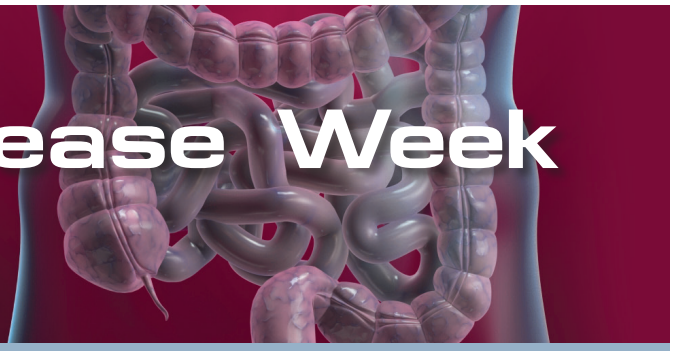
Digestive Disease Week

Conference Review



Making Education Easy

DDW, 19–22 May, 2012, San Diego, USA

In this review:

About the Reviewer

Dr Richard Stein
MD, FACG, AGAF, FRACP

Dr Richard Stein is a gastroenterologist who is originally from the States, but has been living and working in New Zealand since 2007. Richard received his undergraduate degree from Columbia University and his medical degree from the University of Illinois in Chicago. He has an interest in Inflammatory Bowel Disease, but treats all illnesses of the GI tract.

Welcome

to the Digestive Disease Week Conference Review, a locally focused summary of some of the latest and most exciting developments in general gastroenterology.

Digestive Disease Week is considered to be the largest and most prestigious meeting in the world for physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. This year's meeting showcased over 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology.

This Review has been created to allow those unable to attend to access a summary of significant clinical studies presented that are likely to affect current practice. Selection and review of the research has been carried out independently by Dr Richard Stein, Gastroenterologist at Boulcott Hospital, Hutt Valley DHB, and Wairarapa DHB, who attended DDW. Most of the following were designated 'Posters of Distinction'.

I hope you find the conference review stimulating and I look forward to your feedback.

Kind Regards,
Dr Chris Tofield
christofield@researchreview.co.nz

Effect of flexible sigmoidoscopy screening on incidence and mortality from colorectal cancer in the PLCO Screening Trial

Authors: Schoen RE et al

Summary: Outcomes were presented from the US-based Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, in this evaluation of the impact of endoscopic screening with flexible sigmoidoscopy (FSG) with subsequent colonoscopy. From 1993 to 2001, the PLCO study randomised men and women aged 55–74 years to FSG screening with a repeat exam at 3 or 5 years (n=77,445) or to usual care (n=77,455). Participants were followed for a mean 11.2 years. More than 86% underwent ≥1 screen; 50.9% underwent 2 screens. Of the screened population, 28.5% had ≥1 exam positive for a polyp or mass; 80.5% of these underwent diagnostic intervention within 1 year (all but 4.4% underwent subsequent colonoscopy), yielding a colonoscopy rate of 21.9% as a direct result of FSG screening. The incidence of colorectal cancer (CRC) was 11.9 per 10,000 person-years in the screening group and 15.2 per 10,000 person-years in the usual-care group, representing a 21% reduction in cancer incidence (relative risk [RR], 0.79; p<0.0001). The rate of CRC-related death was 3.9 per 10,000 person-years in the usual-care group and 2.9 per 10,000 person-years in the screening group (341 vs 252 deaths) – a 26% reduction in mortality (RR, 0.74; p=0.0003).

Comment: This is a landmark study comparing screening flexible sigmoidoscopy (baseline exam with repeat exam in 3–5 years) to "usual care" in over 150,000 patients. It demonstrated a 21% decrease in the incidence of bowel cancer in the group that received screening and a 26% reduction in mortality (a reduction in mortality from proximal cancers was not demonstrated). The findings are even more impressive, considering that many of the patients in the "usual care" group received screening if they requested it. The best test, however, is the one that people will comply with. In the States, screening colonoscopy has been adopted as the standard of care, based on the assumption that, if flexible sigmoidoscopy is good, full colonoscopy must be better (with the analogy of doing a mammography on just one breast).

It would be interesting to see a study comparing colonoscopy to flexible sigmoidoscopy.

Abstract 588.
www.nejm.org/doi/full/10.1056/NEJMoa1114635

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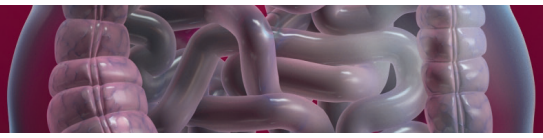


Are sub-centimeter advanced adenomas really significant? A 5-year follow-up study

Authors: Cummins AB et al

Summary: This presentation described outcomes over 5 years of 244 patients with advanced adenomas of all sizes, in an attempt to determine if outcomes differ between patients with adenomas >1 cm and those with sub-centimetre advanced adenomas. Patients were categorised into three groups based on the size of the largest advanced adenoma at their initial exam; Group 1: <5 mm in size, Group 2: 6–9 mm in size and Group 3: ≥10 mm in size. A total of 49% underwent repeat colonoscopy, at an average of 35 months from their baseline examination. In Group 1, 59% had a polyp on repeat exam, 77% of which had adenomas and 21% with advanced adenomas (16% by histology and 5% by size). In Group 2, 68% had a polyp on follow-up, 76% of which had adenomas and 18% with advanced adenomas (13.5% by histology and 4.5% by size). In Group 3, 50% had a polyp on follow-up, of which 68% had adenomas and 18% with advanced adenomas (6% by histology and 12% by size).

Comment: This prospective study lends support for the current recommendation to perform surveillance colonoscopy in patients with sub-centimetre polyps with advanced histology (villous features or high-grade dysplasia) at the same interval that is recommended for polyps greater than 1 cm (i.e., at 3 years). Pts with small advanced adenomas had similar rates of advanced adenomas found on follow-up colonoscopies compared to those with adenomas greater than 1 cm. Size does not make a difference when considering follow-up surveillance with small adenomas with advanced histology.

Abstract Mo1035.
http://ddw.apprisor.org/plnSES.cfm?id=103078

Successful colonoscopy in patients referred for prior incomplete colonoscopy does not require more time but often requires use of a different endoscope

Authors: Keswani RN

Summary: This study sought to determine the differences in endoscope insertion time (EIT) and endoscopes used in 70 patients referred for a subsequent successful repeat colonoscopy (RC) after prior incomplete colonoscopy (IC). The reported causes of the IC were tortuosity (42.9%) or looping (57.1%). The endoscope was changed in 17.9% of patients. RC was successful (caecal intubation) in 68 patients (97.1%), with a mean EIT of 16 min. Successful RC utilised an adult (39.7%) or paediatric (23.5%) colonoscope, upper endoscope (17.6%), or balloon enteroscope (19.1%). The endoscope was changed in 10% of patients during the procedure when caecal intubation was unsuccessful. New adenomas were detected in 31.4% of patients with adenocarcinoma detected in 1 patient. EIT was longer in the majority of the IC procedures (72.4%) compared to the successful RC (mean EIT of 23 min vs 16 min, respectively). In those cases where RC EIT was longer, the median increased time was 7 min. In 37.5% of patients, successful RC used commonly available smaller calibre endoscopes (paediatric, n=12; upper endoscope, n=9) not used during the IC. Successful completion required use of a balloon enteroscope in 23.2% of patients. In patients with an IC due to a tortuosity, 71% of RCs were completed with a paediatric colonoscope or upper endoscope not used during the IC.

Comment: Not surprisingly, repeating an incomplete colonoscopy with a different endoscope often results in a successful procedure. Repeat attempts at caecal intubation were successful in the overwhelming majority of cases (97%), but often required changing to a different endoscope (paediatric colonoscope, gastroscope, or balloon enteroscope). As new adenomas were detected in roughly a third of patients, this study suggests we should routinely change scopes during the initial unsuccessful procedure or perform a repeat colonoscopy in lieu of obtaining a CT colonography. This study, however, was limited by the fact that the initial and repeat exams were performed by different endoscopists.

Abstract Mo1221.
http://ddw.apprisor.org/plnSES.cfm?id=105432

Timing of pre-operative anti-tumor necrosis factor therapy does not affect early post-operative complication rates in inflammatory bowel disease patients undergoing intestinal resection

Authors: Desai PN et al

Summary: These researchers retrospectively reviewed data from 114 patients with inflammatory bowel disease (IBD) who underwent resection of the small or large intestine. Early postoperative complication (EPC) rates with anti-tumour necrosis factor (TNF) therapy (30 remote preoperative and 46 immediate preoperative; patients receiving a TNF dose greater than and less than half of their dosing interval prior to the operation, respectively) were compared to those with immunomodulators (IM) alone (n=38). The study also assessed the effect of remote (RP) versus immediate anti-TNF preoperative (IP) therapy on EPC rates. Despite the anti-TNF group having a higher proportion of patients exposed to steroids and having more severe Crohn's disease, combined EPC rates (defined as any of the following secondary outcomes: infection, anastomotic leak, readmission, reoperation, thrombosis, acute kidney injury, ileus, or new drain within 30 days after surgery) were similar between the preoperative anti-TNF therapy and the IM-alone group (43.4% vs 26.3%; p=0.08), as were individual secondary outcome rates. Similarly, the IP and RP groups did not differ significantly in the combined EPC rate (21.7% vs 30.0%; p=0.16), or in individual secondary outcome complication rates. The average length of postoperative stay was similar in all groups. Use of steroids was not associated with a difference in EPC or length of stay in any group; removing patients on budesonide-alone had no effect.

Comment: While this was a relatively small, retrospective study, it addresses a frequent concern, i.e., whether anti-TNF therapy in the immediate preoperative period affects outcome. Many surgeons and gastroenterologists recommend holding anti-TNF drugs in the perioperative period, due to a perceived increase risk of complications, especially infection. In this study, despite the fact that patients on anti-TNF therapy were more likely to be on concomitant treatment with steroids and had a higher incidence of penetrating disease, there was no difference in early postoperative complication rates or hospital stay when compared to patients on immunomodulators alone.

Abstract Su1560.
http://ddw.apprisor.org/plnSES.cfm?id=105064

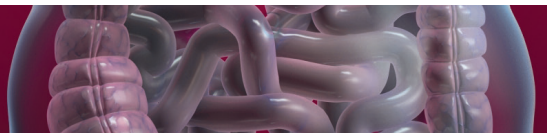
Location, location, location: Does highly dysplastic Barrett's esophagus have a preference?

Authors: Enestvedt BK et al

Summary: These researchers describe the localisation of dysplastic Barrett's oesophagus with high-grade dysplasia (HGD) or intramucosal adenocarcinoma (ImCa) in 119 patients presenting for their first planned eradication endoscopy between December 1997 and May 2010. The oesophageal quadrant (12–3 o' clock, 3–6 o'clock, 6– 9 o'clock or 9–12 o'clock) location of HGD or ImCa involvement for each eradication endoscopy was recorded for each patient and the rates of quadrant involvement were compared across all locations. A total of 57 patients had HGD (47.9%) and 62 had ImCa (52.1%). There was a significantly increased rate of HGD or ImCa pathology in the 12–6 o'clock location (right hemisphere) as compared with the left hemisphere (p<0.0001); the highest rates for both HGD and ImCa were in the 12–3 o'clock quadrant.

Comment: This interesting study looked at the location of dysplasia and intramucosal carcinoma in the setting of Barrett's. It confirms my own experience, i.e., that dysplasia seems to occur more commonly in the 12–6 o'clock hemisphere of the oesophagus than in the 6–12 o'clock position. 84% of HGDs and 93% of intramucosal carcinomas occurred in the 12–6 o'clock hemisphere. The authors had no explanation for this finding, but recommended extra vigilance in surveying this region.

Abstract Tu1563.
http://tinyurl.com/7pbkx87



Major complications during endoscopic eradication therapy (EET) for Barrett's esophagus (BE) with high grade dysplasia (HGD) and early cancer (EC): Results from a large multicenter cohort study

Authors: Wani S et al

Summary: This US-based analysis explored the rate of major complications of endoscopic eradication therapy (EET) including bleeding, strictures, and perforations in 311 patients with Barrett's oesophagus-associated neoplasia (high-grade dysplasia [HGD] or early cancer). Complications were defined as gastrointestinal bleeding requiring hospitalisation, oesophageal stricture requiring dilation, and oesophageal perforation. At baseline, 235 patients had HGD, 56 had intramucosal cancer, and 18 submucosal cancer. During a mean 2-year endoscopic follow-up, a total of 1231 EET sessions were performed: 359 endoscopic mucosal resection only, 37 EMR plus ablative therapy, 684 radiofrequency ablation only, 151 other ablative therapies only (combinations of argon plasma coagulation, cryotherapy, multipolar electrocoagulation, NdYag laser, photodynamic therapy, radiofrequency ablation). Symptomatic oesophageal strictures requiring dilation developed in 46 patients (14.8%), who underwent a total of 108 dilations (mean 2.3/patient). Six (1.9%) developed gastrointestinal haemorrhage that required hospitalisation and 2 (0.6%) patients developed oesophageal perforation. While one of the perforations (post-EMR) required surgical repair after a failed attempt at endoscopic closure, all remaining complications were successfully managed endoscopically. Multivariate analysis failed to identify any independent predictors for complications.

Comment: With more and more patients being referred for non-surgical treatment for Barrett's oesophagus with HGD or early carcinoma, there is limited data regarding safety.

This is a retrospective, multicentre study to specifically address complications following EMR, radiofrequency ablation, and other ablative therapy in 311 patients who underwent 1231 sessions (the majority of which were RFA, followed by EMR). While the complication rate was high (14.8%), almost all were easily treated. The vast majority were strictures, with only 2 perforations and 6 episodes of bleeding. The use of EMR, Barrett's length, and number of sessions did not predict complication rate. Referring doctors should be aware of the relatively high risk of developing symptomatic strictures, although these can generally be treated endoscopically. The risk of serious complications was low.

Abstract Su1108.
http://tinyurl.com/EET-for-Barretts-oesophagus

The safety and efficacy of endoscopic mucosal resection prior to radiofrequency ablation for dysplastic Barrett's esophagus: Results from the U.S. RFA Registry

Authors: Bulsiewicz WJ et al

Summary: This presentation reported the safety and efficacy of endoscopic mucosal resection (EMR) followed by radiofrequency ablation (RFA) using data obtained from the U.S. RFA Registry, a nationwide registry of patients treated with RFA for nodular, dysplastic Barrett's oesophagus. Among 1,248 patients who received RFA for HGD or IMC, 418 (33%) had ≥1 preceding EMRs. Of these subjects undergoing EMR/RFA (n=418), 3.6% developed strictures, 0.7% had bleeding, and 1.4% were hospitalised. No perforations occurred. Stricture, bleeding, and hospitalisation rates were not clinically or statistically different between patients treated with EMR/RFA vs RFA alone. Biopsy data were available at 12 months after enrolment for 554 of 1,248 patients (44%) and were included in the efficacy analysis. Complete eradication of intestinal metaplasia (CEIM) and complete eradication of dysplasia (CED) were achieved by EMR/RFA in 65% and 81% of patients, respectively. Patients undergoing EMR/RFA had similar rates of CED, CEIM, and number of RFA sessions for eradication of high-grade dysplastic Barrett's oesophagus and intramucosal carcinoma when compared to patients with flat Barrett's oesophagus treated with RFA alone.

Comment: At this year's DDW there was a focus on endoscopic treatment of Barrett's with HGD or IC. This is a large, multicentre, prospective study comparing efficacy and complication rates of two subsets of patients with Barrett's with HGD or intramucosal carcinoma. Group 1 received EMR in combination with RFA for nodular, dysplastic Barrett's. Group 2 had non-nodular, dysplastic Barrett's and were treated with RFA alone. Complication rates and eradication of dysplasia and intestinal metaplasia were similar in the two groups (60–85%). Interestingly, only 3.6 % of patients developed strictures, compared with 14% in the previous abstract.

Abstract Su1109.
http://journals.elsevierhealth.com/periodicals/ygast/search/quick

Concomitant use of adalimumab and immunomodulators compared with adalimumab alone: pooled malignancy safety analysis

Authors: Lewis JD et al

Summary: The incidence of treatment-emergent malignancies in patients with Crohn's disease (CD) using adalimumab (ADA) alone or in combination with immunomodulators (IMM) was assessed using the cumulative adverse event data in lead-in and long-term studies of ADA in CD (CLASSIC I and II, CHARM, GAIN, ADHERE, and EXTEND) among patients who received ≥1 dose of ADA. Two categories (non-melanoma skin cancer [NMSC] or all other types of malignancies) were assessed according to receipt of ADA+no IMM (ADA monotherapy without any IMM), ADA+any IMM (defined as azathioprine, mercaptopurine, or methotrexate), or ADA+thiopurine only at lead-in study baseline. The pooled analysis included 1594 patients, representing 3050 patient-years of exposure. The incidence of malignancy with ADA monotherapy was not elevated compared to expected rates, whereas incidence of malignancy with combination therapy was higher than expected in the general population and higher than with ADA monotherapy.

Comment: An ongoing concern both to doctors and, especially patients, is the potential of an increased incidence of neoplasm with the use of biologics. This is a prospective analysis pooled from several large studies, looking at the risk of malignancy in patients with Crohn's disease who received adalimumab alone or in combination with an immunomodulator. Patients on adalimumab monotherapy did not have an increased incidence of malignancy while those on combination therapy did. There were several limitations to this study, however. Patients on immunomodulators alone were not analysed, there was no adjustment for time on immunomodulator therapy, and standardised incidence ratios were based on the general population, not patients with Crohn's disease.

Abstract Su2078.
http://ddw.apprisor.org/plnSES.cfm?id=103505

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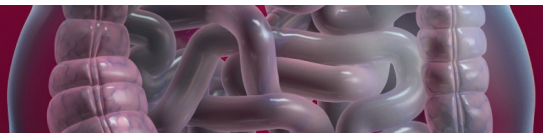

Should diabetes mellitus be an indication for earlier colorectal cancer screening?

Authors: Vu HT et al

Summary: Data were retrospectively analysed from patients undergoing colonoscopy over a 6-year period, comparing 3 cohorts matched for date of exam and gender: 1) aged 40–49 years with diabetes mellitus (DM); 2) aged 40–49 years without DM, and 3) aged 50–59 without DM. The study aimed to determine whether DM is associated with increased risk of developing colorectal adenomas in subjects aged 40–49 years. The adenoma detection rate (ADR) was 14.4% in those aged 40–49 years without DM, 30.4% in those aged 40–49 years with DM, and 32.0% in those aged 50–59 years without DM. Compared to those aged 40–49 years without DM, ADR were significantly higher in those aged 40–49 years with DM (adjusted OR 15.3; p=0.01) and those aged 50–59 years without DM (adjusted OR 14.1; p=0.02). ADR did not differ significantly between those aged 40–49 years with DM and those aged 50–59 years without DM (p=0.88).

Comment: The authors looked at patients with T2DM who underwent colonoscopy in their 40's and compared them to two cohorts, one group without diabetes undergoing colonoscopy in their 40's and a second group in their 50's. The group with diabetes had significantly more adenomas when compared to the younger cohort group and a similar incidence when compared to the older group. T2DM has been associated with an increased risk of bowel cancer, which has been attributed to increased insulin and free IGF-1 levels. Mortality from colon cancer is also higher in this group. Perhaps heightened vigilance of patients with T2DM should be considered as NZ moves towards adopting screening guidelines.

Abstract Tu1185.
http://ddw.apprisor.org/plnSES.cfm?id=103562

Great East Japan earthquake and exacerbation in ulcerative colitis

Authors: Takahashi M et al

Summary: These researchers examined the influence of the Great East Japan Earthquake of 11 March 2011 on the risk of exacerbations among 97 outpatients with quiescent ulcerative colitis (UC) on 11 March residing in the Kanto district, situated 350 kilometres away from the earthquake centre. Quiescent UC was defined as a modified UC disease activity index (UC-DAI) score of ≤2. Modified UC-DAI scores were monitored for 4 weeks after the earthquake and compared with scores obtained during the same 4-week period of 2010, which served as the patients' controls. Exacerbation was defined as a ≥2-point increase in UC-DAI score and patient's complaint of flare. The exacerbation rate over the 4-week post-earthquake period was significantly higher than during the control period (12/97 vs 3/97; p=0.0125). None of the demographic or clinical characteristics of the patients correlated with exacerbations.

Comment: Whether stress can precipitate flares of UC has been an ongoing debate. As stress varies from person to person, studies are difficult to construct. This is an interesting study that was done in Japan following the devastating tsunami and the Fukushima Nuclear Plant disaster. The authors evaluated the disease activity of 97 patients whose disease had been quiescent before the disaster and looked at their disease activity in the four weeks following. 12% of patients flared in those four weeks compared to 3% in the same period one year previously. It supports the hypothesis that stress is an independent risk for colitis flares.

Abstract Tu1257.
http://ddw.apprisor.org/plnSES.cfm?id=105506

Assessment of the efficacy of oral methotrexate in conjunction with infliximab therapy for the treatment of inflammatory bowel disease

Authors: Afzali A et al

Summary: This study investigated the efficacy of oral methotrexate in combination with infliximab for the treatment of inflammatory bowel disease (IBD). Of the 706 study participants, 323 were receiving infliximab monotherapy, 323 were receiving infliximab dual therapy with other immunosuppressants, and 60 were receiving infliximab dual therapy with oral methotrexate. Compared with patients treated with infliximab monotherapy and other dual therapy regimens, patients receiving infliximab plus oral methotrexate had lower average Harvey-Bradshaw Index scores (4.6 and 4.8 vs 2.5, respectively) and higher Short Inflammatory Bowel Disease Questionnaire scores (26.8 and 26.6 vs 54.0, respectively), indicating a reduced disease severity. The proportion of patients tested for human anti-chimeric antibody and serum infliximab concentrations was 2.8% in the infliximab monotherapy group and 3.0% in both the dual therapy with concomitant oral methotrexate and other immunosuppressant groups. The average infliximab concentration was within the appropriate range for therapeutic efficacy with no antibody formation in patients receiving infliximab with concomitant oral methotrexate.

Comment: Despite the statistically very small risk for developing hepatosplenic T cell lymphoma in patients on biologics and azathioprine, many have advocated using low-dose methotrexate as an alternative to decrease immunogenicity. While this is just an initial report with very small patient numbers, the group at the University of Washington is using low-dose oral methotrexate (7.5 mg weekly) in patients on infliximab. Due to the small sample size, there was no statistical analysis. This initial report suggests that low-dose methotrexate, in combination with inifliximab, may have efficacy in reducing the risk for loss of response to therapy with less antibody formation and higher infliximab levels. The authors noted that more data will be forthcoming.

Abstract Tu1309.
http://ddw.apprisor.org/plnSES.cfm?id=102875

Evidence for post-diverticulitis irritable bowel syndrome (Pdv-IBS): longitudinal analysis reveals higher incidence of IBS in DV cases vs. controls

Authors: Cohen ER et al

Summary: This study involved 1102 diverticulitis patients (mean age 64 years; 96% men; 47% white; 8% Latino; 11% black) and 1102 matched controls during the period 1996–2011. The study researchers compared post-diverticulitis irritable bowel syndrome (IBS) and related functional bowel disorder (FBD) diagnoses including functional diarrhoea, constipation, and abdominal pain in diverticulitis cases versus controls. Over a mean 35-month follow-up, diverticulitis patients were 4.6 times more likely to receive an IBS code over the observation period (HR=4.6; p=0.005) and 2.4 times more likely to receive any FBD code (HR=2.4; p<0.0001) after their DV event compared with controls.

Comment: This interesting study looked at over 1000 patients who presented with diverticulitis and their subsequent likelihood of developing IBS or a functional bowel disorder following their illness. Akin to observations that IBS can be triggered by an infectious enterocolitis, the authors found that patients who present with diverticulitis were 4.6 times more likely to receive a diagnosis of IBS over a mean follow-up period of 3 years.

Abstract Tu1363.
http://ddw.apprisor.org/plnSES.cfm?id=102910

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