Risk of advanced adenomas in siblings of individuals with advanced adenomas

Authors: Ng SC et al.

Summary: These researchers compared colonoscopy data from 200 asymptomatic siblings of patients with advanced adenomas (>10mm, high-grade dysplasia, villous or tubulovillous) with those of 400 matched siblings of individuals with normal colonoscopy findings and no family history of CRC in a cross-sectional study. Compared with siblings of individuals with normal colonoscopy findings, siblings of patients with advanced adenomas had a significantly greater prevalence of advanced adenomas (11.5% vs. 2.5%; matched OR 6.05 [95% CI 2.74–13.36]), including adenomas >10mm (10.5% vs. 1.8%; 8.59 [3.44–21.45]), villous adenomas (5.5% vs. 1.3%, 6.28 [2.02–19.53]) and all colonic adenomas (39.0% vs. 19.0%; 3.29 [2.16–5.03]). Cancer was detected in two of the siblings of patients with advanced adenoma and none of the siblings of individuals with normal colonoscopy findings.

Comment: There are very clear data that the risk for CRC is increased in families of patients with CRC. However, it is not as well understood whether the same is true for advanced adenoma, although guidelines do suggest screening in close relatives at a younger age. The current study compared prevalence of advanced adenomas in siblings of patients with advanced adenoma (n=200) as compared with an age- and sex-matched group of siblings of patients without (n=400). Advanced adenoma was defined as a lesion >10mm, high-grade dysplasia, villous or tubulovillous characteristics or any combination of the listed criteria. The results are remarkable in that siblings of advanced adenoma patients had a 2-fold increased risk for adenomas in general and a 6-fold increased risk for advanced adenomas. The risks were higher the younger the original patient with advanced adenoma was and the more lesions that patient had.

Reference: Gastroenterology 2016;150(3):608–16

Abstract
Effects of gluten intake on risk of celiac disease
Authors: Aronsson CA et al.
Summary: This case-control study of 146 cases of coeliac disease from a Swedish birth cohort each matched to three controls investigated whether the risk of coeliac disease is influenced by the amount of dietary gluten during the first 2 years of life. Annual screening for tissue transglutaminase autoantibodies was undertaken in newborns, and for those testing positive, the timepoint of seroconversion was determined from frozen serum samples obtained every 3 months; coeliac disease was confirmed on intestinal biopsy. Compared with tissue transglutaminase autoantibody-negative controls, cases had consumed more gluten at the visit before tissue transglutaminase autoantibody seroconversion (OR 1.28 [95% CI 1.13–1.46]), with more cases than controls in the upper tertile of gluten consumption (>5.0 g/day) before transglutaminase autoantibody seroconversion (2.65 [1.70–4.13]); similar associations were seen in children who were DR3-DQ2 homozygotes (3.19 [1.61–6.30]), heterozygotes (2.24 [1.08–4.62]) and noncarriers (2.43 [0.90–6.54]).

Comment: Genetic predisposition and gluten exposure are required for the development of coeliac disease. However, given that the genetic risk factors are commonly observed even in unafflicted populations and the differences in geographic distribution in similar ethnic groups, environmental factors are likely to be involved. Previous retrospective studies have suggested that gluten exposure at age <6 months may increase the risk. However, subsequent prospective studies have given conflicting results. This nested case-control study showed high gluten intake before 12 months of age to be associated with an increased risk for coeliac disease in childhood irrespective of whether the individual was at high or only moderate genetic risk. Furthermore, genetically at-risk individuals developed coeliac disease a median 12 months earlier than standard-risk individuals. In summary, this prospective study provides further evidence with respect to the risk of coeliac disease in relation to the timing of introducing gluten into a newborn’s diet.

Abstract

Randomised clinical trial: prucalopride, a colonic pro-motility agent, reduces the duration of post-operative ileus after elective gastrointestinal surgery
Authors: Gong J et al.
Summary: Patients undergoing elective GI surgery were randomised to receive oral prucalopride 2 mg/day (n=55) or placebo (n=55) started 24 hours postsurgery and continued until defaecation or a maximum of 7 days in this phase 2 trial. Compared with placebo, prucalopride was associated with shorter times to defaecation (primary outcome; 65.0 vs. 94.5 hours [p=0.001]) and passage of flatus (53.0 vs. 73.0 hours [p<0.001]), a shorter postoperative length of stay (7.0 vs. 8.0 days [p<0.001]), a lower proportion of participants with ileus >5 days (16.4% vs. 34.5% [p<0.026]) and a lower C-reactive protein level on postoperative day 5 (55.67 vs. 59.07 mg/L [p=0.040]). No significant between-group difference was seen for postoperative Clavien–Dindo grade III–IV complications.

Comment: Postoperative ileus has a significant impact on clinical recovery of patients having undergone GI surgery and remains the second most common reason for readmission after surgery in the US (Merkow RP et al., JAMA 2015;313[5]:483–95). This prospective phase 2 randomised controlled trial investigated the application of oral prucalopride, a selective 5-hydroxytryptamine receptor-4 agonist, commenced within 24 hours postsurgery as a means to reduce postoperative ileus. Prucalopride significantly reduced the times to first bowel motion and flatus. More cases of diarrhoea were observed in the prucalopride arm, but no significant CV events were recorded. While larger studies are required, this is important given that several of the traditionally used drugs in the context of postoperative ileus carry the risk of arrhythmias, prolonged corrected QT-interval, etc. Notably, prucalopride seems to mainly act on the colon, as its target is most strongly expressed in colonic but only weakly in intestinal mucosa. In keeping with this, prucalopride did not improve tolerance of solid food, which is related to upper intestinal recovery. Despite its small sample size, this study raises hope for prucalopride to be a new candidate to treat postoperative ileus.

Abstract

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100% cure rate in GT1b non-cirrhotic patients (n=301/301)1,2
100% cure rate in GT1b treatment-naive patients, including compensated cirrhotics (n=232/232)1,2
97% cure rate across GT1 (n=1062/1096)1,2

“In a pooled analysis of patients receiving the recommended VIEKIRA PAK ± RBV closing regimen, cure defined as <25 IU/mL HCV RNA 12 weeks post end-of-treatment (SVR12).”
**Time trends in upper gastrointestinal diseases and *Helicobacter pylori* infection in a multiracial Asian population**

**Authors:** Leow AH-R et al.

**Summary:** These authors studied upper GI disease and *Helicobacter pylori* infection among consecutive patients undergoing first-time gastroscopy at a medical centre in Malaysia over three time periods, namely 1989–1990, 1999–2000 and 2009–2010. Across the time periods, there were reductions in the prevalences of duodenal and gastric ulcers (from 21.1% to 9.5% to 5.0% and from 11.9% to 9.4% to 9.9%, respectively) and *H. pylori* infection (from 51.7% to 30.3% to 11.1%) and in the proportions of *H. pylori*-positive duodenal and gastric ulcers (from 90.1% to 69.8% to 28.9% and from 86.6% to 56.6% to 18.9%, respectively), whereas the prevalence of erosive oesophagitis increased (from 2.0% to 8.4% to 9.5%); the differences were more marked among Malay patients than Chinese or Indian patients. The proportions of patients with gastric and oesophageal cancers also declined over the study period.

**Comment:** This is an interesting study looking at the changing epidemiology of *H. pylori* infection and upper GI disease over time in Malaysia. While prevalence of peptic ulcer disease, *H. pylori* infection and *H. pylori*-associated duodenal ulcers has declined, reflux erosive oesophagitis has steadily become more frequent. Interestingly, gastric and oesophageal cancers seemed to decrease in a similar fashion. The results are in keeping with other studies, but the underlying reasons are not well understood; multiple factors are likely involved such as obesity, better living standards, smoking, alcohol consumption and concomitant medications, such as the increasing use and availability of aspirin and other NSAIDs (nonsteroidal anti-inflammatory drugs).


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**Association between ultrasonography screening and mortality in patients with hepatocellular carcinoma**

**Authors:** Wu C-Y et al.

**Summary:** These researchers conducted a nationwide cohort study in which they classified 52,823 patients with newly diagnosed hepatocellular carcinoma according to the following time intervals during which they received ultrasonography screening: 0–6 months, 7–12 months, 13–24 months, 25–36 months and never screened. The respective chances of receiving curative therapy among these respective time intervals were 24.3%, 26.9%, 22.9%, 21.3% and 18.3%. Compared with the 0–6 month screening interval, the intervals of 7–12, 13–24, 25–36 months and never were associated with increased mortality (respectively HRs 1.11 [95% CI 1.07–1.15], 1.23 [1.19–1.28], 1.31 [1.26–1.37] and 1.47 [1.43–1.51]). The associations between shorter screening intervals and better survival were seen across most subgroups, especially in younger patients, those without diabetes and those with hepatitis B virus infection.

**Comment:** Hepatocellular carcinoma is the fifth most common cancer worldwide (Jemal A et al., J Natl Cancer Inst 2015;108(3):175–201). Further to this, hepatocellular carcinoma remains the third leading cause for cancer-related death and most patients are only diagnosed at an advanced cancer stage (Siegel R et al., CA Cancer J Clin 2012;62(1):10–29 and El-Serag HB et al., Gastroenterology 2008;134(6):1752–63). While guidelines recommend using imaging with or without α-fetoprotein in order to identify lesions earlier and thus allow curative therapy, real-life effectiveness of this screening remains controversial. This population-based cohort study by Wu et al. clearly shows an association between shorter imaging intervals and reduced mortality. This association was particularly strong in younger individuals and patients with chronic hepatitis B virus infection. Importantly, this study also shows that there were a significant number of patients in high-risk groups that did not undergo regular screening. While the study is retrospective in nature, it nevertheless highlights the need for regular screening in order to identify patients early to increase the chance for curative therapy.

Reference: Gut 2016;65(4):693–701

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**Donor species richness determines faecal microbiota transplantation success in inflammatory bowel disease**

**Authors:** Vermeire S et al.

**Summary:** This research involved eight patients with refractory UC and six with refractory CD who had undergone ileocolonoscopy with FMT via a nasojejunal (n=9) or rectal (n=5) tube. Among the CD cohort, no significant improvements were seen at 8 weeks post-FMT, although one patient experienced clinical remission lasting 6 weeks. Two members of the CD cohort experienced endoscopic remission at week 8, and of the others experienced 6-week remission. Predictors of treatment success were donor microbiota richness and the number of transferred phylotypes, whereas treatment failure was predicted by persistently elevated C-reactive protein level at 2 weeks post-FMT. An accompanying editorial by H Sokol discusses the research in the context of rational selection of donors with rich microbiota, but that the findings will need to be confirmed by larger studies.

**Comment:** Dysbiosis, imbalance of the intestinal microbiome, has been considered as part of IBD pathogenesis and seems to contribute to disease activity and treatment response. The proof of principal here is that probiotics seem to have some limited efficacy in mild-to-moderate UC and the impact of antibiotics in terms of inducing remission in UC or CD. FMT has been previously proposed as a therapeutic approach, but the results have been unconvincing so far. Part of the problem in this context is how to select a good donor and the lack of understanding of what makes a good donor a good donor. The study by Vermeire et al. while small and with only a limited response to FMT is interesting, in that they were able to associate donor microbiota richness and number of transferred phylotypes with response. Furthermore, the authors found some suggestion that particular phylotypes may be relevant. Whether these phylotypes themselves or others associated with them play a causal role remains unclear. However, the results of this study point in the right direction, i.e. the identification of what makes a good donor a good donor.


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**Effect of coexisting diabetes mellitus and chronic kidney disease on mortality of cirrhotic patients with esophageal varical bleeding**

**Authors:** Lun C-C et al.

**Summary:** Mortality among 888 patients with cirrhosis hospitalised with a first presentation of oesophageal varical bleeding was investigated in this research. The respective 42-day and 1-year all-cause mortality rates were 21.3% and 45.0%, with the risks increased for any patient with CKD chronic kidney disease; respective HRs 1.80 [95% CI 1.10–2.97] and 1.52 [1.06–2.17]) but not diabetes mellitus (0.79 [0.57–1.10] and 0.88 [0.71–1.09]). The respective 42-day and 1-year mortality risks were also increased in: i) patients with both CKD and diabetes versus those without CKD and diabetes (adjusted HRs 1.99 [95% CI 1.03–3.84] and 1.84 [1.14–2.98]); ii) females with both diabetes and CKD (4.03 [1.40–11.59] and 2.84 [1.31–6.14]); and iii) males with diabetes and CKD (2.93 [1.14–7.57] and 2.42 [1.28–4.57]).

**Comment:** Portal hypertension secondary to liver cirrhosis can result in oesophageal varices. Oesophageal varical bleeding is a major complication with a mortality rate of 57% (D’Amico G et al., J Hepatol 2006;44(1):217–31). Both CKD and diabetes have previously been implicated with varical bleeding, although they are not considered part of the classical risk factors. In the current observational study, patients with a first presentation of oesophageal varical bleeding had mortality assessed over 42 days and 12 months. Both CKD and diabetes mellitus were associated with mortality for both timepoints with an almost 2-fold increased risk if both conditions were present. Subgroup analyses showed that the risk was highest in females with diabetes and CKD, i.e. 4-fold increased mortality at 42 days, but still almost 3-fold in males. Given that both factors are easily identified in at-risk patients, they should be considered when identifying at-risk patients.

Reference: BMC Gastroenterol 2016;16:29

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**Independent commentary by Associate Professor Golo Ahlenstiel**

Gastroenterologist and Hepatologist at Westmead Hospital, Sydney. After completing his medical and doctoral degrees at the University of Bonn, Germany, Golo Ahlenstiel received research fellowship awards from the National Institutes of Health (NIH, USA) and the German Research Foundation (DFG, Germany) to work in the Rehermann laboratory at the NIH on the immunopathogenesis of viral hepatitis. Apart from his clinical duties, he also leads a Liver Immunology group at Westmead Millennium Institute.
Clinical course and outcomes of diagnosing inflammatory bowel disease in children 10 years and under  

Authors: Gasparetto M et al.  
Summary: This retrospective cohort study from UK and Italian tertiary centres investigated differences in paediatric clinical presentation of IBD according to age group. 80 children diagnosed at age 5–10 years were compared with 80 diagnosed at 11–16 years. Children from the younger age group presented with greater disease activity for both CD and UC (OR 1.09 [95% CI 1.02–1.1]) and disease extent, with L2 location more frequent in CD. There were no significant differences between the age groups for GI and extraintestinal signs and symptoms at presentation, or for the number of hospitalisations due to relapse during follow-up. However, the younger group received immunosuppressants earlier and had a greater frequency of endoscopic assessments.  

Comment: IBD may manifest at any age, although 25% of cases are diagnosed during childhood or adolescence. Disease phenotypes and particularly whether there are differences between children versus adolescents remain unclear. In this retrospective study of 160 patients, disease extent and severity were higher in the younger age group at initial presentation, although statistical power was limited based on the cohort size, and thus the results have to be considered with caution. Furthermore, relapse rates seemed to be higher in younger children. A major challenge in this multinational cohort study was significant differences in local practice, such as when to start anti-TNF medications and which would have subsequently affected disease activity, treatment responses, etc. Thus, randomised trials are urgently needed to better understand if IBD in younger children requires a step-up or top-down approach to achieve the best possible outcomes.  

Reference: BMC Gastroenterol 2016;16:38

Abstract

Development and validation of a classification system to identify high-grade dysplasia and esophageal adenocarcinoma in Barrett’s esophagus using narrow-band imaging  

Authors: Sharma P et al.  
Summary: This paper reported on a narrow-band imaging classification system developed by BING (Barrett’s international NBG Group) for identifying dysplasia and cancer in patients with Barrett’s oesophagus. Characterisation of mucosal and vascular patterns visible by narrow-band imaging involved an analysis of data from 60 narrow-band images of nondysplastic Barrett’s oesophagus, high-grade dysplasia and oesophageal adenocarcinoma, which were then used to develop the BING criteria. High-quality narrow-band images and histological analyses of biopsy samples were obtained from adults undergoing surveillance or endoscopic treatment for Barrett’s oesophagus. Fifty narrow-band images were reviewed by experts to validate the BING criteria, and a further 120 narrow-band images were evaluated to determine if the criteria accurately predicted the histological findings. The BING criteria had overall accuracy of 85% for identifying dysplasia, with sensitivity and specificity values of 80% and 88%, respectively, and positive and negative predictive values of 61% and 86%, respectively; these respective values were 92%, 91%, 93%, 89% and 95% when dysplasia was identified with a high level of confidence. Interobserver agreement was strong (κ=0.681).  

Comment: Barrett’s oesophagus is the precursor to oesophageal cancer, for which the incidence is rapidly increasing worldwide. Endoscopic surveillance and quadrant biopsies are usually recommended, but may still miss areas of high-grade dysplasia or cancer. Narrow-band imaging has been suggested to be superior over white light for the identification of suspicious lesions. Previous Barrett’s oesophagus classification systems using narrow-band imaging are complex, and thus results have been variable with significant interobserver variability and often not validated. The current study presents a consensus-based, international, prospectively validated classification system, called the BING criteria, with high accuracy, sensitivity and specificity (92%, 91% and 93%, respectively) and good interobserver agreement (κ=0.681). Notably, this study was based on still images, but the value of an electronic learning approach through predefined images as a baseline should not be underestimated. Ultimately, the BING classification requires further validation in real-life cohorts and long-term follow-up to better understand whether its use will ultimately improve patient outcomes.  

Reference: Gastroenterology 2016;150(3):591–9

Abstract

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*In a pooled analysis of patients receiving the recommended VIEKIRA PAK± RBV dosing regimen, cure defined as <25 IU/mL HCV RNA 12 weeks post-end-of-treatment (SVR12).