Welcome to our December 2015 Newsletter!

During the year of 2015, The Hong Kong Society of Gastroenterology continued to promote the advancement of gastroenterology. Scientific meetings were organized in March, July and September. Our Society participated in the Medical Multispecialty Mega Conference and the IDD Forum. Two newsletters were published in 2015.

I would like to thank Dr. Annie O.O. Chan for organizing the Annual General Meeting cum Scientific Meeting 2015, Dr. Jodis T.W. Lam for organizing the 17th Joint Annual Scientific Meeting 2015, Professor Justin C.Y. Wu for editing the two newsletters, Professor Satish S.C. Rao, Dr. Charlie Lees, Dr. Arthur D.P. Mak, Dr. Kevin K.K. Yau and Dr. Siew C. Ng for their scientific updates in this newsletter. Last but not least, all the sponsors who rendered support and contributions to the Society throughout the year.

The next newsletter will be published in June 2016.

Merry Christmas and Happy New Year!

Dr. Wai Cheung Lao
President, The Hong Kong Society of Gastroenterology

Biofeedback Therapy for Dyssynergic Defecation

Learning objectives:
At the end of this session, participants should be able to:
1) Identify common symptom patterns, demographics, psychosocial issues, and how to diagnose dyssynergic defecation
2) Discuss and understand the role of biofeedback therapy in the treatment of Dyssynergic Defecation
Introduction
Disorders of evacuation are commonly encountered in clinical practice and affect at least 20% of the population. They include a spectrum of disorders that cause difficulty with defecation. Among them are functional disorders such as dyssynergic defecation, or mechanical/structural disorders such as rectocele, solitary rectal ulcer syndrome, excessive perineal descent, and rectal prolapse, or functional anorectal pain syndromes. Here, we will focus on recent advances in the evaluation and treatment of dyssynergic defecation. Dyssynergia is associated with significant psychological distress and impairment of quality of life. Patients with dyssynergia report a variety of complaints that include a constant feeling of incomplete evacuation, bloating, excessive straining, anal pain, feeling of blockage, and the need for digital maneuvers such as disimpaction or vaginal splitting. A detailed rectal exam can provide bedside evidence for the presence of dyssynergia.

Pathophysiology of Dyssynergic Defecation
Dyssynergia is an acquired behavioral disorder of defecation in 2/3rd of patients and the rest may have yet to learn defecation. Most patients with dyssynergic defecation demonstrate the inability to coordinate the abdominal, rectal, anal and pelvic floor muscles to facilitate defecation. This failure of rectoanal coordination may manifest as impaired rectal contraction (61%), paradoxical anal contraction (78%) or inadequate anal relaxation or a combination of these elements. In addition, 2/3rd of patients also demonstrate an impaired rectal sensation. Four types of anorectal dysfunction have been described in patients with dyssynergia.

Type I: Here the patient can generate an adequate pushing force (increase in intra-abdominal pressure) along with a paradoxical increase in anal sphincter pressure.
Type II: Here the patient is unable to generate an adequate pushing force (impaired or absent intra-abdominal pressure) with paradoxical anal contraction.
Type III: Here the patient can generate an adequate pushing force but either has absent or incomplete (<20% sphincter relaxation).
Type IV: Patient is unable to generate an adequate pushing force and has absent or incomplete sphincter relaxation.

Diagnostic Testing
Motility laboratory testing is essential for the diagnosis of dyssynergia, because symptoms alone cannot differentiate between the pathophysiological subtypes of constipation. Anorectal manometry provides information regarding rectal and anal pressure changes at rest and after maneuvers of simulated defecation, rectal sensation, rectal/anal reflexes, and compliance. Minimal standards for performing anorectal manometry have been proposed but there is lack of sound information on normative data. Balloon expulsion test provides a bedside assessment of the patients’ ability to expel a stool. Most normal individuals can expel a 50 ml water filled balloon within one minute. Hence, dyssynergia is best diagnosed in the sitting position and after evoking a sensation of stooling. Both an abnormal balloon expulsion test and abnormal pattern of defecation as evidenced by anorectal manometry or defecography are required to diagnose dyssynergia. A colonic transit study is considered abnormal if more than five markers are present on a plain film of the abdomen taken 120 hours after ingestion of a sitzmark capsule containing 24 markers. About 2/3rd of dysynergics show abnormal colonic transit study. Defecography and Endoanal and dynamic pelvic MRI (MRI defecography which can reveal; poor activation of the levator ani muscles, prolonged retention of barium, inability to expel the barium, absence of rectal stripping wave, rectal mucosal intussusception, rectocele, abnormal perineal descent or rectal prolapse may be useful.

Diagnostic Criteria for Dyssynergic defecation: Patients must fulfill all three criteria
A. Patients must satisfy the diagnostic criteria for functional chronic constipation (Rome III) and
B. Patients must demonstrate dyssynergic or obstructive pattern of defecation (Types 1-4) as defined above on manometry, imaging or EMG during repeated attempts to defecate.
C. Patients must demonstrate one or more of the following abnormalities
1. Inability to expel an artificial stool (50 ml water-filled balloon) within one minute.
2. A prolonged colonic transit time, i.e. greater than 5 markers (>20% marker retention) at 120 hours after one sitzmark capsule containing 24 radio opaque markers.
3. Inability to evacuate or ≥50% retention of barium during defecography.

Treatment
The treatment of patients with dyssynergic defecation consists of standard treatment for constipation, including diet, laxatives, and timed toileting; together with biofeedback therapy. Biofeedback Therapy: Neuromuscular training using biofeedback techniques has been shown to be beneficial. The purpose of biofeedback therapy is to restore a normal pattern of defecation by using an instrument-based education program. Symptomatic improvement has been reported in up to 70% of patients. Other avenues of treatment have included botulinum toxin injection, and surgical approaches such as anal myectomy.

Four recent randomized controlled studies have provided evidence supporting the use of biofeedback therapy in dyssynergic defecation and a summary is provided in table 1.

References

Table 1: Summary of the randomized controlled trials of biofeedback therapy for Dyssynergic Defecation

<table>
<thead>
<tr>
<th>Trial Design</th>
<th>Chiarioni et al</th>
<th>Rao et al</th>
<th>Chiarioni et al</th>
<th>Heymen et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biofeedback vs PEG</td>
<td>Biofeedback vs standard vs. sham biofeedback</td>
<td>Biofeedback for slow transit vs Dyssynergia</td>
<td>Biofeedback vs Diazepam 5 mg vs placebo</td>
<td></td>
</tr>
<tr>
<td>Subjects and Randomization</td>
<td>104 women 54 biofeedback 55 polyethylene glycol</td>
<td>77 (69 women) 1:1:1 distribution</td>
<td>52 (49 women) 34 dyssynergia 12 slow transit 6 mixed</td>
<td>84 (71 women) 30 biofeedback 24 placebo</td>
</tr>
<tr>
<td>Duration &amp; Number of biofeedback sessions</td>
<td>3 months &amp; 1 year, 5 weekly, 30 minute training sessions performed by physician investigator</td>
<td>3 months, Biweekly, one hour, maximum of six sessions over three months, performed by biofeedback nurse therapist</td>
<td>5 weekly 30 minute training sessions, performed by physician investigator</td>
<td>6 bi-weekly, one hour sessions</td>
</tr>
<tr>
<td>Primary outcomes</td>
<td>Global Improvement of symptoms Worse=0  No improvement=1 Mild=2 Fair=3 Major improvement=4</td>
<td>1. Presence of dyssynergia 2. Balloon expulsion time 3. Number of complete spontaneous bowel movements 4. Global satisfaction</td>
<td>Symptom improvement None=1 Mild=2 Fair=3 Major=4</td>
<td>Global Symptom relief</td>
</tr>
<tr>
<td>Dyssynergia corrected or symptoms improved</td>
<td>79.6% reported major improvement at 6 and 12 months 81.5% reported major improvement at 24 months</td>
<td>Dyssynergia corrected at 3 months in 79% with biofeedback vs 4% sham and 6% in Standard group ; CSBM= Biofeedback group vs Sham or Standard, p&lt;0.05</td>
<td>71 % with dyssynergia and 8% with slow transit alone reported fair improvement in symptoms</td>
<td>70% improved with biofeedback compared to 38% with placebo and 30 % with diazepam</td>
</tr>
<tr>
<td>Conclusions</td>
<td>Biofeedback was superior to laxatives</td>
<td>Biofeedback was superior to sham feedback and standard therapy</td>
<td>Biofeedback benefits dyssynergia and not slow transit constipation</td>
<td>Biofeedback is superior to placebo and diazepam</td>
</tr>
</tbody>
</table>
Disease monitoring in inflammatory bowel disease: Optimized to improve patient outcomes

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Treatment goals of Crohn’s disease (CD) are directed towards achieving deep remission, avoiding hospitalization and surgery, preventing complications and bowel damage, and minimizing drug toxicity. Early and effective treatments can improve patient outcomes. Therefore, detecting the disease onset and relapses early is crucial in the management of the disease.

Fecal calprotectin (FC), a calcium binding cytosolic protein found in neutrophils, is increasingly being used as a surrogate marker for intestinal inflammation. A number of studies have demonstrated that FC is significantly elevated in the stool of patients with active inflammatory bowel disease (IBD) compared with controls. In a large retrospective study conducted in Edinburgh, stool samples from 895 patients diagnosed with IBD, abnormal gastrointestinal (GI) condition, or functional GI disease were analyzed for FC. Median FC was shown to be significantly higher in the IBD group (1,251 µg/g, 50 µg/g, and 20 µg/g, respectively; p<0.0001). Using a threshold of FC ≥50 µg/g for IBD versus functional disease yielded a sensitivity of 0.97, specificity of 0.74, positive predictive value of 0.37, and a negative predictive value of 0.99. The sensitivity reached 1.00 when combined with alarm symptoms. These results demonstrated that the use of FC in the initial diagnostic workup is highly accurate in detecting IBD in patients with or without GI symptoms.1

Tight monitoring of disease activity is important to prevent relapses and exacerbations in quiescent disease. Monitoring of treatment by repeated endoscopic and biological assessments is costly and not supported by scientific evidence. In addition, both the Crohn’s disease activity index (CDAI) and the Crohn’s disease endoscopic index of severity (CDEIS) have been shown to be poor predictors of mucosal healing.2,3

FC is an effective tool for CD activity monitoring. In a prospective study involving 140 CD patients, FC was found to be correlated closest with the simple endoscopic score for Crohn’s disease (SES-CD) compared with other noninvasive markers such as C-reactive protein, blood leukocytes, and CDAI. SES-CD is commonly used to predict long term prognosis even in patients with clinical remission.4 In the study, FC was the only marker that reliably discriminated inactive endoscopic disease from mild activity (p<0.001), mild from moderate activity (p=0.008), and moderate from high activity (p<0.001).5

Furthermore, a sub-analysis of another prospective study demonstrated that elevated FC levels were highly predictive of the occurrence of relapse among patients who were in stable remission (Figure 1).6

In conclusion, FC values have been shown to reliably predict disease flare and should be used to optimize management of CD. An intensive monitoring plan will be helpful to achieve long term therapeutic goal (Figure 2).

References
Scientific Updates

**Figure 1:** Calprotectin levels from remission to relapse.

- **n=113**
- Luminal Crohn’s Disease patients
- ≥1 year on infliximab plus immunosuppressant
- In stable remission without steroids ≥6 months

![Graph showing calprotectin levels from remission to relapse](image)

- Relapsers
- Non relapsers

- Time before relapse
- Calprotectin (μg/g)
- p=0.0004

**Figure 2:** An example of a tight monitoring plan (personal practice).

- Mild disease
- Moderate disease
- Severe disease

- - risk factors
- + risk factors

- Clinical review q4m; FC q2m
- FBC, LFT q2m; Clinical review + FC q6m
- Annual review: Clinical review, bloods (FBC, U&E, LFT, Alb, CRP, Fe, Fo, B12), FC*

* Colonoscopy and magnetic resonance enterography in selected individuals at 12 months or if increase CRP/FC indicates active disease

Alb, albumin; B12, vitamin B12; CRP, C-reactive protein; FBC, full blood count; FC, fecal calprotectin; Fe, iron; Fo, folate; LFT, liver function test; U&E, urea and electrolytes
Psychopharmacology for functional gastrointestinal disorders – a psychiatrist’s perspective

Antidepressants and other psychotropic drugs (Table 1) have been increasingly used in the management of functional gastrointestinal disorders (FGIDs). Patients with FGIDs often have psychiatric comorbidities such as generalized anxiety disorder and major depressive disorder. Research suggests that FGIDs involve brain-gut dysregulation, mechanisms of which are associated with visceral hypersensitivity, in turn involving brain and peripheral serotonergic mechanisms. These psychotropic agents are thought to have central and peripheral effects on visceral sensitivity and motor activity as well as central effects on pain modulation.1

Evidence exists to show the effectiveness of antidepressants in the treatment of FGIDs. A Cochrane systematic review demonstrated a beneficial effect of antidepressants versus placebo in the treatment of irritable bowel syndrome (IBS). Improvement in abdominal pain (54% vs 37%; p=0.03), global assessment (59% vs 39%; p<0.001) and symptom score (53% vs 26%; p=0.001) was observed.2

Tricyclic antidepressants (TCAs) have been shown to be efficacious in the treatment of functional dyspepsia (FD). Imipramine was associated with a significantly lower treatment failure rate versus placebo (36.4% vs 55.8%; p=0.04) in refractory FD.3 Amitriptyline provided adequate FD symptom relief in 53% of treatment weeks versus placebo (40%; p=0.05).4 Citalopram – a selective serotonin reuptake inhibitor – was shown to be effective in relieving gastroesophageal reflux disease (GERD) symptoms versus placebo (38.5% vs 66.7%; p=0.021),5 although further studies are required to confirm the use of antidepressants in GERD.

Anticonvulsants, such as pregabalin, are also shown to significantly improve gastrointestinal symptoms in generalized anxiety disorder.6 Other agents, such as antipsychotics and benzodiazepines, may have positive effects on FGIDs but their role in FGIDs has yet to be established, and caution must be exercised concerning their side-effects – for example, benzodiazepines should be limited to short-term use in view of risk of dependence, and antipsychotic medications may have metabolic and extrapyramidal side effects.

Further to pharmacological treatment, a good doctor-patient relationship, education and reassurance are integral to FGID management. Psychotherapy and behavioral interventions (eg, exercise, relaxation, etc) should also be employed to further optimize therapeutic outcomes.

References
Table 1: Psychopharmacological agents commonly used for FGIDs7-10

<table>
<thead>
<tr>
<th>Psychopharmacological agents</th>
<th>Primary action</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td>TCAs eg, imipramine, amitriptyline</td>
<td>• Serotonin and noradrenaline reuptake inhibition</td>
<td>• Marked anticholinergism (may affect gut motility)</td>
</tr>
<tr>
<td></td>
<td>• Effective for depression, GAD, IBS, FD</td>
<td>• Low tolerability</td>
</tr>
<tr>
<td>SSRIs eg, escitalopram, sertraline</td>
<td>Serotonin transporter blockade, which results in reduction in reuptake of serotonin and thereby increasing its availability</td>
<td>• Sexual dysfunction is common in men</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• GI side effects: nausea, vomiting, diarrhea, etc.</td>
</tr>
<tr>
<td>SNRIs eg, desvenlafaxine, duloxetine</td>
<td>• Serotonin reuptake transporter inhibition, NET inhibition and increased dopamine release</td>
<td>• NET inhibition provides pain control in addition to antidepressant effect</td>
</tr>
<tr>
<td>Noradrenergic and specific serotonergic antidepressants eg, mirtazapine</td>
<td>• Mixed actions</td>
<td>• Improvement in insomnia and anxiety</td>
</tr>
<tr>
<td></td>
<td>• Blockade of 5-HT₃ receptors, which reduces nausea and GI side effects</td>
<td>• Weight gain is common</td>
</tr>
<tr>
<td>Norepinephrine and dopamine reuptake inhibitors eg, bupropion</td>
<td>Weak dopamine and norepinephrine reuptake inhibition; metabolites are potent NET inhibitors</td>
<td>• Less sexual dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increase in insomnia, nausea, constipation, etc.</td>
</tr>
<tr>
<td>Anticonvulsants eg, pregabalin</td>
<td>• Voltage-gated calcium channel modulation, presynaptic modulation of several excitatory neurotransmitters</td>
<td>• Effective for fibromyalgia, GAD with gastrointestinal symptoms</td>
</tr>
<tr>
<td>Conventional antipsychotics, eg, haloperidol, flupentixol, chlorpromazine, etc.</td>
<td>Dopamine D₂ receptor blockade</td>
<td>• Extrapyramidal side effects</td>
</tr>
<tr>
<td>Atypical antipsychotics eg, quetiapine</td>
<td>5-HT₂A antagonism, dopamine D₂ receptor blockade</td>
<td>• Tardive dyskinesia, weight gain, hyperglycemia and dyslipidemia are common</td>
</tr>
<tr>
<td>Benzodiazepines eg, diazepam, alprazolam, lorazepam, etc.</td>
<td>Hypnotic and anxiolytic effects</td>
<td>• Use &lt;4 weeks to avoid dependence</td>
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<tr>
<td></td>
<td></td>
<td>• Withdraw slowly</td>
</tr>
</tbody>
</table>

FD, functional dyspepsia; GAD, generalized anxiety disorder; GI, gastrointestinal; IBS, irritable bowel syndrome; NET, norepinephrine transporter; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants.
Hemorrhoids are a common clinical condition that occurs frequently in the adult population. Initial treatment strategy for individuals with mild to moderate degree of hemorrhoids include dietary modifications followed by an oral or topical pharmacotherapy. Severe hemorrhoids can be treated with minimally invasive procedures such as rubber band ligation and sclerotherapy, which can be performed in an outpatient setting. When these treatments fail, surgery should be recommended.

Hemorrhoidectomy has been considered the most definitive and gold standard surgical treatment for grades III and IV hemorrhoids. The most commonly used techniques are the open (Milligan-Morgan) and the closed (Ferguson) hemorrhoidectomy. Some modifications have been made to these techniques in order to reduce their associated postoperative pain and improve treatment outcomes.

In a study comparing Milligan-Morgan hemorrhoidectomy performed with conventional monopolar diathermy versus bipolar energy device dissection (Ligasure™), the patients receiving Ligasure™ (n=146) experienced significantly less postoperative anal pain (p<0.01) and had a significantly lower requirements for oral analgesics. In addition, they returned to work and normal activities significantly faster than those receiving conventional diathermy (n=127). However, larger scale studies are required to validate the advantages of bipolar over monopolar energy source.

Stapled hemorrhoidopexy is a technique developed in the 1990s to reduce the prolapse of hemorrhoidal tissue. This is achieved by excising a band of the prolapsed anal mucosa above the dentate line with the use of a specific circular stapling device. Unlike conventional hemorrhoidectomy which removes only three to four areas of prominent prolapsed hemorrhoidal tissues with large external skin wound, this procedure can remove prolapsed tissues circumferentially with surgical wound remains inside the rectum and above the sensitive perianal area. This makes staple hemorrhoidopexy confer better short-term advantages when compared with open surgery.

Several systematic reviews and meta-analyses have suggested that stapled hemorrhoidopexy is safe and provides short-term benefits such as less postoperative pain and complications. However, the procedure may increase long-term recurrence rate when compared with conventional excisional hemorrhoidectomy. Possible reasons for this observation include different definitions of “recurrence” used among surgeons and the feeling of “recurrence” reported by patients due to retention of skin tags with this procedure.

Recently, some surgeons adopted a modified technique of stapled hemorrhoidopexy – tissue selective therapy (TST) – which has been shown to maintain a healthy bridge of mucosa for regeneration and yet avoid resection of non-prolapsed rectal mucosa. Although the efficacy of TST was found to be comparable to stapled hemorrhoidopexy in the treatment of severe hemorrhoids, TST was associated with faster postoperative recovery and less complications.

The Doppler-guided hemorrhoidal artery ligation is another new technique that can be used to treat hemorrhoids. It is a safe and efficacious procedure and is associated with lower levels of postoperative pain. However, more evidence is needed to establish its long-term outcomes.

References
Prospective Study into the Risk of Colorectal Neoplasms in Asymptomatic Individuals with a Family History of Advanced Adenomas (Summary of Thesis 2014)

Background
Colorectal cancer (CRC) is the third most common cancer worldwide. It is the second most common cancer and second most common cause of cancer death in Hong Kong. It has been estimated that 1 in 20 (5%) and 1 in 33 (3%) Hong Kong males and females, respectively, will develop CRC in their life time. Controlled data showed that CRC screening reduces the incidence of CRC and its associated mortality.1 Previous studies have demonstrated an increased CRC risk in close relatives of a proband with any adenoma or an advanced adenoma (AA).2 Based on these studies, guidelines have recommended screening colonoscopy in close relatives and at a younger age when there is a proband with an adenoma.1 However, most studies cited for risk of CRC in relatives with adenomas were limited by the lack of a suitable comparison group or had instead addressed risk of adenomas in subjects who had a first-degree relative with CRC.3 We conducted a prospective, blinded, cross-sectional study to compare the prevalence of colorectal neoplasms in persons who have a sibling with AA with that in persons who have a normal colonoscopy. We postulated that patients with a sibling diagnosed with AA have an increased risk of AA compared with those without such family history.

Patients and Methods
In this prospective cross-sectional study we compared the frequency of colorectal advanced neoplasms in persons who have siblings with AA (with risk factor; also known as affected siblings) with that in persons who do not have siblings with AA (without risk factor) (Figure 1). The findings in both groups were validated with a colonoscopy. AA were defined as adenomas ≥10 mm in size, had high grade dysplasia, had villous or tubulovillous characteristics, or any combination thereof. Advanced neoplasms were defined as AA and cancer.

From 2010 to 2013, 324 consecutive patients with newly diagnosed AA were identified from our colonoscopy database and referred as index cases. The diagnosis of AA was confirmed from endoscopy and pathology reports. Personal and family histories of CRC were obtained at interview. Subjects with AA were consented to provide details on their number of siblings, their siblings’ contact details, and cause of death in siblings who had deceased. Siblings of patients with advanced adenomas aged between 40 and 70 years old were contacted via phone and invited for an interview and a colonoscopy. Siblings with a family history of CRC, history of hereditary CRC including hereditary non polyposis colorectal cancer syndrome (HNPCC) based on the Amsterdam II criteria, familial adenomatous polyposis (FAP),

![Figure 1. Study design: The cases are individuals who have siblings with advanced adenomas (with risk factor; also known as affected siblings) and the controls are individuals who do not have siblings with advanced adenomas (without risk factor)](image)

1 Index case must not have a family history of CRC.

* Only 1 sibling per family with advanced adenomas will be recruited.
Peutz-Jehger’s syndrome, juvenile polyposis, inflammatory bowel disease, known colonic adenomas, previous colonic surgery, colonoscopy within the last five years, and contraindications to colonoscopy, were excluded.

Controls were siblings aged 40 to 70 years old of asymptomatic average risk subjects who had undergone a colonoscopy in our bowel cancer screening programme between 2010 and 2013 and found to have a normal colonoscopy. The siblings of consecutive subjects with normal colonoscopy were identified from our colonoscopy database and invited to participate by phone calls and invitation letters, to attend a health talk and to undergo a colonoscopy. Controls should have no family history of CRC, personal history of hereditary CRC or IBD, known colonic adenomas or cancer, previous colonic surgery, colonoscopy within the last five years, and contraindications to colonoscopy. Each case was matched by sex- and age (±3 years) with two controls. Controls were matched to cases prior to undergoing a colonoscopy. All siblings recruited were asymptomatic.

The primary outcome was the prevalence of AA and cancers. Secondary outcomes included rates of all colorectal adenomas and rates of AA depending on characteristics of the index case, and the proportion of subjects with proximal AA who also have distal adenomas.

The study protocol was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong and New Territories East Cluster of Hospital Authority of Hong Kong. All study subjects provided informed written consent for participation. The study has been registered at the Clinical Trial Registry (Trial Registration: NCT01593098).

Colonoscopy
Conventional white light colonoscopy was performed within the same time period for cases and controls at the Endoscopy Centre of the Prince of Wales Hospital and The Alice Ho Miu-ling Nethersole Hospital by three experienced endoscopist. Cecal intubation rate was 100%. The size, location and morphology of all colonic lesions were documented. Colorectal neoplasms proximal to splenic flexure on scope withdrawal were classified as proximal lesions. Quality of bowel preparation was graded as good (no or small volume of clear liquid, with >95% of surface seen), fair (between good and poor), and poor (presence of semi-solid stool that could not be washed away, and <90% of surface seen). Large adenomas were defined as adenomas ≥10 mm in size. Multiple adenomas were defined as ≥3 adenomas. In subjects with multiple lesions, the most advanced lesion was considered. Endoscopists and pathologist were blinded to the history of the study subjects. Endoscopists were not provided with information on the family history of the patient or given any indication of colonoscopy during procedure.

Statistical Analysis and Sample Size Calculation
Statistical analyses were performed using SPSS software (version 15.0; SPSS, Chicago, Illinois) and LogXact software (version 9.00; Cytel Software Corp., Cambridge, Massachusetts). Sample size calculation was performed using the StatsDirect statistical package (version 2.7.7; www.statsdirect.com). Screening colonoscopic studies in asymptomatic subjects in Asia and the West showed that the prevalence of advanced neoplasms was approximately 5 percent. Assuming a 2.5-fold increased risk of advanced neoplasms in siblings of patients with advanced adenomas, the recruitment of a minimum of 185 cases and 370 controls was required to achieve 80% power to detect difference at a 5% significance level.

Table 1. Baseline characteristics of the studied population

<table>
<thead>
<tr>
<th></th>
<th>Affected siblings (n=188)</th>
<th>Matched controls (n=323)</th>
<th>P value</th>
<th>mOR (95% CI)</th>
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<tbody>
<tr>
<td><strong>Age (years), mean (SD)</strong></td>
<td></td>
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<tr>
<td>&lt; 50, n (%)</td>
<td>58 (6.4)</td>
<td>57.6 (5.9)</td>
<td></td>
<td>Matched</td>
</tr>
<tr>
<td>50-59, n (%)</td>
<td>16 (8.5)</td>
<td>23 (7.1)</td>
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<tr>
<td>≥ 60, n (%)</td>
<td>94 (50)</td>
<td>176 (54.5)</td>
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<tr>
<td></td>
<td>78 (41.5)</td>
<td>124 (38.4)</td>
<td></td>
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</tr>
<tr>
<td><strong>Sex, Male, n (%)</strong></td>
<td>85 (45.2)</td>
<td>152 (47.1)</td>
<td></td>
<td>Matched</td>
</tr>
<tr>
<td><strong>Diabetes mellitus, n (%)</strong></td>
<td>20 (10.6)</td>
<td>21 (6.5)</td>
<td>0.127</td>
<td>1.67 (0.87, 3.21)</td>
</tr>
<tr>
<td><strong>Cardiovascular accident, n (%)</strong></td>
<td>4 (2.1)</td>
<td>4 (1.2)</td>
<td>0.362</td>
<td>2.04 (0.44, 9.48)</td>
</tr>
<tr>
<td><strong>Ischemic heart disease, n (%)</strong></td>
<td>6 (3.2)</td>
<td>13 (4.0)</td>
<td>0.526</td>
<td>0.73 (0.27, 1.94)</td>
</tr>
<tr>
<td><strong>Non steroidal anti-inflammatory drugs, n (%)</strong></td>
<td>3 (1.6)</td>
<td>5 (1.5)</td>
<td>0.901</td>
<td>1.10 (0.26, 4.63)</td>
</tr>
<tr>
<td><strong>Aspirin usage, n (%)</strong></td>
<td>7 (3.7)</td>
<td>15 (4.6)</td>
<td>0.595</td>
<td>0.78 (0.31, 1.96)</td>
</tr>
<tr>
<td><strong>Smoker, n (%)</strong></td>
<td>16 (8.5)</td>
<td>33 (10.2)</td>
<td>0.781</td>
<td>0.91 (0.47, 1.76)</td>
</tr>
<tr>
<td><strong>Alcohol intake, n (%)</strong></td>
<td>12 (6.4)</td>
<td>11 (3.4)</td>
<td>0.085</td>
<td>2.06 (0.91, 4.68)</td>
</tr>
<tr>
<td><strong>Body mass index≥25, n (%)</strong></td>
<td>64 (34)</td>
<td>109 (33.7)</td>
<td>0.742</td>
<td>1.07 (0.73, 1.57)</td>
</tr>
</tbody>
</table>

*Aspirin usage: use of aspirin ≥75 mg in the past seven days.
*Alcohol intake: any alcohol consumption of greater than twice per week
Bold figures indicated p<0.05.
mOR: matched odds ratio; CI: confidence interval.
Data were presented as mean, standard deviation (SD) or frequency (%). Univariable analysis was conducted by computing matched odds ratios and their 95% confidence intervals (CI) to compare affected siblings and matched controls for each variable through conditional logistic regression. For multivariable analyses, baseline factors that showed an association with p<0.1 in unadjusted analyses were entered into regression model. In these analyses, the most severe colonoscopic finding was represented as an independent variable in a number of ways (2). It was considered as a binary variable (all adenomas vs. no adenomas), or a three-level categorical variable (advanced adenomas vs. non-advanced adenomas vs. no adenomas). Stratified conditional logistic regression analyses were performed according to age and characteristics of index case at diagnosis. Significance was defined by a two-sided alpha level of 0.05. P values were not adjusted for multiple subgroup analyses.

### Results
#### Study population
Between 2010 and 2013, 324 consecutive subjects with newly diagnosed advanced adenomas were recruited and referred as index cases. Amongst them, 421 siblings from 188 families were contacted. Altogether 188 siblings from 188 families fulfilled eligibility criteria and underwent a colonoscopy. A total of 323 controls from 323 families participated in a colonoscopy and were included in the final analysis. Figure 2 shows the study population consisting of affected siblings and matched controls. 135 affected siblings were age- and sex-matched with two controls each and 53 siblings with one control each (Table 1).

Screening uptake rate in affected siblings was 78.7% (188/239; 188 had a colonoscopy; 51 declined participation or failed to attend for colonoscopy; Figure 2). Screening uptake rate in matched controls was 78.6% (323/411; 411 eligible to participate; 88 declined participation or failed to attend for colonoscopy). None of the deceased siblings had been diagnosed with CRC. Quality of bowel preparation did not differ between both groups (p=0.966). The three endoscopists performed similar number of procedures. Adenoma detection rates were comparable between the endoscopists (Endoscopist 1, 27.4% vs. endoscopist 2, 31.6% vs. endoscopist 3, 23.7%; p= 0.411).

**Figure 2. Study population (affected siblings and matched controls)**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>324 index cases with advanced neoplasm identified</td>
<td>450 asymptomatic subjects who had normal screening colonoscopy between 2010 and 2013 were identified</td>
</tr>
<tr>
<td>250 index cases consented to provide family information</td>
<td>368 families of subjects with normal colonoscopy</td>
</tr>
<tr>
<td>319 siblings identified</td>
<td>459 siblings identified</td>
</tr>
<tr>
<td>197 siblings (age 40-70 years old)</td>
<td>392 controls age and sex matched and agreed to have colonoscopy*</td>
</tr>
<tr>
<td>188 siblings (from 188 families) with screening colonoscopy were included*</td>
<td>323 siblings (from 323 families) underwent screening colonoscopy were included in final analysis</td>
</tr>
<tr>
<td>12 unable to contact index case</td>
<td>18 unable to contact</td>
</tr>
<tr>
<td>36 family history of CRC</td>
<td>28 family history of CRC</td>
</tr>
<tr>
<td>26 nil sibling</td>
<td>36 nil sibling</td>
</tr>
<tr>
<td>25 deceased</td>
<td>22 deceased</td>
</tr>
<tr>
<td>27 with age &lt;40 or &gt;70</td>
<td>30 with age &lt;40 or &gt;70</td>
</tr>
<tr>
<td>42 declined participation</td>
<td>82 declined participation</td>
</tr>
<tr>
<td>28 sibling participated</td>
<td>32 sibling participated</td>
</tr>
<tr>
<td>6 patients did not attend colonoscopy</td>
<td>9 defaulted colonoscopy</td>
</tr>
</tbody>
</table>

*6 patients did not attend colonoscopy.
adenomas
AA in sibling was particularly high when the index case had
respectively. The risk of having AA in siblings was higher when
Advanced Adenomas
Influence of Index Patient's Characteristics on Risk of
1.8%). Affected siblings were more likely to have distal adenomas
Among patients with adenomas, the average number of
95% CI, 1.51 – 3.41; p<0.001)
controlled with hemoclips; 1 transient hypotension; 2 mild
prevalence of hyperplastic polyps was however not different
The stage I cancer had endoscopic submucosal dissection of the lesion
controls. The two patients had stage I and stage III cancer and
Table 2
Prevalence of Colorectal Advanced Adenomas
Study population
characteristics of index case at diagnosis. Significance was defined
three-level categorical variable (advanced adenomas vs.
as a binary variable (all adenomas vs. no adenomas), or a
an independent variable in a number of ways (2). It was considered
matched odds ratios and their 95% confidence intervals (CI) to
values were not adjusted for
advanced adenomas is 3.0 to 4.5%6-9 and 3.1 to 11.7% respectively.
of advanced adenomas in probands with AA.
studies of a higher prevalence of CRC in these relatives supporting
higher prevalence of advanced neoplasms is consistent with prior
colonoscopy in these families. Furthermore, demonstrating a
literature and anchors the guideline recommendations for
population-based study from Utah found a 35% increased risk of
United States showed a modest and non-significant increase in the
adenomas or CRC in the first degree relatives of patients with large
Our data are consistent with studies showing an increased risk of
colonoscopy. Siblings to subjects with a normal colonoscopy
study is that findings in control subjects were fully validated using
affected siblings and matched controls. 135 affected
Figure 2
Colorectal cancer (CRC) is the third most common cancer
Background
have demonstrated an increased CRC risk in close relatives of a
Proximal adenomas
Siblings to subjects with a normal colonoscopy
number of patients with adenomas in any first-degree relative of
no significant difference between index case and control

discussed in this report. Siblings were considered affected by
adenomas or CRC if they had a diagnosis of adenoma or CRC
The two provinces included 2662 cases of CRC from which a

Table 2. Risk of advanced adenomas and cancer among siblings of patients with advanced adenomas

<table>
<thead>
<tr>
<th></th>
<th>Affected siblings n=188 (%)</th>
<th>Matched controls n=323 (%)</th>
<th>Adjusted mOR* (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No adenomas</td>
<td>116 (61.7)</td>
<td>253 (78.3)</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>All adenomas</td>
<td>72 (38.3)</td>
<td>70 (21.7)</td>
<td>2.27 (1.51, 3.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Advanced neoplasms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenomas ≥10 mm&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21 (11.2)</td>
<td>6 (1.9)</td>
<td>6.62 (2.61, 16.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;25% villous features&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11 (5.9)</td>
<td>4 (1.2)</td>
<td>5.01 (1.57, 16.04)</td>
<td>0.007</td>
</tr>
<tr>
<td>High grade dysplasia&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3 (1.6)</td>
<td>2 (0.6)</td>
<td>2.94 (0.47, 18.42)</td>
<td>0.249</td>
</tr>
<tr>
<td>Cancer</td>
<td>2 (1.1)</td>
<td>0 (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Multiple adenomas&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12 (6.4)</td>
<td>8 (2.5)</td>
<td>3.24 (1.28, 8.18)</td>
<td>0.013</td>
</tr>
<tr>
<td>Distal adenomas&lt;sup&gt;b&lt;/sup&gt;</td>
<td>35 (18.6)</td>
<td>27 (8.4)</td>
<td>3.22 (1.77, 5.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proximal adenomas&lt;sup&gt;c&lt;/sup&gt;</td>
<td>24 (12.8)</td>
<td>31 (9.6)</td>
<td>1.79 (0.99, 3.22)</td>
<td>0.054</td>
</tr>
<tr>
<td>Synchronous adenomas&lt;sup&gt;d&lt;/sup&gt;</td>
<td>13 (6.9)</td>
<td>12 (3.7)</td>
<td>1.75 (0.77, 3.99)</td>
<td>0.181</td>
</tr>
</tbody>
</table>

<sup>a</sup>Adjusted for alcohol history of affected siblings and matched controls using conditional logistic regression.
<sup>b</sup> These features are not mutually exclusive
<sup>c</sup>≥3 adenomas.
<sup>d</sup>Distant to the splenic flexure.
<sup>e</sup>Proximal to the splenic flexure.
<sup>f</sup>Adenomas detected in both proximal and distal colons.

Table 3. Prevalence of advanced neoplasms and all colorectal adenomas according to the age of affected siblings

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>All Colorectal Adenomas</th>
<th>Advanced Neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Affected siblings (%)</td>
<td>Matched controls (%)</td>
</tr>
<tr>
<td>&lt; 50</td>
<td>3/16 (18.7)</td>
<td>5/29 (17.2)</td>
</tr>
<tr>
<td>50-59</td>
<td>38/94 (40.4)</td>
<td>34/167 (20.4)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>31/78 (39.7)</td>
<td>31/127 (24.4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Adjusted for alcohol history of affected siblings and matched controls using conditional logistic regression.
<sup>b</sup> Bold figures indicated p<0.05.
mOR: matched odds ratio; CI: confidence interval.
Table 4. Prevalence of advanced neoplasms and all colorectal adenomas according to index case characteristics

<table>
<thead>
<tr>
<th>Index case characteristics</th>
<th>All Colorectal Adenomas</th>
<th>Advanced Neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Affected cases n (%)</td>
<td>Matched controls n (%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60</td>
<td>41/107 (38.3)</td>
<td>46/201 (22.9)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>31/81 (38.2)</td>
<td>24/122 (19.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>33/102 (32.4)</td>
<td>37/171 (21.6)</td>
</tr>
<tr>
<td>Female</td>
<td>39/86 (45.3)</td>
<td>33/152 (21.7)</td>
</tr>
<tr>
<td>Advanced adenoma site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal*</td>
<td>38/103 (36.9)</td>
<td>40/179 (22.3)</td>
</tr>
<tr>
<td>Proximal</td>
<td>30/78 (38.5)</td>
<td>29/133 (21.8)</td>
</tr>
<tr>
<td>Synchronous</td>
<td>4/7 (57.2)</td>
<td>1/11 (9.1)</td>
</tr>
<tr>
<td>Number of adenomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>15/35 (42.9)</td>
<td>11/65 (16.9)</td>
</tr>
<tr>
<td>&lt; 3</td>
<td>57/153 (37.3)</td>
<td>59/258 (22.9)</td>
</tr>
<tr>
<td>Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>58/153 (37.9)</td>
<td>59/261 (22.6)</td>
</tr>
<tr>
<td>&gt;25% villous</td>
<td>31/89 (34.8)</td>
<td>34/156 (21.8)</td>
</tr>
<tr>
<td>High grade dysplasia</td>
<td>15/37 (40.5)</td>
<td>12/64 (18.8)</td>
</tr>
</tbody>
</table>

*Adjusted for alcohol history of affected siblings and matched controls using conditional logistic regression.

*Distal to the splenic flexure.

Proximal to the splenic flexure.

Lesions detected in both proximal and distal colons.

Bold figures indicated p<0.05.

mOR: matched odds ratio; CI: confidence interval.
Prevalence of Colorectal Advanced Adenomas

The prevalence of advanced adenomas and cancer was higher in siblings of subjects with advanced adenomas than controls [11.7% vs. 2.8%; Matched odds ratio (mOR) 4.58; 95% CI, 2.07–10.14; p<0.001]. Affected siblings also had a higher prevalence of all colorectal adenomas (38.3% vs. 21.7%), adenomas ≥10 mm in size (11.2% vs. 1.9%), adenomas with >25% villous architecture (5.9% vs. 1.2%) and high grade dysplasia (1.6% vs. 0.6%), than controls. **Table 2** shows the risk of advanced adenomas and all colorectal adenomas among siblings of patients with advanced adenomas. CRC was identified in two affected siblings and none of the controls. The two patients had stage I and stage III cancer and both of the cancers were detected in the rectum. The patient with stage I cancer had endoscopic submucosal dissection of the lesion and has been followed-up every six months with colonoscopic surveillance. The patient with stage III cancer underwent neoadjuvant chemotherapy followed up laparoscopic low anterior resection. There were significantly more distal adenomas (18.6% vs. 8.4%; p<0.001) in affected siblings than controls (Table 2). The prevalence of hyperplastic polyyps was however not different between both groups (8% vs. 13.6%; p=0.502). Adverse effects were reported in five subjects (2 post-polypectomy bleeding controlled with hemoclip; 1 transient hypotension; 2 mild abdominal discomfort which spontaneously resolved).

**Table 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases (n=10)</th>
<th>Controls (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced adenomas</td>
<td>5</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All colorectal adenomas</td>
<td>8</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adenomas ≥10 mm</td>
<td>5</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adenomas with &gt;25% villous</td>
<td>3</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High grade dysplasia</td>
<td>2</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Risk Factors Associated with Advanced Adenomas and Cancer**

A history of AA in siblings remained an independent factor associated with increased risk for AA and cancer (mOR 4.58; 95% CI, 2.07 – 10.14; p<0.001) and any colorectal adenomas (mOR 2.27; 95% CI, 1.51 – 3.41; p<0.001) (Table 2). Affected siblings were more likely to have higher numbers of adenomas than controls. Among patients with adenomas, the average number of adenomas per subject was 1.82 in affected siblings and 1.6 in controls.

The prevalence of AA and cancer was higher in male than female in affected siblings (14.1% vs. 9.7%) and matched controls (3.9% vs. 1.8%). Affected siblings were more likely to have distal adenomas (Table 2). After stratification by age, affected siblings aged 50 to 59 years had a higher prevalence of AA and cancer (11.7% vs. 2.4%; mOR 6.39; p=0.002) and all colorectal adenomas (40.4% vs 20.4%; mOR 3.19; p<0.001) than controls. Affected siblings aged older than 59 years old also had a higher prevalence of AA (14.1% vs. 3.9%, mOR 3.53; p=0.022) and all colorectal adenomas (39.7% vs. 24.4%; mOR 1.8; p=0.047) than controls. In subjects less than 50 years of age, there was no difference in the prevalence of all colorectal adenomas in affected siblings and controls (18.7% vs. 17.2%; p=0.942) (Table 3).

**Influence of Index Patient’s Characteristics on Risk of Advanced Adenomas**

AA in the distal colon, the proximal colon and synchronous adenomas, were present in 54.8%, 41.5% and 3.7% of index cases, respectively. The risk of having AA in siblings was higher when their index case was female (mOR 6.4; 95% CI 2.07-20.46). The risk of AA in sibling was particularly high when the index case had adenomas ≥10 mm (mOR 4.58; 95% CI 1.86–11.3) or villous adenomas (mOR 7.58; 95% CI 1.6–36.05). The odds ratio of advanced adenomas in siblings was 3.6 (95% CI 1.29–10.04) and 5.13 (95% CI 1.29–20.5) when the index case had AA in the distal and proximal colon, respectively (Table 4).

**Discussion**

This study showed that siblings of subjects with AA have a greater than four-fold increased risk of advanced colorectal neoplasms and a more than two-fold increased risk of all colorectal adenomas. This risk is higher if the index case had large adenomas, villous adenomas and multiple adenomas. To the best of our knowledge, this is the first prospective study to offer colonoscopy to siblings of polyp-free subjects. Second, the findings of AA in all index cases were confirmed on endoscopy and histology. Third, to limit the effect of familial clustering only one sibling per family was recruited for cases and controls and none of the subjects had a family history of CRC. Fourth, the rate of participation was relatively high and did not differ between cases and controls. Lastly, the prevalence of hyperplastic polyps in both groups was similar which makes ascertainment bias less likely. The main strength of this study is that findings in control subjects were fully validated using colonoscopy. Siblings to subjects with a normal colonoscopy represent a group more comparable to affected siblings and a better control group.

Our data are consistent with studies showing an increased risk of CRC or AA in relatives of subjects with adenomas. Two case-control design studies from France reported an elevated risk of developing adenomas or CRC in the first degree relatives of patients with large adenomas (≥10mm in size). A separate smaller study from the United States showed a modest and non-significant increase in the risk of CRC in the relatives of patients with small tubular adenomas and a significant increase in relatives of patients with AA. A recent population-based study from Utah found a 35% increased risk of CRC in first-degree relatives of patients with adenoma (OR, 1.35) and a close to 70% elevated risk of CRC in first-degree relatives of patients with villous adenomas (OR, 1.68).

This study has several clinical implications. The higher prevalence of advanced adenomas and cancers found on colonoscopy in affected siblings provides a major contribution to the existing literature and anchors the guideline recommendations for colonoscopy in these families. Furthermore, demonstrating a higher prevalence of advanced neoplasms is consistent with prior studies of a higher prevalence of CRC in these relatives supporting our present understanding of the adenoma-carcinoma relationship, and strengthening the concept of familial risk with adenoma proband. Prior studies have reported family risk of CRC with adenoma proband whereas our study has reported family risk of advanced adenomas in probands with AA.

Studies of screening colonoscopy in average risk asymptomatic subjects in Asia and the West showed that the prevalence of advanced adenomas is 3.0 to 4.5% and 3.1 to 11.7% respectively. Here the prevalence of AA in asymptomatic affected siblings (11.7%) is one of the highest in published colonoscopy screening studies from Asia. We also found that the prevalence rates of AA and any adenomas were higher in males than females. The risk of...
AA and any colorectal adenomas was particularly high in siblings between 50 to 60 years of age. After the age of 60, the risk of AA remained higher in affected siblings than controls. These data suggest that screening colonoscopy in patients with a first degree relative with AA is strongly indicated. Lastly, screening is indicated in siblings regardless of the age of the index case when AA were diagnosed. Colonoscopy is likely to be the most appropriate modality in this group given the high likelihood of finding advanced adenomas and the need for polypectomy.

In conclusion, siblings of patients with advanced adenomas have a substantially increased risk of advanced adenomas and cancer, and this risk is higher if the index case was female, and had large or villous adenomas. These data enhance our knowledge of familial risk in adenoma proband and support the recommendation of screening in families when an index patient has an advanced adenoma on colonoscopy.

References

Cancer prevalence of hyperplastic polyps was however not different (Table 2) vs. 8.4%; p<0.001) in affected siblings than controls. After stratification by age, affected siblings aged 50 to 59 (14.1% vs 9.7%) and matched controls (3.9% vs. 2.9%).

Affected siblings were more likely to be diagnosed with advanced adenomas than controls. The odds ratio of advanced colorectal adenomas (mOR 7.58; 95% CI 1.6–36.05). The odds ratio of ≥10 mm in size). 2;4 A separate smaller study from the same site also demonstrated a higher prevalence of CRC in these relatives supporting the recommendation for screening colonoscopy in these families. Furthermore, demonstrating a familial risk of advanced colorectal adenomas or CRC in the first degree relatives of patients with large adenomas or CRC. Two case-control studies have shown an increased CRC risk in close relatives of a patient with a first degree relative with CRC. In conclusion, siblings of patients with advanced adenomas have a greater risk for advanced adenomas and the need for polypectomy.

Prevalence of Colorectal Advanced Adenomas

Study population

Results

analyses, the most severe colonoscopic finding was represented as polyp-free subjects. Second, the findings of AA in all index cases suggest that screening colonoscopy in patients with a first degree relative with CRC or AA in relatives of subjects with adenomas. Two case-control studies have shown an increased CRC risk in close relatives of a patient with a first degree relative with CRC. In conclusion, siblings of patients with advanced adenomas have a greater risk for advanced adenomas and the need for polypectomy.

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analyses, the most severe colonoscopic finding was represented as polyp-free subjects. Second, the findings of AA in all index cases suggest that screening colonoscopy in patients with a first degree relative with CRC or AA in relatives of subjects with adenomas. Two case-control studies have shown an increased CRC risk in close relatives of a patient with a first degree relative with CRC. In conclusion, siblings of patients with advanced adenomas have a greater risk for advanced adenomas and the need for polypectomy.
17th JOINT ANNUAL SCIENTIFIC MEETING 2015

Date: 6 September 2015
Venue: Level 7, Cordis Hong Kong at Langham Place
Kowloon, Hong Kong
Organizing Chairman: Dr. Jodis T.W. Lam

Co-organized by:
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

Sponsors: Abbott, Abbvie, AstraZeneca, Ferring, Fujifilm, Gilead, Meda, Menarini, Novartis, Sandoz & Takeda

Dr. Jodis Lam welcomed the delegates and thanked the co-organizing societies and sponsors for their support and contributions to the 17th Joint Annual Scientific Meeting.

There were 8 lectures covering hot topics in gastroenterology, hepatology and endoscopy delivered by renowned speakers.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symposium I</strong>&lt;br&gt;Chairs: Prof. Wai-Keung Leung &amp; Dr. Kam-Chuen Lai</td>
<td><strong>Symposium II</strong>&lt;br&gt;Chairs: Dr. Angus C.W. Chan &amp; Dr. Cliff C.C. Chung</td>
</tr>
<tr>
<td><em>H. pylori</em> therapy circa 2015: Putting different options in perspective</td>
<td>Recent advances in endoscopic treatment of achalasia and oesophageal submucosal mass lesions</td>
</tr>
<tr>
<td>Prof. Ernst J. Kuipers (Netherlands)</td>
<td>Prof. Pinghong Zhou (China)</td>
</tr>
<tr>
<td>Gastroparesis</td>
<td>Colorectal ESD</td>
</tr>
<tr>
<td>Prof. Justin Che-Yuen Wu (CUHK)</td>
<td>Dr. Thomas Ka-Luen Lui (TMH)</td>
</tr>
<tr>
<td>Risk for upper GI cancer: Implications for intervention and surveillance</td>
<td>Endoscopic submucosal dissection and full-thickness resection for gastric tumours</td>
</tr>
<tr>
<td>Prof. Ernst J. Kuipers (Netherlands)</td>
<td>Prof. Pinghong Zhou (China)</td>
</tr>
<tr>
<td><strong>Symposium III</strong>&lt;br&gt;Chairs: Dr. Francis T.W. Li &amp; Dr. Yee-Tak Hui</td>
<td></td>
</tr>
<tr>
<td>Treatment of Chronic Hepatitis C: Local Experience in Hong Kong</td>
<td>Cancer and Infection Risks in IBD: What should we tell our patients?</td>
</tr>
<tr>
<td>Dr. Wing-Yan Mak (QEH)</td>
<td>Dr. Siew C. Ng (CUHK)</td>
</tr>
</tbody>
</table>

The Meeting was attended by 243 healthcare professionals. Panel discussions were actively participated. Souvenirs were presented to the speakers and sponsors in appreciation of their contributions.
8-10 December 2015
30th International Workshop on Therapeutic Endoscopy
Organizers: CUHK Institute of Digestive Disease, CUHK The Nethersole 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.hkide.org/workshop.htm

18-20 December 2015
APASL Single Theme Conference: HCV Infection and Disease & Recent Advances in Liver Diseases
Hosted by: Institute of Liver & Biliary Sciences & Indian Society of Gastroenterology
Location: New Delhi, India
Website: http://apasilndia.com

21-22 January 2016
Falk Workshop: Communications and System Relevance in Liver Damage And Regeneration
Organizer: Falk Foundation
Location: Dusseldorf, Germany
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

21-23 January 2016
2016 Gastrointestinal Cancers Symposium: Insight on Novel Mechanisms and Precision Care
Location: San Francisco, California, USA
Website: http://gicsym.org/

24-26 January 2016
16th International Colorectal Forum
Location: Villars-sur-Ollon, Switzerland
Website: www.icf-colorectal.com/

11-13 February 2016
18th Dusseldorf International Endoscopy Symposium
Location: Dusseldorf, Germany
Website: www.endo-dusseldorf.com/english/conference.php

20-24 February 2016
25th Conference of Asian Pacific Association for the Study of the Liver: Modern Hepatology
Organizer: Asian Pacific Association for the Study of the Liver (APASL)
Location: Tokyo, Japan
Website: www.apasil2016.org/

21 February 2016
Endoscopy Summit
Organizer: World Endoscopy Organization, Asian Institute of Gastroenterology
Location: Hyderabad, India
Website: www.aiajindia.net/images/endos%20summit%20flex.pdf

25-26 February 2016
9th Sydney International Endoscopy Symposium (SIES)
Incorporating the Westminster Endoscopy Symposium Nurses’ Workshop on 24 February 2016
Location: Sydney, NSW, Australia
Website: www.sies.org.au/

26-29 February 2016
Canadian Digestive Diseases Week (CDDW 2016) & and the Annual CASL Winter Meeting
Organizers: Canadian Association of Gastroenterology (CAG) & Canadian Association for the Study of the Liver (CASL)
Location: Montreal, QC, Canada
Website: www.cag-acg.org/cddw

11-12 March 2016
Falk Symposium 201: Gut-Liver Interactions: From IBD to NASH
Organizer: Falk Foundation
Location: Innsbruck, Austria
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

16-19 March 2016
11th Congress of ECCO on Inflammatory Bowel Diseases 2016
Organizer: European Crohn’s and Colitis Organisation
Location: Amsterdam, The Netherlands
Website: www.ecco-ibd.eu/ecco16

31 March 2016 (Thursday)
35th Annual General Meeting cum Scientific Meeting of The Hong Kong Society of Gastroenterology
Organizer: The Hong Kong Society of Gastroenterology
Location: Cordis Hong Kong at Langham Place
Kowloon, Hong Kong
Website: www.hksge.org/event.htm

8-10 April 2016
APASL STC 2016: Recent Advances in Prevention and Management of Cirrhotic Complications
Organizers: Asian Pacific Association for the Study of the Liver
Location: Busan, Korea
Website: www.apaslstc2016.org/main.php

8-10 April 2016
Endoscopy 2016: Expanding the Horizons of Therapeutic Endoscopy
Organizer: Malaysian Society of Gastroenterology and Hepatology, University of Malaya
Location: Kuala Lumpur, Malaysia
Website: www.msgh.org.my/

13-17 April 2016
The International Liver Congress 2016 & 51st annual meeting of the European Association for the Study of the Liver
Organizer: European Association for the Study of the Liver (EASL)
Location: Barcelona, Spain

14-15 April 2016
EURO EUS Congress 2016
Location: Manuille, France
Website: www.euro-eus.com

15-16 April 2016
Quality in Endoscopy Upper GI Endoscopy & Neoplasia Symposium
Organizers: European Society of Gastrointestinal Endoscopy (ESGE) & European Society of Digestive Oncology (ESDO)
Location: Berlin, Germany
Website: www.quality-in-endoscopy.org/symposium-upper-gi-qe90.html

20 April 2016
The 7th Asian-Pacific Topic Conference (APTC): Advanced Imaging in Gastroenterology
Organizers: Japanese Society of Gastroenterology and APAGE
Location: Tokyo, Japan
Website: www.jjou.com/APTC7/

20-23 April 2016
12th World Congress of International Hepato-Pancreato-Biliary Association
Location: São Paulo, Brazil
Website: www.hpba2016.com/

21-23 April 2016
Korea International Gastric Cancer Week (KINGCA 2016) & 6th Asia Pacific Gastroesophageal Cancer Congress (APGCC 2016)
Organizer: The Korean Gastric Cancer Association
Location: Seoul, Korea
Website: www.kingca.org/

22-23 April 2016
The 5th International Forum
Organizer: Japanese Society of Gastroenterology
Location: Tokyo, Japan
Email: 10jigojc@convention.co.jp

29-30 April 2016
Falk Symposium 202: Evolving Therapies in Clinical Practice in IBD
Organizer: Falk Foundation
Location: Prague, Czech Republic
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

30 April – 4 May 2016
2016 ASCRS Annual Scientific Meeting
Organizer: The American Society of Colon and Rectal Surgeons
Location: Los Angeles, California, USA
Website: www.fascrs.org

21-24 May 2016
Dietetic Disease Week (DDW 2016)
Organizers: American Association for the Study of Liver Diseases (AASLD), American Gastroenterology Association (AGA), American Society for Gastrointestinal Endoscopy (ASGE) and The Society for Surgery of the Alimentary Tract (SSAT)
Location: San Diego, CA, USA
Website: www.ddw.org

10-12 June 2016
APASL STC on HCV 2016: Hepatitis C: Before and Beyond Cure
Organizers: Asian Pacific Association for the Study of the Liver
Location: Kaohsiung, Taiwan
Website: www.apasl-hcv-2016.org/

17-18 June 2016
Falk Symposium 203: XXIV International Bile Acid Meeting: Bile Acids in Health and Disease
Organizer: Falk Foundation
Location: Dusseldorf, Germany
Website: www.falk-foundation-symposia.org/symposia-and-workshops/2016/?L=1

15-19 October 2016
24th UEG Week
Organizer: United European Gastroenterology (UEG)
Location: Vienna, Austria
Website: www.ueg.eu/week

21-26 October 2016
ACG 2016 Annual Scientific Meeting and Postgraduate Course
Organizer: American College of Gastroenterology (ACG)
Location: Las Vegas, Nevada, USA
Website: http://acgmeetings.git/

2-5 November 2016
Asian Pacific Digestive Week (APDW 2016)
Organizer: Organization of JDDW
Location: Kobe, Japan
Website: www.apdw2016.org

17-19 November 2016
Gastro 2016: EQHS/WSG International Congress
Organizers: World Gastroenterology Organization, Emirates Gastroenterology & Hepatology Society
Location: Abu Dhabi, United Arab Emirates
Website: www.worldgastroenterology.org/meetings-and-events/wgci-international-conferences
(More information is available from www.hksge.org/event.htm)