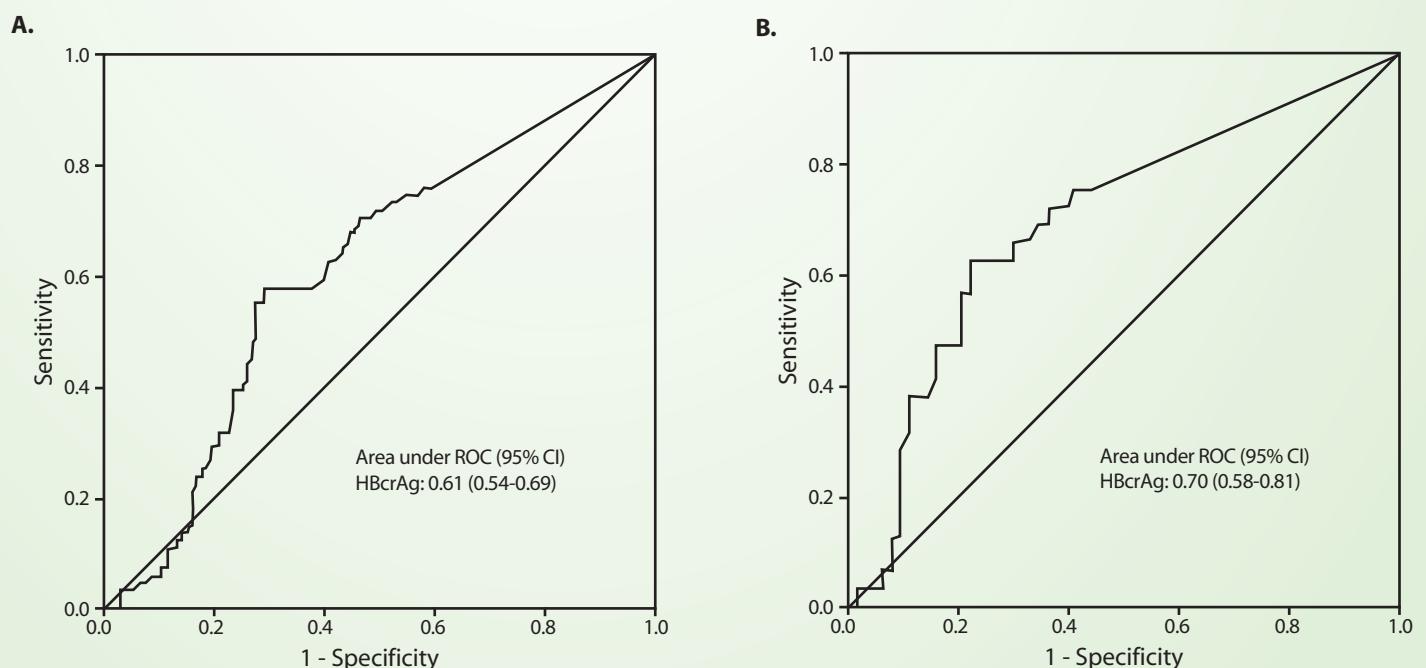
Comparison of pre-treatment HBV DNA levels between the HCC and control groups

There existed a significant difference in the pre-treatment HBV DNA levels between the HCC and control groups (6.1 and 5.7 log IU/mL, respectively, $p=0.039$). By using a cutoff value of ≥ 5 log IU/mL, the OR of HCC development of was 2.39 (95% CI: 1.11-5.36).

Comparison of rates of drop in HBcrAg levels between HCC and control groups

The HCC group had a significantly faster rate of drop in HBcrAg level (i.e. the difference between pre-treatment and post-treatment HBcrAg divided by the duration of NA therapy) than the control group (79.5 kU/mL per year and 7.3 kU/mL per year, respectively, $p=0.016$).

Figure 3. AUROC of post-treatment HBcrAg for HCC prediction in (A) HBV carriers (whole cohort); (B) HBV carriers (non-cirrhotic)



AUROC, area under receiver operating curve; HBcrAg, hepatitis B core-related antigen; HCC, hepatocellular carcinoma; HBV, hepatitis B virus; CI, confidence interval

Table 4. Predictive accuracy of HCC for different cutoff values of post-treatment HBcrAg in different groups of patients

	Whole cohort (HBcrAg ≥ 7.8 kU/mL)	Cirrhosis-negative (HBcrAg ≥ 7.9 kU/mL)
Sensitivity	57.9%	62.5%
Specificity	70.4%	78.1%
Positive-predictive value	49.4%	58.8%
Negative-predictive value	77.0%	80.6%

HCC, hepatocellular carcinoma; HBcrAg, hepatitis B core-related antigen

Table 5. Univariate and multivariate analysis of pre-treatment factors associated with HCC development in patients with undetectable serum HBV DNA while on NA therapy

	Crude OR (95% CI)	p value	Adjusted OR (95% CI)	p value
HBcrAg level (kU/mL)				
< 47.1	1.0		1.0	
≥ 47.1	3.29 (1.66-6.52)	0.001	3.53 (1.45-8.62)	0.005
HBV DNA level (log IU/mL)				
< 5	1.0		1.0	
≥ 5	2.39 (1.11-5.36)	0.024	1.74 (0.70-4.37)	0.236

HCC, hepatocellular carcinoma; HBV, hepatitis B virus; NA, nucleos(t)ide analogue; OR, odds ratio; HBcrAg, hepatitis B core-related antigen

Pre-treatment factors affecting HCC risk

As age, gender, HBeAg and cirrhosis status were well matched, pre-treatment HBV DNA levels and HBcrAg were the only factors found to be associated with HCC development by univariate analysis. Further multivariate analysis showed that pre-treatment HBcrAg level ≥ 47.1 kU/mL remained as an independent risk factor for HCC with an OR of 3.53 (95% CI: 1.45-8.62), but not pre-treatment DNA levels (Table 5).

Discussion

To our best knowledge, this is the first study to investigate the association between HBV serologic markers (HBsAg, HQ-HBsAg and HBcrAg levels) and the development of HCC in HBV patients achieving the optimal HBV DNA suppression under NA therapy.

High HBsAg has been shown to be associated with HCC development in treatment-naïve HBV carriers who have serum HBV DNA level $< 2,000$ IU/mL.⁸ However, in the present study, such relationship was not observed in our patients (with both the conventional HBsAg and HQ-HBsAg measurements) who achieved undetectable serum HBV DNA while on NA therapy. The difference in the findings between the two studies may be due to the differences in the patient population. Firstly, the former study

analyzed the subgroup of patients with serum HBV DNA level $< 2,000$ IU/mL. In fact, 59% of patients had HBV DNA levels between 200 and 1999 IU/mL whereas all the patients in the present study had HBV DNA levels < 20 IU/mL. Secondly, the former study excluded patients who had underlying cirrhosis. Thirdly, patients in the former study were treatment-naïve, while all the patients in the present study received NA therapy because of either active hepatitis or cirrhosis. Therefore, patients in the present study had a pre-existent higher risk of HCC development. Nevertheless, the findings of the present study suggest that HBsAg has no predictive role in HCC development in patients who are on NA treatment with good viral suppression.

HBcrAg is another viral marker that has been shown to be associated with HCC development in different scenarios.^{15,16} Our study is the first to study patients with undetectable HBV DNA under NA treatment, in whom the risk factors for HCC development are less well-defined. We found that both pre- and post-treatment HBcrAg were important risk factors in HBV carriers on NA therapy, as illustrated by the significant difference in the median values observed between the HCC and control groups (pre-treatment: 279.0 and 35.4 kU/mL, respectively; post-treatment: 10.2 and 1.7 kU/mL, respectively). However, there

was no statistically significant difference in pre- and post-treatment HBcrAg levels when only patients with cirrhosis were analyzed (although the median value of HBcrAg levels was still higher in cirrhotic patients with HCC). It may indicate that the value of HBcrAg in predicting HCC was relatively lower in patients with established cirrhosis. Cirrhosis per se is a major risk factor for HCC development (HCC incidence: 0.3-0.6% per year in non-cirrhotic patients; 3-8% per year in cirrhotic patients).²⁰ This may render the power of the present study insufficient to isolate the potential role of HBcrAg in cirrhotic patients. Further studies with larger sample sizes of cirrhotic patients are required.

One interesting observation from this study is that the rate of drop in HBcrAg level in HCC group was faster than that in control groups (79.5 kU/mL per year and 7.3 kU/mL per year, respectively). This may be because the HCC group had a much higher pre-treatment HBcrAg levels and was able to achieve greater suppression of HBcrAg levels once given NA treatment.

The OR of HCC development with post-treatment HBcrAg level $\geq$ 7.8 kU/mL was 3.27 (95% CI: 1.84-5.80). With this cutoff value, the NPV to rule out HCC development was 77.0%. At a cutoff value of $\geq$ 7.9 kU/mL, the NPV reached 80.6% in non-cirrhotic patients. If the HBcrAg level is below the suggested cutoff value, the chance of HCC development will be low. All these results suggest that HBcrAg level has a role in stratifying the risk for the development of HCC in patients who with undetectable HBV DNA under NA therapy.

It is not known whether HBcrAg plays a direct functional role in hepatocarcinogenesis. We hypothesize that, compared with HBsAg, HBcrAg may be a better marker for the level of intrahepatic replication, which may be associated with hepatocarcinogenesis. Unlike HBsAg which is the translational product from the mRNAs for the large, middle, and small hepatitis B surface proteins and is often produced in excess quantities, HBcrAg is the translational product from both the e mRNA and the core mRNA, the latter of which also serves as the pregenomic RNA. Thus, compared with HBsAg level, HBcrAg level may have a higher correlation with the level of pregenomic RNA production, which reflects the level of cccDNA inside the hepatocytes.¹⁴ The application of HBcrAg should therefore be further studied in particular for whether it can increase the accuracy of risk prediction of development of HCC and cirrhosis, apart from the commonly used surrogates (e.g. serum HBV DNA level). Furthermore, its role in prediction of HCC development in those with undetectable serum HBV DNA should also be further evaluated.

There are several limitations of the present study. Firstly, as it is not a prospective study, it may be susceptible to various biases. However, the major risk factors of HCC development (e.g. age, sex, cirrhosis status, HBeAg status) were well matched with the control group. Secondly, HBV genotyping (which is a risk factor for HCC development)²¹ was not performed in this study.

In conclusion, the present study shows that HBcrAg (but not HBsAg or HQ-HBsAg) could predict HCC risk in HBV carriers with undetectable serum HBV DNA while receiving NA therapy. HBcrAg

may serve as a novel risk marker for HCC in this special group of patients. Future prospective studies should be performed to further define the role of HBcrAg levels in other populations of chronic HBV infection.

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World Cancer Research Fund CUP Report on Stomach Cancer

<http://wcrf.org/int/research-we-fund/continuous-update-project-findings-reports/stomach-cancer>

Welcome! New Fellow and Members

Honorary Fellow



**Professor Suk-Kyun Yang,
M.D.**

*Department of Gastroenterology
University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea*

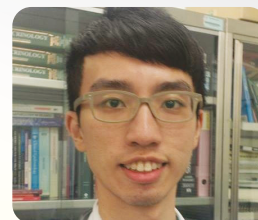
Member



Dr. Yip-Shun LAM

*Department of Medicine
Queen Elizabeth Hospital
Kowloon, Hong Kong*

Member



Dr. Yau-Yui LAM

*Department of Medicine
Queen Elizabeth Hospital
Kowloon, Hong Kong*

Coming Soon

18th JOINT ANNUAL SCIENTIFIC MEETING 2016 Sunday, 28 August 2016

Date : Sunday, 28 August 2016

Venue : The Ballroom, Level 7
Cordis, Hong Kong at Langham Place
555 Shanghai Street, Mongkok
Kowloon, Hong Kong

Organizing Chairman: Dr. Jodis Ting-Wa Lam

Sponsors: AbbVie, AstraZeneca, Gilead, Menarini, Novartis, Otsuka, Takeda

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
Hong Kong IBD Society

Topics	Speakers
New treatments of autoimmune liver diseases	Dr. George Webster (UK)
FMT - current practice and future perspectives	Dr. Kelvin L.Y. Lam (PWH)
Controversies in management of primary sclerosing cholangitis	Dr. George Webster (UK)
To be Confirmed	Dr. Marta Jimenez (Spain)
Sessile Serrated Adenoma/Polyp	Prof. Wai-Keung Leung (HKU)
To be Confirmed	Dr. Marta Jimenez (Spain)
Recent Advances In the Endoscopic Biliary Intervention	Dr. Raymond S.Y. Tang (CUHK)
Recent advances in biologic therapy in IBD	Dr. Heyson C.H. Chan (PWH)

35th Annual General Meeting cum Scientific Meeting of The Hong Kong Society of Gastroenterology

Date: 31 March 2016

Venue: Cordis, Hong Kong at Langham Place, Kowloon

Organizing Chairperson: Dr. Wai-Fan Luk

Sponsored by: Abbott, AbbVie, AstraZeneca, Eisai, Ferring, Gilead, A.Menarini, Novartis & Takeda

The annual scientific meeting was successful and attended by 133 healthcare professionals. The honorary fellowship of our Society was bestowed upon distinguished guest, Prof. Suk-Kyun Yang, The Chief of Department of Gastroenterology, Asan Medical Center, Seoul, South Korea. He is among the 19 honorary fellows of our Society who are renowned scholars in the specialty.

Prof. Yang delivered an enlightening lecture on “Inflammatory Bowel Disease in Korea” and joined a panel discussion with Prof. Wai-Keung Leung and Dr. Hester Y.S. Cheung on a case with “IBD” presented by Dr. Patrick K.F. Tsang. Delegates participated actively throughout the discussion.

The annual general meeting then followed was attended by 42 fellows and members during which the Society’s annual report and financial statements for the year of 2015 were presented. Seven fellows were elected to the Council for the term of 2016-2018.

A Certificate of Appreciation was presented to each of the nine sponsors in appreciation of their support and contributions towards the Meeting and they were Abbott, AbbVie, AstraZeneca, Eisai, Ferring, Gilead, A.Menarini, Novartis and Takeda.

Most participants stayed for the dinner and continued exchanging their views.



More photographs are available online <http://www.hksge.org/photogallery.htm>

Major Meetings

30 June – 3 July 2016

11th Edition of GIHeP Singapore 2016

Organizers: Gastroenterological Society of Singapore
Location: Singapore
Website: www.gihp.org.sg

6-9 July 2016

48th Annual Meeting of the European Pancreatic Club

Organizer: European Pancreatic Club
Location: Liverpool, United Kingdom
Website: <http://epc2016.com/>

7-9 July 2016

The 4th Annual Meeting of Asian Organization for Crohn's & Colitis

Location: Kyoto, Japan
Website: <http://aocc2016.org/>

8-10 July 2016

2nd Singapore Society of Oncology AGM

Organizer: Singapore Society of Oncology
Location: Singapore
Website: www.bascoasia.com/#home/z8a7b

8-9 July 2016

3rd Athens International Symposium 2016 – Gastrointestinal Cancer

Organizer: Hellenic Society of Gastroenterology
Location: Athens, Greece
Website: <http://athens-symposium2016.com/>

8-10 July 2016

7th Asia-Pacific Primary Liver Cancer Expert (APPLE) Meeting

Host: Hong Kong Liver Cancer and Gastrointestinal Cancer Foundation
Location: Crowne Plaza Hong Kong
Website: www.applecongress2016.org/index.html

20-21 July 2016

Singapore Gastric Cancer Consortium 9th Annual Scientific Meeting: Latest Advances in Gastric Cancer Research

Location: Singapore
Website: www.sgcc.sg/asm

26-27 August 2016

APAGE 2nd Clinical Forum on Inflammatory Bowel Disease 2016: IBD in the Asia Pacific

Organizer: The Gastroenterological Association of Thailand and Asian Pacific Association of Gastroenterology
Location: Chiang Mai, Thailand
Website: www.apage.org/files/APAGE_IBD_Aug2016.pdf

26-28 August 2016

FNM 2016 Federation Joint International Meeting

Organizer: Federation of Neurogastroenterology and Motility
Location: San Francisco, CA, USA
Website: www.esnm.eu/congresses/joint-international-meetings/

2-3 September 2016

Falk Symposium 204: Clinical Hepatology Practice in 2016: From Science to Therapy

Organizer: Falk Foundation
Location: Birmingham, United Kingdom
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

8-10 September 2016

26th World Congress of the International Association of Surgeons, Gastroenterologists and Oncologists (IASGO 2016)

Organizer: International Association of Surgeons, Gastroenterologists and Oncologists
Location: Seoul, Korea
Website: <http://iasgo2016.org/>

15-17 September 2016

XXIXth International Workshop on Helicobacter and Microbiota in Inflammation and Cancer

Organization: European Helicobacter and Microbiota Study Group (EHMSG)
Location: Magdeburg, Germany
Website: www.helicobacter.org/2016/

19-21 September 2016

15th World Congress of the International Society for Diseases of the Esophagus

Organizer: The International Society for Diseases of the Esophagus
Location: Singapore
Website: www.isde.net/singapore_2016_world-congress

22-24 September 2016

EUS2016, 20th International Symposium on Endoscopic Ultrasonography

Organizer: European Society of Gastrointestinal Endoscopy
Location: Budapest, Hungary
Website: www.eus2016.org

22-24 September 2016

APASL Single Topic Conference on Non-Responders: Chronic Viral Hepatitis, Liver Cirrhosis, HCC

Organized by: Asian Pacific Association for the Study of the Liver (APASL)
Location: Istanbul, Turkey
Website: www.apaslTurkey2016.org

29 September – 1 Oct 2016

10th Australasian Viral Hepatitis 2016 Conference

Location: Gold Coast Convention Centre, Queensland, Australia
Website: www.hepatitis.org.au/

30 September – 2 October 2016

Taiwan Digestive Disease Week (TDDW 2016)

Organizer: The Gastroenterological Society of Taiwan
Location: Taipei, Taiwan
Website: www.tddw.org/

10-12 October 2016

Australian Gastrointestinal Week 2016 – Innovations in Medicine

Organizers: Gastroenterological Society of Australia
Location: Adelaide, South Australia
Website: www.agw2016.org.au/

15-19 October 2016

24th UEG Week

Organizer: United European Gastroenterology (UEG)
Location: Vienna, Austria
Website: www.ueg.eu/week

14-19 October 2016

ACG 2016 Annual Scientific Meeting and Postgraduate Course

Organizer: American College of Gastroenterology (ACG)
Location: Las Vegas, Nevada, USA
Website: <http://acgmeetings.gi.org/>

21-22 October 2016

Falk Symposium 205: New Treatment Targets in Gut and Liver Diseases

Organizer: Falk Foundation
Location: Lucerne, Switzerland
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

2-5 November 2016 / 3-6 November 2016

Asian Pacific Digestive Week (APDW 2016) / Japan Digestive Disease Week (JDDW 2016)

Organizer: Organization of JDDW
Location: Kobe, Japan
Websites: www.apdw2016.org/ / www.jddw.jp/jddw2016/en/index.html

11-15 November 2016

The AASLD Liver Meeting

Organizer: The American Association for the Study of Liver Diseases
Location: Boston, USA
Website: www.aasld.org/events-professional-development/liver-meeting

17-19 November 2016

Gastro 2016: EGHG/WGO International Congress

Organizers: World Gastroenterology Organization, Emirates Gastroenterology & Hepatology Society
Location: Abu Dhabi, United Arab Emirates
Website: www.worldgastroenterology.org/meetings-and-events/wgo-international-conferences

22-25 November 2016

14th Annual International Congress: Frontiers in Intestinal and Colorectal Disease 2016

Organized by: St Mark's Hospital Academic Institute
Location: St Mark's Hospital, Middlesex, UK
Website: www.stmarksacademicinstitute.org.uk/courses/frontiers-in-intestinal-and-colorectal-disease/

23-25 November 2016

Annual Scientific Meeting 2016 of The New Zealand Society of Gastroenterology & NZNO Gastroenterology Nurses Section

Location: Hamilton, New Zealand
Website: www.gastro2016.co.nz

24-25 November 2016

Seoul International Digestive Disease Symposium (SIDDs 2016)

Organizers: Korean Society of Gastroenterology
Location: Seoul, Korea
Website: www.sidds.org/

6-8 December 2016

31st International Workshop on Therapeutic Endoscopy

Organizers: CUHK Institute of Digestive Disease, CUHK The Netherlands School of Nursing, Hong Kong Society of Digestive Endoscopy & CUHK Jockey Club Minimally Invasive Surgical Skills Centre
Location: Prince of Wales Hospital, Shatin, Hong Kong
Website: www.hksde.org/workshop.htm

15-18 December 2016

57th Annual Conference of Indian Society of Gastroenterology (ISGCON 2016)

Organizer: Indian Society of Gastroenterology
Location: Hotel Pullman, Aerocity, New Delhi, India
Website: <http://isgcon-2016.com/>

16-19 February 2017

ENDO 2017 World Congress of GI Endoscopy

Host: World Endoscopy Organisation
Location: Hyderabad, India
Website: www.endo-2017.org/

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

HKSge Secretariat

Room C, 7/F, Thomson Commercial Building, 8 Thomson Road, Wanchai, Hong Kong

Tel: (852) 2869 5933

Fax: (852) 2869 9533

E-mail: gastro@hksge.org

Website: www.hksge.org

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