President Message

Welcome to our December 2017 Newsletter!

The year 2017 has proven to be another fruitful year for The Hong Kong Society of Gastroenterology in promoting the advancement of gastroenterology, with the organization of two successful Scientific Meetings in March and September, as well as the support of the Medical Multispecialty Mega Conference. The Society was also proud to be one of the host organizations of Asian Pacific Digestive Week 2017. With a very comprehensive programme and excellent faculty members, the Conference was a great success and proved to be a valuable platform for local and overseas professionals to exchange knowledge and experience.

On behalf of the Society, I wish to express my gratitude to Dr. Wai-Fan Luk for organizing the Annual General Meeting cum Scientific Meeting 2017, Dr. Jodis T.W. Lam for organizing the 19th Joint Annual Scientific Meeting, Professor Wai-Keung Leung for editing the two newsletters, and Dr. Marta Jiménez Toscano, Professor Siew Ng, Dr. George Webster, Professor Wai-Keung Leung and Dr Wilson Yip-Shun Lam for their scientific updates in this newsletter. Thanks also to all fellows and members for attending the scientific meetings, and friends from the pharmaceutical industry for their generous sponsorship and support.

The next newsletter will be published in June 2018.

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

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

Scientific Updates

Transanal-transabdominal total mesorectal excision for rectal cancer

Innovation in the management of rectal cancer has led to better outcomes for patients, but it could potentially be improved even further. Early studies indicated that cancers of the colon, rectum and anus were associated with high mortality and recurrence rates. A few decades ago, just 43% of patients with cancer of the colon, rectum or anus were still alive 1 year after diagnosis and the 5-year mortality rate was as high as 70%. Local recurrence rates ranged from 12–20% in specialized centres and up to 40%
generally. Laparoscopic total mesorectal excision (TME) changed the balance, reducing the local recurrence rate to <10% and improving the overall 5-year survival rate to 80%, and it is currently the gold standard treatment. However, morbidity rates for rectal cancer surgery remain high.

**TaTME reduces morbidity associated with laparoscopic TME**

Transanal TME (TaTME) is a technique that can provide better postoperative outcomes and oncological results by allowing rectum mobilization using a ‘bottom-up’ approach to resection and accessing the peritoneal cavity via the anastomotic site. First trialled in pigs, the technique was shown to be both feasible and safe for humans in trials using cadavers. The first clinical trials were performed in 2009 at Clinic Hospital in Barcelona, Spain, and 250 procedures have been performed since, leading to standardization of the technique.2-4

The indications for TaTME are the same as those for laparoscopic TME, meaning it is suitable for every patient with rectal cancer. However, some situations can be challenging, such as patients with bulky tumours or T4 disease, recurrent rectal cancer, infiltration of surrounding organs, a large anterior tumour or a predicted circumferential resection margin (CRM) ≤1 mm on magnetic resonance imaging. Men who have a narrow pelvis and/or obesity and those with a ‘hostile abdomen’ may also be difficult to treat.

**“Transanal TME can provide better postoperative outcomes and oncological results”**

**Key considerations**

Key considerations include determining whether one or two teams are required for surgery, the platform used for transanal access, ensuring distal margin and sphincter preservation, rectal sectioning and lumen closure, and preservation of vessels, nerves and surrounding organs. Two teams working simultaneously is recommended since surgery time is reduced (mean 154 min, range 55–320 min vs mean 240 min, range 184–300 min with laparoscopy reported in the COLOR II study), which is much safer for the patient.5-8

TEM™ and TEO™ platforms can be expensive; flexible accesses are preferred for financial reasons, but also because the triangular position of the trocars enables greater control when cutting. The TaTME technique can be modified depending on the height of the tumour as it enables better visualization of the distal margin, better evaluation of the sphincter, and the flexibility to choose a hand-sewn or mechanical anastomosis. The sphincter can generally be preserved if the tumour is higher than 1.0 or 1.5 cm from the anal verge.2-3 Rectal lumen closure avoids tumour spillage and contamination during the surgical procedure and reduces specimen manipulation, while sectioning should ensure sufficient distal margin from the tumour. TaTME also enables better visualization of vessels, nerves and surrounding organs, as well as better haemostasis. Postoperative complications such as bleeding, leakage, anastomotic stenosis and chronic sinus can also be avoided with TaTME.

Essential points to remember when considering TaTME are a focus on circumferential and progressive resection, use of a three-dimensional viewing device and valveless insufflator trocars that stabilize pressure in the pelvis, and selection of a flexible rather than rigid platform.

**Management of sessile serrated polyp/adenoma lesions**

Serrated lesions are a heterogeneous group characterized by the presence of serrated epithelial architecture in the epithelium of the colon crypts; they include hyperplastic polyps, sessile serrated polyp/adenoma and serrated adenoma. Hyperplastic polyps are the most common serrated lesions and are generally found in the distal colon. They are not associated with cytological dysplasia and can be further classified into microvesicular and goblet cell hyperplastic polyps. Sessile serrated polyp/adenoma lesions are the second most common type of serrated lesions. They are usually flat and sessile and are more common in the proximal colon than hyperplastic polyps. Dysplastic components are present in 15–30% of cases. Traditional serrated adenomas are rare and account for less than 1% of lesions. They can be flat or pedunculated, and are often found in the distal colon. They have a complex and distorted terminal villous and villous configuration. Prominent serration and ectopic crypt foci are present, as well as dysplasia in most instances.3

**Serrated neoplasia pathway**

The serrated neoplasia pathway has traditionally been less well understood than the conventional adenoma to carcinoma pathway. It is usually triggered by BRAF mutations and can result in microsatellite unstable (MSI) or stable (MSS) colorectal cancer.3 RNF43 mutations have recently been found in many sessile serrated polyp/adenoma lesions, as well as in traditional serrated adenomas (Figure).3

Sessile serrated polyp/adenoma is associated with advanced neoplasm and interval cancers, ie, lesions that are missed by colonoscopy. A meta-analysis of 12 studies that collectively included 7,912 interval cancers reported a pooled prevalence of 3.7%.5 Interval cancers were more than twice as likely to be located in the proximal colon, and were more common in older patients (odds ratio [OR] 1.15, 95% confidence interval [CI] 1.02–1.30) and those with more comorbidities (OR 2.00, 95% CI 1.77–2.27) and diverticular disease (OR 4.25, 95% CI 2.58–7.00).5

**Risk of colorectal cancer and detection**

The 10-year risk of colorectal cancer (CRC) in patients with sessile serrated polyp/adenoma is similar to that for conventional adenomas (2.5% vs 2.3%, respectively). The risk is lower for hyperplastic polyps (1.2%) but much higher for traditional serrated adenomas (4.5%).6

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**References**

Image-enhanced endoscopy may facilitate detection of sessile serrated poly/adenoma lesions. A systematic review and meta-analysis of 13 studies of patients undergoing colonoscopy with endoscopy-based image enhancement revealed a range of sensitivities (38% to 100%), with sensitivity ≥90% observed in four of 10 narrow band imaging (NBI) or magnification-NBI studies. Pooled sensitivities for discriminating sessile serrated poly/adenomas and non-neoplastic lesions were 80% for magnification-NBI and 60% for NBI, but 49% for autofluorescence and 47% for flexible spectral imaging colour enhancement.7

**Surveillance**

There are currently no data on optimal surveillance for sessile serrated poly/adenoma lesions, but a multi-society task force on CRC made some recommendations in 2012 based on expert opinion. The recommended surveillance interval was once every 5 years for sessile serrated polyyps <10 mm in diameter with no dysplasia, but once every 3 years for lesions ≥10 mm or associated with dysplasia, as well as traditional serrated adenomas.6 A recent comparison of recommended surveillance intervals from multiple societies clearly shows the present lack of consensus, with intervals ranging from annually to once every 10 years (Table).8

**Conclusion**

Sessile serrated poly/adenoma lesions have traditionally been underdiagnosed, but they carry a similar risk of progression to CRC as conventional adenomas and are frequently associated with advanced neoplasm in the colon. It is possible that they account for the majority of missed lesions, particularly in the right colon. Image-enhanced endoscopy may help detect these lesions, but the optimal surveillance intervals remain to be defined.

**References**


**Table. Recommended surveillance intervals for serrated lesions**

<table>
<thead>
<tr>
<th>US multisociety taskforce</th>
<th>NIH working group</th>
<th>ESGE</th>
<th>European Union/ IARC</th>
<th>Surveillance interval, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPS</td>
<td>SPS</td>
<td>N/A</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>SSA/SSP ≥10 mm, SSA/SSP with dysplasia, or TSA</td>
<td>SSA/SSP or TSA ≥10 mm or 3 or more in number. Two or more SSA/SSP 10 mm in sizes* or any SSA/SSP with dysplasia α</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>SSA/SSP &lt;10 mm with no dysplasia</td>
<td>≤4 HPs any size proximal to sigmoid, or any proximal HP &gt;5 mm in size, or 1-2 SSPs or TSAs &lt;10 mm</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>-</td>
<td>HP &lt;10 mm in recto-sigmoid, or ≤3 HP ≤5 mm proximal to sigmoid</td>
<td>Serrated polyp &lt;10 mm with no dysplasia</td>
<td>All serrated lesions of any size without adenomatous dysplasia (no recommendation for surveillance)</td>
<td>10 (routine screening)</td>
</tr>
</tbody>
</table>

* This proposed strategy considers HPs, SSA/SSPs and TSAs as serrated polyps.

1-3 years recommended depending on clinical circumstances. SPS should be considered.

ESGE, European Society of Gastrointestinal Endoscopy; HP, hyperplastic poly; IARC, International Agency For Research on Cancer; NIH, National Institutes of Health (USA); SPS, serrated polyposis syndrome; SSA, sessile serrated adenoma; SSP, sessile serrated poly; TSA, traditional serrated adenoma.

**Figure.** The serrated neoplasia pathway is generally triggered by BRAF and/or RNF43 mutations.4

<table>
<thead>
<tr>
<th>Conventional Pathway</th>
<th>Serrated Pathway</th>
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<tbody>
<tr>
<td>Familial Germline APC</td>
<td>APC 2nd hit KRA S</td>
</tr>
<tr>
<td>Sporadic</td>
<td>APC KRA S</td>
</tr>
<tr>
<td>AD</td>
<td>HP</td>
</tr>
<tr>
<td>MSS CRC</td>
<td>SSA/TSA</td>
</tr>
<tr>
<td>MSS CRC</td>
<td>RNF43 2nd hit BRAF</td>
</tr>
<tr>
<td>MSS/MSI CRC</td>
<td>MSS CRC</td>
</tr>
</tbody>
</table>

AD, adenoma; CIMP, CpG island methylator phenotype; CRC, colorectal cancer; HP, hyperplastic poly; MSI, microsatellite instability; MSS, microsatellite stable; SSA, sessile serrated adenoma; TSA, traditional serrated adenoma.
 Colonoscopy would be carried out for hemostasis. A polyp was categorized as proximal if it was found proximal to the splenic flexure. The colonoscope, polypectomy snare and electrosurgical device were used. Bridging therapy would be withheld for 48 to 72 hours. Bridging therapy is to use parenteral, anticoagulant preparation that mimics the effects of warfarin. UFH: Continuous intravenous heparin infusion was given with bridging therapy if the INR was >2.2. UFH bridging therapy was used. The high incidence of PPB was similar to what was published in the literatures. The rate of thromboembolism (1%) in our study was comparable to the incidence rate in published studies. The incidence and predictors of post-polypectomy bleeding. Factors applied where appropriate. Univariate analysis was performed for comparing the effectiveness of prophylactic anticoagulant therapies (or with mucosal biopsies) alone, as it is now widely accepted. **Conclusion**

In this pilot open-label randomised trial, FMT was not superior to vancomycin in subjects with an initial episode of CDI. A restoration of healthy control enriched bacteria in recipients was observed after FMT, with a decrease in abundance of CDI-enriched bacteria.

**Abstract of Research Project “Fecal Microbiota Transplantation Versus Vancomycin for Initial Clostridium difficile Infection: An Open-label Randomised Controlled Trial”**

### Background
Fecal microbiota transplantation (FMT) is effective for the treatment of patients with recurrent *Clostridium difficile* infection (CDI). We studied the effect of FMT in patients with an initial episode of CDI compared with standard vancomycin regimen.

### Methods
In a single-center, open-label, randomised study, we assigned patients with an initial episode of CDI to receive either: oral vancomycin (500mg four times daily) followed by FMT consisting of a single infusion of donor feces through a nasoduodenal tube; or a standard oral vancomycin regimen (500mg four times daily for 10 days). The primary end point was resolution of diarrhea associated with *C. difficile* infection without relapse within 10 weeks after initiation of therapy. Secondary outcomes included 30-day mortality, and adverse effects.

### Results
Resolution of *C. difficile* infection occurred in 11 of 15 patients (73.3%) receiving FMT and in 10 of 15 patients (66.7%) receiving vancomycin (p=1.0). Two deaths occurred in the vancomycin group and none in the FMT group within 30 days of recruitment. No serious adverse events attributed to FMT were observed. A restoration of healthy control enriched bacteria in recipients was observed after FMT, with a decrease in the abundance of CDI-enriched bacteria.

### Conclusions
In this pilot open-label randomised trial, FMT was not superior to vancomycin in subjects with an initial episode of CDI. A restoration of healthy control enriched bacteria in recipients was observed after FMT, with a decrease in abundance of CDI-enriched bacteria.

**Table 1. Subjects (including patients and donors) baseline characteristics**

<table>
<thead>
<tr>
<th></th>
<th>FMT (n=15)</th>
<th>Vancomycin (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>8 (53.0%)</td>
<td>7 (46.7%)</td>
</tr>
<tr>
<td>Median age, years (IQR)</td>
<td>68(52-84)</td>
<td>83(76-92)</td>
</tr>
<tr>
<td>Severe CDI*, n (%)</td>
<td>7 (46.7%)</td>
<td>9 (60.0%)</td>
</tr>
<tr>
<td>Smoker/ Ex-smoker, n (%)</td>
<td>2 (13.3%)</td>
<td>3 (20.0%)</td>
</tr>
<tr>
<td>Alcohol drinker/ ex-drinker, n (%)</td>
<td>2 (13.3%)</td>
<td>3 (20.0%)</td>
</tr>
<tr>
<td>History of appendectomy, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*Definition of Severe CDI: Any of white blood cell (WBC) count ≥15 x 109/L, temperature > 38.5°C, blood creatinine >50% increase above baseline or evidence of severe colitis (abdominal signs, radiology).

**Table 2. Outcome Measures Comparing Fecal Microbial Transplantation With Vancomycin**

<table>
<thead>
<tr>
<th></th>
<th>FMT (n=15)</th>
<th>Vancomycin (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure without relapse, n (%)</td>
<td>11 (73.3%)</td>
<td>10 (66.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>30 days mortality, n (%)</td>
<td>0 (0%)</td>
<td>2 (13.3%)</td>
<td>0.483</td>
</tr>
<tr>
<td>Median length of hospital stay (IQR)</td>
<td>15 (8-34)</td>
<td>13 (5-33)</td>
<td>0.756</td>
</tr>
</tbody>
</table>

**References**

Differentiating between primary sclerosing cholangitis (PSC) and IgG4-related sclerosing cholangitis (IgG4-SC) is difficult using cholangiography alone. A study of cholangiograms in patients with PSC, cholangiocarcinoma or IgG4-SC showed a sensitivity of 45% for diagnosing PSC and poor interobserver agreement (0.18, kappa statistic), which suggests that many cases of IgG4-SC could be misdiagnosed as PSC or cancer if physicians rely on cholangiogram alone.1 This would also mean that many patients may miss out on effective treatment.1 However, PSC can also be distinguished from IgG4-SC by the presence of elevated IgG levels in serum and tissue, as well as by treatment response since true PSC will not characteristically respond to steroids, and only a small proportion of PSC patients have elevated IgG4.2

Assessment and management of dominant strictures
Approximately 36–50% of patients with PSC will develop dominant strictures, but determining whether these are benign or malignant may be particularly challenging. In patients with PSC whose initial presentation is with a dominant stricture, the stricture will be malignant in 50% of cases.3,4 Although disease progression is unpredictable, malignancy is a major cause of mortality.

Routine biliary cytology and cancer antigen 19.9 testing are of poor sensitivity in assessing biliary strictures in PSC, and better diagnostic tests are needed for assessing malignancy risk.3 In PSC, clinicians should increasingly strive to make a pathological diagnosis of indeterminate strictures, by means of cholangiography and/or fluoroscopy-directed endobiliary biopsies.5–9 Indeed, cholangiography is increasingly used for PSC strictures and has a reported sensitivity of 92% and specificity of 93% compared with 66% and 51%, respectively, for endoscopic retrograde cholangiopancreatography.10 In terms of structure management, there is a move away from stenting towards balloon dilatation alone.

“Pathological diagnosis by cholangioscopic or endobiliary biopsy is more effective than cytology for assessing malignancy risk in PSC”

Medical therapy
Immunosuppression is not suitable for PSC patients except in the context of an overlap syndrome such as PSC/autoimmune hepatitis. Although intermediate doses of ursodeoxycholic acid (UDCA) have been shown to improve biochemistry and histology, this does not affect clinical outcomes. Indeed, a trial of high-dose UDCA in PSC patients reported a doubling of the risk of death or transplantation versus placebo.11 The 2010 American Association for the Study of the Liver Diseases (AASLD) guidelines therefore recommend against the use of UDCA in adult PSC patients.12 However, the 2016 European Association for the Study of the Liver guidelines suggest that UDCA may be beneficial for pediatric PSC.13 At present, there are insufficient data to allow a specific recommendation for the general use of UDCA in PSC, although all agree that high-dose UDCA (eg >25 mg/kg/day) should not be used.

In patients with IgG4+ PSC, a trial of steroid therapy may show some benefit, although complications appear common, and more than 50% of patients relapse once steroid therapy is stopped.14 Osteoporosis occurs in approximately 4–10% of PSC patients, so an assessment of bone densitometry should be made at diagnosis and every 2–3 years thereafter. Supplementation with calcium, vitamin D and bisphosphonates may be effective for prevention.

Disease surveillance
The 10-year survival rate from initial diagnosis is 65% among PSC patients and the mean time to death or transplantation is 10–18 years. Cholangiocarcinoma is the leading cause of death in patients who do not receive transplants. The standard incidence ratio for colorectal cancer is 10.3, while the ratios for hepatobiliary and pancreatic cancer are 160.6 and 9.7, respectively.15

Surveillance for hepatobiliary and colonic malignancy is vital and is extremely important in patients with PSC and ulcerative colitis, as PSC dramatically increases the risk of colorectal neoplasia.16

“Surveillance is extremely important in patients with PSC and ulcerative colitis, as PSC dramatically increases the risk of colorectal neoplasia”

Surgery/transplantation
Transplantation is the only effective means of treating end-stage PSC.17 Although more than 80% of patients remain alive 5 years after transplantation, PSC recurrence in the graft occurs in 20–25% after 10 years. Cholangiocarcinoma also recurs in 80% of transplanted patients. A highly select group of patients may benefit from transplant following chemotherapy and radiotherapy, but sadly cholangiocarcinoma usually precludes consideration of transplantation in PSC.18

References
Background & Aims
Heparin bridging therapy is commonly used in patients with high thromboembolic risk undergoing colonoscopy. Specific data on its use remains limited. We aim to evaluate the safety and efficacy of bridging therapy in this group of patients.

Methods
Consecutive warfarinized patients who underwent colonoscopy in a regional hospital from Jan 2006 to Dec 2015 were retrieved. Unfractionated heparin (UFH) group was compared with low-molecular-weight heparin (LMWH) group for assessment of thromboembolic risk. The 2 bridged groups were compared as a whole to a control group of those who received warfarin anticoagulation but not bridging for assessment of the bleeding risk.

Results
A total of 392 patients who was taking warfarin underwent colonoscopic procedure. Half of them (50.5%) received bridging therapy and in which 62.1% of them were given LMWH. For those patients with a high thromboembolic risk, an overall 1% of thromboembolic event and an overall post-polypectomy bleeding rate of 16.7% were noted. Though the post-polypectomy bleeding (PPB) rate was similar between UFH and LMWH groups (17.1% vs. 16.4%; P=0.92), the whole bridged populations had a significantly higher PPB rate than the controls who did not receive bridging therapy (3.6%; P<0.01). On multivariate analysis, risk factors of post-polypectomy bleeding included a polyp size ≥10 mm (OR 3.58; CI 95% 1.32-9.72; P=0.01) and the use of bridging therapy (OR 5.03; CI 95% 1.39-18.2; P=0.01). The use of LMWH as bridging therapy in elective colonoscopy was associated with a shorter median length of stay. (5 vs. 7 days for UFH; P=0.01).

Conclusion
The use of UFH and LMWH were comparable as bridging therapy for patients who underwent colonoscopy. However, under the effect of anticoagulation, the post-polypectomy bleeding risk remained high and special precautions should be taken to minimize such adverse events.

1. Introduction
Warfarin is commonly used for the treatment of venous thromboembolism, or prevention of thromboembolic events in patients with atrial fibrillation and mechanical heart valve replacement. Cessation of warfarin before invasive procedures may increase the risk of peri-procedural thromboembolism, whereas continuation of anticoagulation will increase the risk of procedure-related bleeding. Bridging therapy is to use parenteral, short-acting heparin derivatives during the peri-procedural period, which aims to reduce thromboembolic risk. Unfractionated heparin, and recently low-molecular-weight heparin are used for this purpose.

Colonoscopy and polypectomy is a commonly performed procedure in the field of gastroenterology. Specific efficacy and safety data of bridging therapy in this field is, however, lacking. Poor adherence was reported from recent surveying studies despite the recommendations of international guidelines. With this regard, we would like to report our experience of using bridging therapy in patients with high thromboembolic risk who underwent colonoscopy.

2. Study Design & Patient Populations
This is a single-center, retrospective cohort study conducted in Queen Elizabeth Hospital, Hong Kong, evaluating the use of bridging anticoagulation therapy in warfarinized patients who underwent colonoscopy between the period 2006 to 2015. Study population was identified from a computerized Clinical Data Analysis and Reporting System. Consecutive patients with age equal to or more than 18 years old, who had received continuous warfarin anticoagulation for at least 4 weeks prior colonoscopy procedure, were included into analysis.

The study is divided into 2 parts:
1. Assessment of the thromboembolic risk in which the LMWH-bridged group was compared with the UFH group. Since bridging therapy is now the standard of care in patients with high thromboembolic risk^1-4, the two different types of BT were compared to see if they differ in the thromboembolic risk.
2. Assessment of the significance of post-polypectomy bleeding risk in relation to the use of bridging therapy, and the difference, if any, between the two groups of BT.

The study group included patients who received peri-procedural bridging anticoagulation therapy, either unfractionated heparin (UFH) or low molecular weight heparin (LMWH). All subjects were having high thromboembolic risk, namely atrial fibrillation (AF) with high thromboembolic risk as defined by a CHA2DS2-VASc score ≥2,^ recent venous thromboembolic episode within 3 months, chronic rheumatic heart disease (CRHD) with AF, thrombophilia, mitral valvular replacement (MVR), aortic valvular replacement (AVR) with AF or prior thromboembolic event, and double (mitral and aortic) valvular replacement (DVR). They were divided into 2 groups according to the type of bridging therapy used and between them the peri-procedural thromboembolic risk was compared. The assessment of post-polypectomy bleeding risk was achieved by comparing the bridged population against patients who was taking warfarin but did not receive bridging anticoagulation around time of colonoscopy.

Patients were excluded if 1) both UFH & LMWH were used concomitantly within the same admission, 2) using a LMWH other than Enoxaparin, or 3) colonoscopy was done in the context of acute gastrointestinal (GI) bleeding in which no bridging therapy was given, or 4) bridging therapy was not given because of adequate INR before the colonoscopy procedure, or 5) receiving novel oral anticoagulants (NOACs) at baseline, instead of warfarin.

2.1 Peri-procedural Management of Anticoagulation
The peri-procedural management was done according to our own hospital management protocol. Before colonoscopy, warfarin was stopped for 3 to 5 days. PT-INR was determined 2 days thereafter. Bridging therapy would be started once the INR level had fallen ≤ 1.5, which included either:

1. LMWH: Enoxaparin sodium (Clexane; Sanofi-Aventis) administered at 0.1ml/10kg subcutaneously every 12 hours (with or without renal adjustment). LMWH was stopped for 24 hours before the procedure.
2. UFH: Continuous intravenous heparin infusion was given with regular monitoring of activated partial thromboplastin time (aPTT) at 6-8 hour interval, aimed to achieve an aPTT of 1.5 to 2-fold the upper limit of normal. UFH was stopped for 6 hours before the procedure.

For uncomplicated cases after colonoscopy, warfarin would be resumed within 1 day and BT would be started when indicated. In cases with anticipated high risk of bleeding, both warfarin & bridging therapy would be withheld for 48 to 72 hours. Bridging anticoagulation would be continued until the PT-INR level returned to therapeutic range.

2.2 Colonoscopy Procedure, Lesions & Follow-up
All colonoscopies were performed in our endoscopy unit by the hospital-accredited endoscopists. Moderate sedation was usually employed and cardiopulmonary status of the patient being closely monitored. Polypectomy was performed with the standard colonoscope, polypectomy snare and electrosurgical device. The colonic polyp was categorized as proximal if it was found proximal to the splenic flexure, or distal if the polyp was located in descending colon, sigmoid colon and rectum. The type of polyp was classified as pedunculated or sessile according to Paris classification. For large sessile polyps, submucosal cushion might be created using normal saline, or adrenaline, or mixture of them, before polypectomy procedure to minimize the risk of perforation. Detachable snare (Endoloop) or prophylactic clipping might be applied at discretion of individual endoscopist. Bleeding immediate after polypectomy was secured by adrenaline injection, hemoclip or argon plasma coagulation.

After colonoscopy, patient was usually discharged on the same day. If there was anticipated risk of bleeding, or bleeding had occurred immediate after polypectomy, or bridging therapy (especially UFH) was required, the patient would be admitted for observation and warfarin titration. In case of PPB, an emergency colonoscopy would be carried out for hemostasis. Patient who required LMWH as bridging therapy might receive injections in day ward facilities, or to be taught for doing injections themselves, on a case-by-case basis. An early clinic appointment, usually within 2-4 weeks, would be arranged for the review of histology reports of mucosal biopsies and resected polyps when appropriate.

2.3 Study Variables
The baseline clinical and demographic variables recorded included age, gender, presence or absence of atrial fibrillation, hypertension, diabetes, prior coronary artery disease or acute coronary syndrome, cerebrovascular accident, venous thromboembolic episodes, baseline hemoglobin, platelet count, prothrombin time-international normalized ratio prior to colonoscopy. The glomerular filtration rate (eGFR) of the study populations was estimated using the Modification of Diet in Renal Disease (MDRD) formula. Colonoscopy reports and the details of polypectomy procedure were recorded. The duration of peri-procedural bridging anticoagulation and the timing of warfarin resumption were reviewed.

2.4 Outcome Measurements
The primary outcome of the study was to compare thromboembolic events between patients who received LMWH versus UFH bridging therapy, and secondly, the bleeding adverse events occurring among the bridged population within 30 days of colonoscopy. To evaluate the significance of bleeding complications, the post-polypectomy bleeding results were compared between bridging therapy groups and the historic warfarinized controls but without peri-procedural bridging therapy. Arterial thromboembolism was defined as the occurrence of either an cardiovascular accident or transient ischemic attack, an acute coronary syndrome, or an arterial ischemic event involving a limb or viscerla. Venous thromboembolism was defined as deep vein thrombosis, or pulmonary embolism. Post-polypectomy bleeding was classified as early if it occurred within 24 hours of colonoscopy, or delayed if bleeding was between 24 hours to 30 days. Bleeding outside the colon was also studied. A major bleeding episode was defined as a bleeding resulted in a drop in hemoglobin of 2g/dL or need of 2 units of packed cell transfusion. Secondary outcome included length of stay and mortality within 30 days of the colonoscopy procedure between the 2 bridged population groups.

2.5 Statistical Analysis
All statistical analysis was done using IBM SPSS Statistics software (version 23). Continuous variables were expressed as mean (± standard deviation) if they were parametric, or median (interquartile range) if they were non-parametric. Categorical variables were expressed as frequency or number of that particular group. Independent sample T-test was used for comparison of continuous variables with normal distribution, while Mann-Whitney U test was used for comparison of continuous variables with skewed distribution. Chi-square test was used for comparison of categorical variables, and Fisher’s exact test was applied where appropriate. Univariate analysis was performed for studying the predictors of post-polypectomy bleeding. Factors with a P value <0.2 would be included for subsequent multivariate analysis using logistic regression. All P values were two-sided and a value of <0.05 was considered significant.
Table 1. Baseline Characteristics (UFH vs. LMWH) for Assessment of Thromboembolism

<table>
<thead>
<tr>
<th></th>
<th>UFH (N=75)</th>
<th>LMWH (N=123)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, Years (IQR)</td>
<td>64 (58-74)</td>
<td>64 (57-72)</td>
<td>0.47</td>
</tr>
<tr>
<td>Age ≥75 (% No.)</td>
<td>22.7 (17)</td>
<td>16.3 (20)</td>
<td>0.26</td>
</tr>
<tr>
<td>Male (% No.)</td>
<td>41.3 (31)</td>
<td>46.3 (57)</td>
<td>0.49</td>
</tr>
</tbody>
</table>

**Medical History**

- **Atrial fibrillation (% No.)**
  - UFH 73.3 (55)
  - LMWH 68.3 (84)
  - P value 0.45
- **Medication CHA2DS2-VASc score (IQR)**
  - UFH 3 (2-4)
  - LMWH 3 (2-4)
  - P value 0.79
- **Hypertension (% No.)**
  - UFH 37.3 (28)
  - LMWH 35 (43)
  - P value 0.74
- **Diabetes Mellitus (% No.)**
  - UFH 26.7 (20)
  - LMWH 28.5 (35)
  - P value 0.79
- **Congestive Heart Failure (% No.)**
  - UFH 24 (18)
  - LMWH 23.6 (29)
  - P value 0.95
- **History of CVA (% No.)**
  - UFH 18.7 (14)
  - LMWH 13.8 (17)
  - P value 0.36
- **History of AMI (% No.)**
  - UFH 6.7 (5)
  - LMWH 5.7 (7)
  - P value 0.77*
- **History of VTE (% No.)**
  - UFH 9.3 (7)
  - LMWH 13.16 (16)
  - P value 0.43
- **History of Malignancy (% No.)**
  - UFH 16 (12)
  - LMWH 16.3 (20)
  - P value 0.96
- **History of Variceal Veins (% No.)**
  - UFH 5.3 (4)
  - LMWH 2.4 (3)
  - P value 0.43*

**Indication of Anticoagulation (i.e. high thromboembolic risk factors)**

- AF with high thromboembolic risk (% No.)
  - UFH 57.3 (43)
  - LMWH 51.2 (63)
  - P value 0.4
- VTE Within 3 Months (% No.)
  - UFH 0 (0)
  - LMWH 2.4 (3)
  - P value 0.29*
- CRHD with AF (% No.)
  - UFH 9.3 (7)
  - LMWH 7.3 (9)
  - P value 0.61
- Thrombophilia (% No.)
  - UFH 1.3 (1)
  - LMWH 0.8 (1)
  - P value 1*
- Mechanical MVR (% No.)
  - UFH 41.3 (31)
  - LMWH 49.3 (54)
  - P value 0.72
- AVR with AF or thromboembolic events (% No.)
  - UFH 14.7 (11)
  - LMWH 7.3 (9)
  - P value 0.1
- Mechanical DVR (% No.)
  - UFH 29.3 (22)
  - LMWH 23.6 (29)
  - P value 0.37

**Concomitant Medications**

- Aspirin (% No.)
  - UFH 20 (15)
  - LMWH 14.6 (18)
  - P value 0.33
- NSAID (% No.)
  - UFH 2.7 (2)
  - LMWH 2.4 (3)
  - P value 1*

**Indication of Colonoscopy**

- Anaemia (% No.)
  - UFH 16 (12)
  - LMWH 35 (43)
  - P value <0.01
- Positive FOB (% No.)
  - UFH 2.7 (2)
  - LMWH 0.8 (1)
  - P value 0.56*
- Gastrointestinal bleeding (% No.)
  - UFH 40 (30)
  - LMWH 22.27 (27)
  - P value <0.01
- Screening of CA colon (% No.)
  - UFH 36 (27)
  - LMWH 37.4 (46)
  - P value 0.84
- Others (% No.)
  - UFH 5.3 (4)
  - LMWH 5.7 (7)
  - P value 1*

**Pre-procedure Laboratory Parameters**

- Median haemoglobin (IQR)
  - UFH 12 (9.8-13.3)
  - LMWH 11.9 (9.9-13.2)
  - P value 0.04
- Median platelet (IQR)
  - UFH 203 (158-245)
  - LMWH 186 (133-234)
  - P value 0.09
- Median creatinine (IQR)
  - UFH 87 (64-101)
  - LMWH 83 (69-110)
  - P value 0.71
- Median eGFR (IQR)
  - UFH 71.7 (52.6-89.4)
  - LMWH 68.5 (50.1-87.4)
  - P value 0.71
- Median INR (IQR)
  - UFH 1.27 (1.18-1.43)
  - LMWH 1.32 (1.21-1.49)
  - P value 0.16

**Colonoscopy Procedure**

- Diagnostic Procedure Only (% No.)
  - UFH 50.7 (38)
  - LMWH 39.8 (49)
  - P value 0.14
- Mucosal Biopsy (% No.)
  - UFH 6.7 (5)
  - LMWH 17.1 (21)
  - P value 0.04
- Polypectomy (% No.)
  - UFH 46.7 (35)
  - LMWH 49.6 (61)
  - P value 0.69
- Hemostasis (If any)
  - Argon Plasma Coagulation (% No.)
    - UFH 40 (0)
    - LMWH 4.9 (6)
    - P value 0.09*
  - Adrenaline injection (% No.)
    - UFH 6.7 (5)
    - LMWH 8.1 (10)
    - P value 0.71
  - Normal Saline injection (% No.)
    - UFH 2.7 (2)
    - LMWH 12.2 (15)
    - P value 0.02
  - Endoloop (% No.)
    - UFH 0 (0)
    - LMWH 1.6 (2)
    - P value 0.53*
  - Clipping (% No.)
    - UFH 5.3 (4)
    - LMWH 8.9 (11)
    - P value 0.35

**Peri-procedural Bridging Therapy**

- Median Duration of Pre-CLN BT, Days (IQR)
  - UFH 2 (1-3)
  - LMWH 1 (1-2)
  - P value 0.19
- Median Time to Start Post-CLN BT, Days (IQR)
  - UFH 0 (0-0)
  - LMWH 0 (0-1)
  - P value 0.01
- Median Duration of Post-CLN BT, Days (IQR)
  - UFH 4 (3-5)
  - LMWH 4 (3-6)
  - P value 0.52
- Median Time to Resume Warfarin, Days (IQR)
  - UFH 1 (0-1)
  - LMWH 1 (0-1)
  - P value 0.84
- Median length of stay for elective procedures, Days (IQR)
  - UFH 7 (5-9)
  - LMWH 5 (1-9)
  - P value 0.01


* Fisher Exact Test
3. Results
During the period 2006-2015, a total of 502 warfarinized patients underwent colonoscopy procedure in Queen Elizabeth Hospital. Seventy-six cases were excluded from the analysis for colonoscopy being performed in the context of acute gastrointestinal bleeding; because warfarin was started for less than 4 weeks (26 patients); because of concomitant use of UFH & LMWH in the same admission (4 patients); mechanical valve replacement were not given heparin bridging because INR remained ≥1.5 the day before procedure (3 patients). A total of 198 patients received bridging anticoagulation, and among them 75 patients (37.9%) received UFH and 123 patients (62.1%) received LMWH. For comparison of the PPB risk related to the use of bridging therapy (BT), 194 warfarinized patients in whom bridging heparin therapy was not given were identified as the control. All 392 patients had been followed-up for at least 2 months after the colonoscopy procedure at the time of data analysis. (Figure 1)

A. UFH versus LMWH for Thromboembolic Risk Assessment
1. Patient Characteristics
Table 1 depicted the baseline demographics and clinical characteristics of patients who had received bridging anticoagulation. The UFH group and the LMWH group patients were comparable in terms of median age, gender, past medical history. A comparable proportion of patients were taking aspirin (20% in UFH vs. 14.6% in LMWH; P=0.33). The commonest indication for anticoagulation was mechanical valve replacement (85.3% in UFH vs. 74.8% in LMWH). All three patients who experienced recent venous thromboembolic event within 3 months received LMWH as bridging therapy (P=0.29). A significantly higher percentage of patients (40%) in UFH group had colonoscopy done because of overt GI bleeding (vs. 22% in LMWH group; P<0.01), while 16% of the UFH-bridged group had colonoscopy done for anemia (vs. 35% in LMWH group; P<0.01). The baseline laboratory results before colonoscopy were comparable. The median duration of pre- and post-colonoscopy bridging therapy and the median time of warfarin resumption were also similar between the two groups.

2. Clinical Outcome
The overall rate of thromboembolism was 1% (2 out of 198 patients). Two patients in the UFH group developed ischemic stroke within 30 days after endoscopic procedure (vs. 0% in the LMWH group; P=0.14; Table 2). One patient with underlying dual mechanical valve replacement and AF developed ischemic stroke on day 2 after colonoscopy while she was waiting for re-scope as the first colonoscopy failed to pass through an obstructive malignant lesion. UFH was started on day 0 with INR of 1.13s & aPTT of 33s prior to the episode. Another patient with prosthetic heart valves developed ischemic stroke on day 20 after the procedure. Therapeutic level of PT-INR was achieved before she was discharged from hospital. Subsequently, however, the patient was noted to have a suboptimal level of anticoagulation (INR 1.59) at the onset of stroke. There was no acute coronary syndrome or venous thromboembolism in our cohort.

One patient developed severe spontaneous retroperitoneal hemorrhage on day 7 after colonoscopy. The aPTT level remained within therapeutic range at the diagnosis of the bleeding event. One patient died of severe pneumonia with streptococcus pneumoniae bacteremia within same admission episode. For patients undergoing elective procedure, the use of LMWH was associated with a significantly shorter median length of hospital stay (5 vs. 7 days; P=0.01).

B. Post-polypectomy Bleeding Risk (Bridging Therapy Groups versus Controls)
1. Patient Characteristics
The baseline demographics and clinical characteristics of the bridged population and the controls were shown on Table 3. Both groups of patient had comparable characteristic in terms of the indications for colonoscopy, namely cancer screening, overt gastrointestinal bleeding and anemia. The control group had a higher median age of 71 (vs. 64; P<0.01) and higher proportion of male sex (37.1% vs. 18.7%; P<0.01). Significantly more patients (27.3% vs. 16.7%; P=0.01) in the control population were taking aspirin concomitantly. The control group patients had a similar baseline median platelet count (203 vs. 192; P=0.09) & median INR (1.32 vs. 1.31; P=0.91), and a higher median baseline haemoglobin (12.7 g/dL vs. 12 g/dL; P<0.01), and a slightly less median eGFR (65 ml/min vs. 69 ml/min; P<0.01) when compared to their heparin-bridged counterparts. Significantly shorter in terms of median time of warfarin resumption (day 0 vs. day 1; P<0.01) was noted in the controls.

Table 2. Clinical Outcome within 30 Days Of Colonoscopy

<table>
<thead>
<tr>
<th>Thromboembolic Complications</th>
<th>UFH (N=75)</th>
<th>LMWH (N=123)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Stroke (%. No.)</td>
<td>2.7 (2)</td>
<td>0 (0)</td>
<td>0.14*</td>
</tr>
</tbody>
</table>

Table 3. Baseline Characteristics (Bridging Therapy vs. Controls)

<table>
<thead>
<tr>
<th>Bridging Therapy (N=198)</th>
<th>Control (N=194)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age (IQR)</td>
<td>64 (58-73)</td>
<td>71 (60-77)</td>
</tr>
<tr>
<td>Age &gt;=75 (%). No.</td>
<td>18.7 (37)</td>
<td>37.1 (72)</td>
</tr>
<tr>
<td>Male (%). No.</td>
<td>44.4 (88)</td>
<td>56.7 (110)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concomitant Medications</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (%. No.)</td>
<td>0.01</td>
</tr>
<tr>
<td>Thienopyridines (%. No.)</td>
<td>0.49*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication of Colonoscopy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia (%. No.)</td>
<td>0.16</td>
</tr>
<tr>
<td>Positive FOB (%. No.)</td>
<td>0.04</td>
</tr>
<tr>
<td>Gastrointestinal bleeding (%. No.)</td>
<td>0.83</td>
</tr>
<tr>
<td>Screening of CA colon (%. No.)</td>
<td>0.5</td>
</tr>
<tr>
<td>Others (%. No.)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-CLN laboratory parameters</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median platelet (10^3)</td>
<td>192 (148-243)</td>
</tr>
<tr>
<td>Median eGFR (IQR)</td>
<td>69 (51-88)</td>
</tr>
<tr>
<td>Median INR (IQR)</td>
<td>1.31 (1.19-1.48)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coloscopy Procedure</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal Biopsy (%. No.)</td>
<td>1.0 (26)</td>
</tr>
<tr>
<td>Polypotomy (%. No.)</td>
<td>48.5 (96)</td>
</tr>
<tr>
<td>Median Max. Size of Polyp</td>
<td>5 (3-10)</td>
</tr>
<tr>
<td>Resected, mm (IQR)</td>
<td></td>
</tr>
<tr>
<td>Endoscopic Submucosal Dissection (%. No.)</td>
<td>1.5 (3)</td>
</tr>
<tr>
<td>Hemostasis (If any)</td>
<td></td>
</tr>
<tr>
<td>Argon Plasma Coagulation (%. No.)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Adrenaline injection (%. No.)</td>
<td>7.6 (15)</td>
</tr>
<tr>
<td>Normal Saline injection (%. No.)</td>
<td>8.6 (17)</td>
</tr>
<tr>
<td>Endoloop (%. No.)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Clipping (%. No.)</td>
<td>7.6 (15)</td>
</tr>
<tr>
<td>Median Time to Resume Warfarin, Days (IQR)</td>
<td>1 (0-1)</td>
</tr>
<tr>
<td>Median length of stay, Days (IQR)</td>
<td>6 (3-9)</td>
</tr>
</tbody>
</table>

IQR=interquartile range. %.=percentage. No.=number
*Fisher Exact Test
Table 4. Clinical Outcome Within 30 Days Of Colonoscopy

<table>
<thead>
<tr>
<th>Bleeding Complications</th>
<th>UFH (N=75)</th>
<th>LMWH (N=123)</th>
<th>P value</th>
<th>Bridging Therapy (N=198)</th>
<th>Control (N=194)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypectomy (%; No.)</td>
<td>46.7 (35)</td>
<td>49.6 (61)</td>
<td>0.69</td>
<td>48.5 (96)</td>
<td>42.8 (83)</td>
<td>0.26</td>
</tr>
<tr>
<td>Post-Polypectomy Bleeding (%; No.)</td>
<td>17.1 (6)</td>
<td>16.4 (10)</td>
<td>0.92</td>
<td>16.7 (16)</td>
<td>3.6 (3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Median Onset of Bleeding, Days (IQR)</td>
<td>3.5 (1-5)</td>
<td>3 (1-5)</td>
<td>0.06</td>
<td>3 (1-4)</td>
<td>5 (3-6)</td>
<td>0.31</td>
</tr>
<tr>
<td>Major PPB (%; No.)</td>
<td>83 (5)</td>
<td>20 (2)</td>
<td>1*</td>
<td>43.8 (7)</td>
<td>33.3 (1)</td>
<td>0.07*</td>
</tr>
<tr>
<td>Median Hemoglobin Drop, g/dL (IQR)</td>
<td>1.4 (0-3.5)</td>
<td>2.5 (0.9-3.1)</td>
<td>1</td>
<td>1.8 (0.5-3.3)</td>
<td>0.0 (0-1.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>Median Units of Packed Cells Transfused (IQR)</td>
<td>0 (0-2)</td>
<td>0 (0-3)</td>
<td>0.9</td>
<td>0 (0-2.5)</td>
<td>1 (0.5-1.5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Endoscopic Hemostasis (%; No.)</td>
<td>66.6 (4)</td>
<td>80 (8)</td>
<td>0.6</td>
<td>75 (12)</td>
<td>33.3 (1)</td>
<td>0.22</td>
</tr>
<tr>
<td>Bleeding Other Than GI Tract (%; No.)</td>
<td>1.3 (1)</td>
<td>0 (0)</td>
<td>0.38*</td>
<td>0.5 (1)</td>
<td>0.5 (1)</td>
<td>1*</td>
</tr>
</tbody>
</table>

IQR=interverquartile range, %=percentage, No.=number

*Fisher Exact Test

Figure 2. Post-polypectomy bleeding rate between study groups

2. Clinical Outcome
Colonic polypectomy (Table 4) was performed in 96 out of 198 colonoscopic procedures, and was similar between the UFH and LMWH group (46.7% vs. 49.6%; P=0.69). The polypectomy rate was also comparable between bridged patients and the controls (48.5% and 42.8% respectively; P=0.26). Post-polypectomy bleeding rate was high and was comparable between the 2 groups (Table 4; 17.1% in UFH vs. 16.4% in LMWH; P=0.92; Figure 2). There was no significant difference between UFH and LMWH group for the onset and severity of bleeding, median level of hemoglobin drop and the need for blood transfusion.

When compared to control group populations, post-polypectomy bleeding rate was significantly higher in heparin-bridged patients (16.7% vs. 3.6% control; P<0.01; Figure 2), and there was a tendency towards a major bleeding episode (43.8% N=7 vs. 33.3% control N=1; P=0.07). There was no significant difference between the median onset times of bleeding. One elderly lady of 85 years old in the control group died of hospital acquired pneumonia after prolonged stay for management of her persistent transfusion-dependent anemia due to the newly diagnosed CA sigmoid.

3. Predictors of Post-Polypectomy Bleeding
With univariate analysis of the whole study populations, it was shown that a polyp size ≥10 mm (OR 9.8; CI 95% 3.75-25.61; P<0.01), polypectomy site at distal colon (OR 3.16; CI 95% 1.25-8.01; P=0.01), use of aspirin (OR 5.6; CI 95% 1.6-19.5; P=0.01), early resumption of bridging therapy within 48 hours (OR 2.82; CI 95% 1.05-7.59; P=0.03) were associated with post-polypectomy bleeding (Table 5). Multivariate logistic regression analysis showed that only polyp size ≥10 mm (OR 3.58; CI 95% 1.32-9.72; P=0.01) and the use of bridging therapy (OR 5.03; CI 95% 1.39-18.2; P=0.01) were independently associated with increased risk of post-polypectomy bleeding (Table 5).
4. Discussion
Existing evidence of direct comparison between unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH) are limited and most were retrospective studies on prosthetic heart valves. Our cohort is the first study in Hong Kong comparing the use of LMWH and UFH as bridging therapy. Only patients with high thromboembolic risk were included and most patients received bridging therapy (78.7%) had prosthetic heart valve. This provides important evidence supporting the use of LMWH in this regard.

Unlike the other studies, we also analyzed the clinical outcome of the colonoscopic procedure. As Enoxaparin was the only LMWH preparation used, the bias caused by the various LMWH preparations with different anticoagulant activities was minimized.

4.1 Bridging Therapy & Thromboembolism
The use of UFH was 2-fold greater than LMWH, which is consistent with previous studies. Our study demonstrated that the use of UFH was associated with a significantly shorter median length of hospital stay (4 days vs. 5 days). The peri-procedural management was done according to our own protocol.

4.2 Bridging Therapy & Post-polypectomy Bleeding
Post-polypectomy bleeding (PPB) is a crucial complication associated with colonoscopy procedures. We found that the PPB rate was similar between UFH and LMWH. The primary outcome of the study was to compare the PPB risk related to the use of bridging therapy (BT), and the results were as follows:

### 4.3 Measures to Reduce Post-polypectomy Bleeding
During the colonoscopic procedure, prophylactic hemostatic measures are helpful for high risk case like resection of large-sized polyp. A recent meta-analysis of 7 RCTs showed that prophylactic haemostatic measures such as the use of hemoclips, detachable snare or adrenaline injection were associated with a lower risk of PPB, with a pooled prophylactic ratio (RR) of 0.35; number needed to treat (NNT) 13.6; p<0.0001. The use of mechanical prophylactic measures was also found to be better than use of adrenaline injection alone (RR 0.28, NNT 12.3; p<0.0001). All studies excluded patients on anticoagulation.

However, another recent RCT, which comprised of 156 patients with 288 colonic neoplasms; with 14 large lesions of size ≥2cm, has failed to demonstrated the beneficial effect of prophylactic clipping on PPB. Eight patients in this study took anticoagulants and none of them developed PPB. Besides, the percentage of patients that had received bridging therapy was not mentioned. Guideline on the high risk of PPB associated with the use of bridging therapy, the application of prophylactic hemoclip, detachable snare, or a combination of both, should also be considered in high risk cases, especially if the polyp size was larger than 1cm. Further large scale randomized controlled trials should be conducted to confirm the efficacy.

Several studies have shown that half-therapeutic dose of LMWH is equally effective in preventing thromboembolic events. However it remains unclear if such approach can be used to reduce the risk of PPB. If hemostasis is insecure, it would be safer to withhold the bridging heparins for 48 to 72 hours after polypectomy procedure. In this cohort, early resumption of bridging therapy within 48 hours was associated with post-polypectomy bleeding (OR 2.82; CI 95% 1.05-7.59; p=0.03) on univariate analysis but not multivariate analysis. To clarify the issue, large-scale prospective studies would be required.

4.4 Indications for Bridging Therapy
Identifying the correct population for bridging therapy is essential to protect the patient from thromboembolic events and to avoid unnecessary bleeding complications. BT is currently indicated in patients with high thromboembolic risk, defined as >10% annual risk. They include patients with 1) any mitral valve prosthesis, 2) any caged-ball or tilting disc aortic valve prosthesis, 3) AF with rheumatic valvular heart disease, 4) recent venous thromboembolism within 3 months, and 5) thrombophilia for example protein C or S deficiency.

There have been differences between recommendations from the latest guidelines. In the most recently updated European guideline, thrombophilia was re-classified as low risk condition that bridging therapy is not required during warfarin interruption. Meanwhile these disorders remains under the high risk category in the latest guideline by American Society for Gastrointestinal Endoscopy (ASGE)1. Another controversy between the two authorities is found in non-valvular AF, which is defined as AF in the absence of rheumatic mitral stenosis, prosthetic heart valve or mitral valve repair. ASGE suggested bridging therapy in all patients with a CHADS2-VASc score ≥2, whereas the European guideline classified non-valvular AF as a low risk condition and bridging therapy is therefore not indicated. The recent BRIDGE trial attempted to resolve this issue. It randomized 1884 patients with atrial fibrillation into bridging (using Danaparoid) or non-bridging groups. The result showed that the bridging group had a more incidence of major bleeding (3.2% vs. 1.3%) with similar rate of arterial thromboembolism (0.3% vs. 0.4%). It should be noted that half of the study population underwent GI endoscopies and it did not specified how many patients had received diagnostic procedures (or with mucosal biopsies) alone, as it is now widely accepted that warfarin interruption are not necessary in this situation. The substantial increase in risk of PPB associated with the use of bridging therapy, the application of prophylactic hemoclip, detachable snare, or a combination of both, should also be considered in high risk cases, especially if the polyp size was larger than 1cm. Further large scale randomized controlled trials should be conducted to confirm the efficacy.

Patients with conditions like bileaflet aortic valve prosthesis without AF or prior stroke, xenograft heart valve, or a history of venous thromboembolism episode >12 months are classified as low risk2, and bridging therapy is not indicated. For other patients who did not fulfill the criteria mentioned above, for example a case of recurrent venous thromboembolism or venous thrombosis in active malignancies, they are referred to the moderate risk group. Late guidelines suggest a case-based approach.
In real life practice, the indication, purpose and potential adverse events of bridging therapy should be clearly explained to our patients. It could be devastating if people suffer from a major thromboembolic event (e.g. stroke) after warfarin interruption merely for a diagnostic procedure. As almost half of the colonoscopy procedures (45.7%) were associated with polypectomy procedures, one should get prepared for therapeutic interventions for every colonoscopy.

4.5 Study Implications
The findings of current study add to the body of evidence that both UFH and LMWH bridging therapy are equally effective in preventing thromboembolic events in high thromboembolic risk patients undergoing colonoscopy. The significant increase in PPB in the bridged group means we must be cautious when performing colonic polypectomy in this group of patients. If large polyps are encountered, prophylactic mechanical hemostasis e.g. hemoclip should be considered and patient should be closely monitored afterwards.

4.6 Limitations
This study had several limitations. First, it was a retrospective single center analysis. The choice of BT between LMWH and UFH was not randomized and this might result in selection bias. On the other hand, polypectomy techniques and use of prophylactic clipping were not standardized. This might potentially influence the chance of PPB. Thirdly, the follow-up schedule after colonoscopy was not standardized and was decided at the discretion of individual physicians. Occasionally, patients may develop mild PPB and do not require re-admission. However, given the fact that no patient (except those with mortality) was lost on follow-up in our cohort, the possibility of under-reporting a major bleeding event should be negligible. Lastly, due to inadequate sample size in certain high risk groups (e.g. thrombophilia), the results cannot be extrapolated to these special populations.

5. Conclusions
In patients on long term warfarin who undergoes colonoscopy, bridging therapy with LMWH is equally effective as UFH in the prevention of thromboembolic complications. However, under the effect of anticoagulation, the risk of post-polypectomy bleeding was excessively high, especially in colonic polyps sized >10mm, and special precautions should be taken to minimize such adverse events.

References
WARD facilities, or to be taught for doing injections themselves, on a
(particularly UFH) was required, the patient would be admitted for
occurred immediate after polypectomy, or bridging therapy
hemoclip or argon plasma coagulation.

was classified as pedunculated or sessile according to Paris

2.2 Colonoscopy Procedure, Lesions & Follow-up

sigmoid.

prolonged stay for management of her persistent
old in the control group died of hospital acquired pneumonia after

Figure 2

bleeding rate was significantly higher in heparin-bridged patients
(48.5% and 42.8% respectively; P=0.26). Post-polypectomy
(Table 4)

2. Clinical Outcome

regular monitoring of activated partial thromboplastin time

CI 95% 1.32-9.72; P=0.01) and the use of bridging therapy (OR 5.03;
regression analysis showed that only polyp size
studying the predictors of post-polypectomy bleeding. Factors

versus UFH bridging therapy, and secondly, the bleeding adverse
peri-procedural bridging anticoagulation and the timing of
studies10, we also found that polypectomy of large-sized polyps
the UFH (17.1%) and the LMWH groups (16.4%). Overall
post-polypectomy bleeding (PPB). The risk was similar between
the non-bridging groups. The result showed that the bridging group

procedures (or with mucosal biopsies) alone, as it is now widely
example protein C or S deficiency.

12. Dokoshi, T., et al.,
Half-dose enoxaparin vs. full-dose enoxaparin for postoperative
bleeding in colorectal polyps larger than 10 mm.

4.6 Limitations

patients with high thromboembolic risk, defined as >10% annual
performing colonic polypectomy in this group of patients. If large
snares or adrenaline injection were associated with a lower risk of
suspension of bridging therapy. Therefore, the bridging agent
replacement (AVR) with AF or prior thromboembolic event, and
months, chronic rheumatic heart disease (CRHD) with AF,
non-bridging groups. The result showed that the bridging group

The Asian Pacific Digestive Week 2017 (APDW 2017) themed “The Future in Digestive Diseases” was held in Hong Kong 23 - 26 September 2017 at the Hong Kong Convention and Exhibition Centre. APDW 2017 was the concerted effort of 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 and Hong Kong Society of Endoscopy Nurses.

It was a very successful Conference with over 2,800 participants from 44 countries/cities including 197 invited speakers. Japan, China and Korea ranked top 3 for the number of participants.

The scientific programme was very comprehensive with the postgraduate course, the Nurses Program and 7 parallel workshops on the pre-congress day on 23 September. Named lectures, the live endoscopy workshop, Young Clinician/Investigator Program, sponsored symposia and workshops and 56 parallel scientific sessions were conducted over 3 days, 24-26 September.
Out of 1,002 abstracts received, 786 were accepted for presentation in different categories, the Young Investigator Awards, Posters of Distinction Awards, Best of APDW Plenary Abstracts, Moderated e-Poster, Pure e-Poster Display and Video Display.

It was good opportunities for participants to meet during the welcome reception, opening ceremony and faculty dinner.

Industry partners, faculty and delegates enjoyed the participation in the Conference, friendship, and cultural experience in Hong Kong.

19th Joint Annual Scientific Meeting

Date: 23 September 2017

Venue: Hong Kong Convention and Exhibition Centre

Organizing Chairperson: Dr. Jodis Ting-Wa Lam

The 19th Joint Annual Scientific Meeting was successfully held on 23 September 2017 and attended by more than 100 healthcare professionals. The Meeting is an annual scientific event jointly organized by six societies for gastrointestinal and hepatobiliary diseases in Hong Kong, namely 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 and the Hong Kong IBD Society.

This year, the Meeting was incorporated into Asian Pacific Digestive Week 2017. Two case discussions were presented. The first case presented by Dr. Michael Ko was a young patient with Wilson’s Disease complicated by pregnancy. The second case presented by Dr. Kevin Liu was a patient with signet ring cell carcinoma of the stomach with peritoneal metastasis mimicking Crohn’s Disease. Both panelists and delegates participated actively throughout the discussions.

<table>
<thead>
<tr>
<th>Case Presentation I</th>
<th>Case Presentation II</th>
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<tbody>
<tr>
<td>Chairman: Dr. Francis Tat-Wing Li</td>
<td>Chairman: Dr. Wai-Man Yip</td>
</tr>
<tr>
<td><strong>A pregnant lady with hereditary liver disease</strong>&lt;br&gt;Dr. Michael Kwan-Lung Ko (QMH)</td>
<td><strong>A young man with dyspepsia</strong>&lt;br&gt;Dr. Kevin Sze-Hang Liu (QMH)</td>
</tr>
<tr>
<td><strong>Panel Discussion</strong>&lt;br&gt;Dr. Ambrose Chi-Pong Kwan (Private) &lt;br&gt;Dr. Michael Hang-Hoi Wong (UCH)</td>
<td><strong>Panel Discussion</strong>&lt;br&gt;Dr. Yuk-Tong Lee (Private) &lt;br&gt;Dr. Kevin Kwok-Kay Yau (Private)</td>
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The Hong Kong Society of Gastroenterology
37th Annual General Meeting cum Scientific Meeting
Thursday, 22 March 2018  6:15 pm

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

Organizing Chairperson: Dr. Wai-Fan Luk

Presentation of Honorary Fellowship by President, Professor Justin C.Y. Wu

The gut microbiome and GI disease: where are we now?
Professor Emad M El-Omar
Professor of Medicine
Editor in Chief, GUT
St George & Sutherland Clinical School
University of New South Wales
Sydney, Australia

A case discussion: Endoscopic management of early gastric cancer in a regional hospital
Dr Ka-Luen Lui
Assistant Consultant
Department of Medicine and Geriatrics
Tuen Mun Hospital
Hong Kong

Annual General Meeting
(More information will be available soon from www.hksge.org)