Welcome to this edition of Gastroenterology Research Review, issue 21.

We are delighted to introduce Associate Professor Golo Ahlenstiel, Gastroenterologist and Hepatologist at Westmead Hospital, Sydney, who has provided the selections and expert commentary. We trust that you will find his insights and wealth of knowledge valuable in your everyday practice. The issue includes research reporting safe, long-term symptom relief of achalasia using POEM (peroral endoscopic myotomy), a pilot study showing that FMT (faecal microbiota transplantation) through mid-gut holds promise as rescue therapy for patients with refractory CD, and research reporting that EUS detects more pancreatic lesions in patients with MEN1 (multiple endocrine neoplasia type 1) syndrome than CT/MRI plus SRS (somatostatin receptor scintigraphy).

We are always happy to receive your comments, feedback and suggestions.

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Long-term outcomes of peroral endoscopic myotomy for achalasia in pediatric patients

Authors: Chen W-F et al.

Summary: The feasibility, safety and efficacy of POEM was evaluated in 27 paediatric patients with achalasia in this prospective, single-centre study. There was one procedure failure due to serious inflammation and adhesion, and there were no serious procedure-related adverse events. All successful procedures resulted in treatment success at mean follow-up of 24.6 months.

Comment: Achalasia is a rare oesophageal motility disorder including inability of the lower oesophageal sphincter to relax. The most definitive treatment currently is laparoscopic myotomy. Recently, POEM, which involves endoscopy, submucosal tunneling and endoscopic myotomy, has been described as an alternative to surgery in adults, but its efficacy in paediatric populations is unknown. The current prospective study by Chen et al. included 27 children, aged 6–17 years, with an Eckardt score of 8.3, with successful POEM in 26 of 27 cases. As a result, symptom scores improved from 8.3 to 0.7 and lower oesophageal sphincter pressures fell from 31.6 to 12.9mm Hg. Postoperative complications were low, and only five patients (19.2%) developed clinical reflux disease. This study highlights the high success rate and comparable safety of POEM in children. However, important challenges remain. Firstly, POEM is a technically challenging procedure requiring an experienced endoscopist in a high-volume centre. Secondly, reflux is a common complication for both POEM and surgical myotomy, with potential lifetime risks of stricture, Barrett’s oesophagus and even cancer. The potential benefit for prophylactic fundoplication in this context warrants further study. Overall, the current study provides evidence for POEM to become a suitable, minimally invasive alternative to surgery for achalasia in children and adolescents.

Reference: Gastrointest Endosc 2015;81(1):91–100

Abstract
Colon capsule versus CT colonography in patients with incomplete colonoscopy

Authors: Spada C et al.

Summary: CCE was compared with CT colonography in a prospective cohort of patients with incomplete colonoscopy. Compared with CT colonography, CCE was comparable for completing colon evaluation while providing a better overall diagnostic yield. No cancers had been missed at mean clinical follow-up of 20 months.

Comment: Colonoscopy completion rates range from 86% to >95%. Patients with incomplete colonoscopy may undergo additional imaging such as CT colonography to exclude significant lesions. The current study evaluated CCE in direct comparison with CT colonography as an alternative in patients with incomplete colonoscopy (n=100). Repeat colonoscopy was performed only if a lesion >6mm was identified. Completion rates were high (98% for both modalities) without any severe adverse events. CCE identified significant polyps 24 (24.5%) as compared with 12 (12.2%) of patients available for analysis (n=97) with a relative sensitivity for CCE of 2.0. False positives were found in one CCE and two CT colonographic procedures resulting in high predictive values for both procedures (86% for CCE and 85.7% for CT colonography). Of note, in this study only those patients with findings on CCE or CT colonography underwent repeat colonoscopy and the follow-up time was only 1 year, meaning that in the CCE and CT colonography double-negative patients, lesions may have remained undiagnosed. The results are encouraging as they suggest that CCE may become an alternative to CT colonography, including potentially a higher yield in terms of colonic polyps and the benefit of direct visualisation of the lesion. However, this comes at the known cost of CCE requiring more challenging bowel preparation and the substantial expense for the device.

Reference: Gut 2015;64(2):272–81

Fecal microbiota transplantation through mid-gut for refractory Crohn’s disease

Authors: Cui B et al.

Summary: These researchers assessed the safety, feasibility and efficacy of single FMT (faecal microbiota transplantation) through mid-gut in patients with refractory CD. The respective 1-month rates of clinical improvement and remission based on clinical activity were 86.7% and 76.7%.

Comment: Gut microbiota has been linked to inflammatory bowel disease. Therefore, the use of FMT has been proposed as a rescue therapy for refractory inflammatory bowel disease. The current study evaluated the safety, feasibility and efficacy of FMT through mid-gut for refractory CD. Patients with refractory CD with Harvey-Bradshaw Index score ≥ 7 were enrolled for this study. Thirty patients qualified for the present analysis. The rates of clinical improvement and remission based on clinical activity peaked within 1 month at 86.7% (26/30) and 76.7% (23/30), respectively, and were sustained, albeit at a lower level, over 15 months follow-up. FMT resulted in improved bodyweight, lipid profiles and haemoglobin level as well as serum albumin level. C-reactive protein level and erythrocyte sedimentation rate decreased. Of note, the definition of treatment-refractory CD in this study was broad and not all patients had been trialled on immunomodulators (67%) or anti-TNF (tumour necrosis factor) therapy (20%). In summary, this study is encouraging as it suggests that FMT may be a safe, low-risk, feasible and efficacious therapy for CD, particularly refractory CD. Future formal, randomised, double-blinded trials in well-defined CD cohorts will be essential to further define the role of FMT in CD.


Probiotic VSL#3 reduces liver disease severity and hospitalization in patients with cirrhosis

Authors: Dhiman RK et al.

Summary: In this randomised controlled trial, patients with cirrhosis who had recovered from a hepatic encephalopathy episode within the prior month received a probiotic preparation consisting of 9 x 10^9 bacteria or placebo daily for 6 months. Significant improvements were seen in the probiotic group in terms of quality of life and hospitalization rates for cirrhosis, in comparison with current standard therapies such as lactulose and rifaximin. Importantly, participants’ ethnicity, sex, body mass index, smoking status, alcohol intake and diabetes status did not seem to significantly impact on these associations. In summary, increased coffee consumption was associated with reduced risks of both incident hepatocellular carcinoma and chronic liver disease-related mortality (p<0.0002 for trend).

Comment: The incidence of hepatocellular carcinoma is steadily rising, with the greatest annual increase in mortality amongst all cancers. Coffee consumption has been previously described to lower liver function tests and lower severity and progression of liver disease. Epidemiological data suggest a lower risk for HCC related to coffee intake. This study assessed the possible association of coffee intake with hepatocellular carcinoma and chronic liver disease in the US Multiethnic Cohort. During an 18-year follow-up period, 451 incident cases of hepatocellular carcinoma and 654 deaths from chronic liver disease were documented. The risks of incident hepatocellular carcinoma and chronic liver disease mortality were reduced with high levels of coffee consumption; compared with coffee non-drinkers, participants who consumed ≥4 and 2–3 cups of coffee daily had 41% and 38% reductions in hepatocellular carcinoma risk, respectively. A similar impact was seen on chronic liver disease-related mortality, with a 71% reduction with ≥4 cups per day and a 46% reduction with 2–3 cups per day. Importantly, participants’ ethnicity, sex, body mass index, smoking status, alcohol intake and diabetes status did not seem to significantly impact on these associations. In summary, increased coffee consumption reduces the risk of hepatocellular carcinoma and chronic liver disease, an interesting observation given the beneficial influence of coffee in other cancers, Alzheimer’s disease and Parkinson’s disease.


Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation

Authors: Curry MP et al.

Summary: Patients with HCV infection (any genotype) and cirrhosis (CTP score, <7) awaiting liver transplantation for hepatocellular carcinoma received ≤48 weeks of sofosbuvir 400mg and ribavirin in this phase 2 open-label study. Among transplant recipients who had an HCV-RNA level <25 IU/mL at transplantation (n=43), the 12-week post-transplantation virological response rate was 70%, the recurrent infection rate was 23% and the mortality rate was 7%. Among all sofosbuvir and ribavirin recipients, the post-transplantation virological response rate was 49%, and recurrence was inversely associated with the number of consecutive pretransplant days of undetectable HCV-RNA. Fatigue, headache and anaemia were the most frequently reported adverse events.

Comment: Patients with HCV viraemia at the time of liver transplantation universally experience recurrent HCV infection with a major impact on graft function and survival. HCV eradication prior to transplant can prevent HCV recurrence in the graft. Interferon-based antiviral treatment, however, is often poorly tolerated or contraindicated before transplantation. This phase 2, open-label study included patients with liver cirrhosis (CTP score <7), with chronic HCV infection (73% genotype 1) awaiting liver transplantation for hepatocellular carcinoma. The patients received ≤48 weeks of sofosbuvir and ribavirin. Forty-six patients eventually received a liver transplant. Of 43 patients achieving virological suppression, 30 (70%) had a post-transplantation virological response at 12 weeks, ten (23%) had recurrent infection and three (7%) died of non-HCV-related reasons. Eighty-nine percent of patients experienced adverse events, severe in 11 cases with two subjects having to discontinue treatment. In summary, in this very ill, difficult-to-treat patient group, treatment with sofosbuvir and ribavirin was highly successful in preventing post-transplant HCV recurrence and more successful than an interferon-based regimen (20–28%).

Reference: Gastroenterology 2015;148(1):100–7

Association of coffee intake with reduced incidence of liver cancer and death from chronic liver disease in the US Multiethnic Cohort

Authors: Setiawan VW et al.

Summary: The relationships of coffee intake with hepatocellular carcinoma and chronic liver disease were explored in 162,022 African Americans, Native Hawaiians, Japanese Americans, Latinos and whites from the US Multiethnic Cohort. During an 18-year follow-up period, 451 incident cases of hepatocellular carcinoma and 654 deaths from chronic liver disease were documented. The risks of incident hepatocellular carcinoma and chronic liver disease mortality were reduced with high levels of coffee consumption; compared with coffee non-drinkers, participants who consumed ≥4 and 2–3 cups of coffee daily had 41% and 38% reductions in hepatocellular carcinoma risk, respectively. A similar impact was seen on chronic liver disease-related mortality, with a 71% reduction with ≥4 cups per day and a 46% reduction with 2–3 cups per day. Importantly, participants’ ethnicity, sex, body mass index, smoking status, alcohol intake and diabetes status did not seem to significantly impact on these associations. In summary, increased coffee consumption reduces the risk of hepatocellular carcinoma and chronic liver disease, an interesting observation given the beneficial influence of coffee in other cancers, Alzheimer’s disease and Parkinson’s disease.

Comment: The incidence of hepatocellular carcinoma is steadily rising, with the greatest annual increase in mortality amongst all cancers. Coffee consumption has been previously described to lower liver function tests and lower severity and progression of liver disease. Epidemiological data suggest a lower risk for HCC related to coffee intake. This study assessed the possible association of coffee intake with hepatocellular carcinoma and chronic liver disease in a well-characterised cohort of 162,022 African Americans, Native Hawaiians, Japanese Americans, Latinos and whites from the US Multiethnic Cohort. During an 18-year follow-up period, 451 incident cases of hepatocellular carcinoma and 654 deaths from chronic liver disease were documented. The risks of incident hepatocellular carcinoma and chronic liver disease mortality were reduced with high levels of coffee consumption; compared with coffee non-drinkers, participants who consumed ≥4 and 2–3 cups of coffee daily had 41% and 38% reductions in hepatocellular carcinoma risk, respectively. A similar impact was seen on chronic liver disease-related mortality, with a 71% reduction with ≥4 cups per day and a 46% reduction with 2–3 cups per day. Importantly, participants’ ethnicity, sex, body mass index, smoking status, alcohol intake and diabetes status did not seem to significantly impact on these associations. In summary, increased coffee consumption reduces the risk of hepatocellular carcinoma and chronic liver disease, an interesting observation given the beneficial influence of coffee in other cancers, Alzheimer’s disease and Parkinson’s disease.

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Prepared January 2015. PM2015.005 FA4014

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Women with celiac disease present with fertility problems no more often than women in the general population

Authors: Dhalwani NN et al.

Summary: This large population-based study of UK women found no differences in recorded fertility problems between women with versus without celiac disease, either before or after diagnosis, with the exception of more reported fertility problems in women with celiac disease diagnosed when they were aged 25–39 years.

Comment: For a long time, celiac disease has been associated with infertility in women, even though the data remain controversial and the studies have been relatively small. Dhalwani et al. performed a large population-based study of infertility and celiac disease in 4,262,225 women from the UK using prospective primary-care records between 1990 and 2015 during child-bearing years from the Health Improvement Network database. Women with celiac disease were more likely to be underweight and have higher incidences of type 1 diabetes mellitus, rheumatoid arthritis and thyroid disorders. Overall rates of fertility problems in 6,506 women with celiac disease (4.4%) were similar to women without celiac disease (4.1%) as well as age-specific rates of new fertility problems (incidence rate ratio 1.12). Rates of infertility in women with celiac disease before and after diagnosis were similar to those without celiac disease. However, women diagnosed with celiac disease when they were aged 25–29 years had a 41% higher rate than women in the same age group without celiac disease (incidence rate ratio 1.41). This study confirmed patients diagnosed within the primary-care setting, and thus may be more reflective of a population-based risk for fertility problems in celiac disease instead of a preselected group of patients presenting to a specialist centre, and thus minimises selection bias. However, it has to be noted that due to study design and the type of data used, undiagnosed celiac disease is not unlikely, given the incidence of only 0.3% in this cohort, whereas it is known that around 15% of women in the UK have serological evidence of celiac disease. While the current study does not include a contribution of celiac disease to fertility problems in some women, the data are reassuring that overall celiac disease does not have a greater likelihood of clinically significant fertility problems, except for higher reports of fertility problems between 25–29 years.

Reference: Gastroenterology 2014;147(6):1267–74
Abstract

The incidence of esophageal adenocarcinoma in a national veterans cohort with Barrett’s esophagus

Authors: Shakhateh MH et al.

Summary: These researchers sought to determine the risk of developing esophageal adenocarcinoma in a retrospective cohort of US veterans with Barrett’s esophagus. The incidence rate of esophageal adenocarcinoma during 144,949 person-years of follow-up was lower than previous estimates at 3.21 per 1000 person-years; the incidence rate fell to 1.75 per 1000 person-years on exclusion of patients who developed oesophageal adenocarcinoma ≤1 year of their Barrett’s oesophagus index date and increased on the incidence rate decreased on exclusion of patients who underwent endoscopic ablation or oesophagectomy for adenocarcinoma in a retrospective cohort of 29,536 patients with Barrett’s oesophagus from a total national veterans cohort with Barrett’s esophagus.

Comment: For a long time, celiac disease has been associated with infertility in women, even though the data remain controversial and the studies have been relatively small. Dhalwani et al. performed a large population-based study of infertility and celiac disease in 4,262,225 women from the UK using prospective primary-care records between 1990 and 2015 during child-bearing years from the Health Improvement Network database. Women with celiac disease were more likely to be underweight and have higher incidences of type 1 diabetes mellitus, rheumatoid arthritis and thyroid disorders. Overall rates of fertility problems in 6,506 women with celiac disease (4.4%) were similar to women without celiac disease (4.1%) as well as age-specific rates of new fertility problems (incidence rate ratio 1.12). Rates of infertility in women with celiac disease before and after diagnosis were similar to those without celiac disease. However, women diagnosed with celiac disease when they were aged 25–29 years had a 41% higher rate than women in the same age group without celiac disease (incidence rate ratio 1.41). This study confirmed patients diagnosed within the primary-care setting, and thus may be more reflective of a population-based risk for fertility problems in celiac disease instead of a preselected group of patients presenting to a specialist centre, and thus minimises selection bias. However, it has to be noted that due to study design and the type of data used, undiagnosed celiac disease is not unlikely, given the incidence of only 0.3% in this cohort, whereas it is known that around 15% of women in the UK have serological evidence of celiac disease. While the current study does not include a contribution of celiac disease to fertility problems in some women, the data are reassuring that overall celiac disease does not have a greater likelihood of clinically significant fertility problems, except for higher reports of fertility problems between 25–29 years.

Reference: Gastroenterology 2014;147(6):1267–74
Abstract

Residual lower esophageal sphincter pressure as a prognostic factor in the pneumatic balloon treatment of achalasia

Authors: Park JH et al.

Summary: These researchers retrospectively reviewed 52 patients who underwent pneumatic balloon dilation for achalasia, among whom the treatment was unsuccessful in nine. They identified lower resting and relaxation pressure (4sRIP) as a possible prognostic indicator for poor outcomes after pneumatic balloon dilation.

Comment: Pneumatic balloon dilation is a standard, cost-effective treatment for achalasia, but has significant procedural risk for major complications. To identify predictive factors for successful treatment, 76 patients with a diagnosis of achalasia who underwent pneumatic balloon dilation were retrospectively reviewed, including Edwards score for clinical symptoms and manometry data using resting and relaxation pressure of the lower esophageal sphincter and the distal contractile integral. Pneumatic balloon dilation was administered to 52/76 patients, among whom it was unsuccessful in nine (six in Chicago class I and three in III). Compared with the successful treatment group, the unsuccessful treatment group had a significantly lower mean value for 4sRIP (p<0.05), but there was no difference for resting lower esophageal sphincter pressure, distal contractile integral or pull-through size. The primary outcome of treatment was considered successful if the data suggest that lower 4sRIP may be a prognostic indicator for treatment outcome after pneumatic balloon dilation.

Reference: J Gastroenterol Hepatol 2015;30(9):59–63
Abstract

EUS is superior for detection of pancreatic lesions compared with standard imaging in patients with multiple endocrine neoplasia type 1

Authors: van Asselt SJ et al.

Summary: EUS and 11C-5-HTP (C-5-hydroxytryptophan)-PET were compared with recommended screening techniques for early detection of pancreatic neuroendocrine tumours in 41 patients with a MEN1 gene mutation or one MEN1 syndrome manifestation and a MEN1 mutation carrier in a first-degree family member. For the 107 pancreatic lesions detected, EUS detected 101, whereas 11C-5-HTP-PET and CT/MR+ +SRS detected 35 and 32 lesions, respectively. The performance of 11C-5-HTP-PET was similar to CT/MRI+SRS and better than SRS only at both patient- and lesion-based levels.

Comment: MEN1 syndrome, a rare, inherited condition related to mutation of the MEN1 gene encoding menin, is associated with neoplasms of pituitary and parathyroid glands and the pancreas. Pancreatic neuroendocrine tumours are common in MEN1 syndrome at 30–70%, and are the leading cause of death. Diagnostics are difficult especially with respect to the pancreas. Screening for pancreatic neuroendocrine tumours is recommended in MEN1 syndrome to allow detection, as they can have malignant potential and surgery is only curative treatment. Standard screening techniques include abdominal CT or MR+ +SRS. The current study compared the utility of EUS and 11C-5-HTP-PET with standard screening techniques in MEN1 syndrome patients for the early detection of pancreatic neuroendocrine tumours. Forty-one patients with a proven MEN1 mutation or with one MEN1 syndrome manifestation and a MEN1 mutation carrier as a first-degree family member and recent standard screening were prospectively recruited and underwent EUS and 11C-5-HTP-PET. One hundred and seven pancreatic lesions were detected in 35/41 patients. Notably, 101 pancreatic lesions were detected in 54 patients by EUS, 35 lesions in 19 patients by 11C-5-HTP-PET and 32 lesions in 18 patients by CT/MRI+SRS, a highly significant difference. 11C-5-HTP-PET performance was similar to CT/MRI+SRS, but was better than SRS alone (13 lesions in 12 patients). As the majority of lesions were only identified on EUS and the study only included one timepoint per patient, the clinical significance of detecting more lesions remains unclear. Despite its small study size, the data would suggest that EUS is superior to current standard screening with CT/MRI+SRS for pancreatic lesion detection in patients with MEN1 syndrome and thus should be considered for screening in this rare but important patient group. Furthermore, given that pancreatic neuroendocrine tumours also occur sporadically and in Hippel–Lindau disease, EUS should also be considered in such circumstances to exclude further lesions.

Abstract