Highlights from the literature

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Beta blockers decrease decompensation in cirrhosis

The PREDESCI trial,¹ published in *The Lancet*, is the first randomised controlled trial (RCT) to evaluate the efficacy of non-selective beta-blockers in the primary prevention of hepatic decompensation in patients with compensated cirrhosis and clinically significant portal hypertension (CSPH).

Two hundred and one patients with compensated cirrhosis and CSPH (baseline hepatic venous pressure gradient (HVPG) ≥ 10 mm Hg), no previous decompensation and no high-risk oesophageal varices were recruited. Acute HVPG responders to intravenous propranolol were randomised to propranolol or placebo and non-responders to carvedilol or placebo. The primary endpoint was decompensation (ascites, variceal bleeding or overt encephalopathy) or liver-related death.

Decompensation or death occurred in 16% (16/100) in the beta-blocker group versus 27% (27/101) in the placebo group (HR 0.51, 95% CI 0.26 to 0.97, $p=0.04$). This difference was largely attributable to a significant reduction in the incidence of ascites (HR 0.42, 95% CI 0.19 to 0.92, $p=0.03$). There was a greater reduction in HVPG in the carvedilol group compared to propranolol (16% vs 10%, $p=0.036$) and no significant reduction in the placebo group.

The development of ascites heralds a dramatic deterioration in prognosis; therefore, a potential primary prevention strategy is promising. In real-world practice where HVPG is not widely available, the pertinent issue will be patient selection. Non-invasive markers can effectively be used to identify low-risk cirrhotics but the optimal combination to 'rule in' CSPH remains to be elucidated.

Endoscopic duodenal mucosal resurfacing for type 2 diabetes mellitus

The duodenum is a potential therapeutic target for various metabolic disorders. Duodenal mucosal resurfacing (DMR) is a novel endoscopic technique involving circumferential hydrothermal ablation of duodenal mucosa with subsequent regeneration. This multicentre, open-label study, published in *Gut*, evaluated the

safety and efficacy of DMR for improving glycaemic control in type 2 diabetes mellitus (T2D).²

Forty six patients with T2D, with a body mass index of 24–40 and glycated haemoglobin (HbA1C) of 59–86 mmol/mol who were on stable oral glucose-lowering medication were recruited, of which 36 were included in the final per-protocol analysis. The primary endpoint was HbA1C at 24 weeks, which reduced by mean 10 mmol/mol from baseline (SE 2 mmol/mol, $p<0.001$). Reduced fasting plasma glucose, a fall in transaminases and modest weight loss were also significant during the study, with effects sustained at 12 months.

Twenty four patients had adverse events, mainly gastrointestinal symptoms, of which 81% were mild. There was one serious procedure-related adverse event (systemic inflammatory response postprocedure). A significant number of patients were excluded from the final analysis, mostly due to technical issues during the procedure.

DMR potentially offers a safer, less invasive approach to the burgeoning problem of T2D compared to bariatric surgery. However, an RCT is needed to confirm these results and investigate the role of weight loss which may have been an important confounder in this data. Moreover, improvements to the technology and upscaling of endoscopic training will be needed to make this a practical solution to such a prevalent disease.

Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis

There are few trials assessing biologics head-to-head in the treatment of ulcerative colitis (UC). The VARSITY trial,³ published in the *New England Journal of Medicine*, sought to address this with an RCT comparing the gut-selective anti-integrin vedolizumab with adalimumab.

Seven hundred and sixty-nine adults with moderate-to-severe UC were randomised to either vedolizumab or adalimumab. In patients taking corticosteroids, inability to taper these after week 6 was considered treatment failure. Primary outcome was clinical remission at week 52, with secondary outcomes of endoscopic

improvement and corticosteroid-free remission.

At week 52, 120/383 (31.3%) vedolizumab patients and 87/386 (22.5%) adalimumab patients were in clinical remission (difference 8.8%, 95% CI 2.5% to 15.0%, $p=0.006$). Endoscopic improvement was observed in 39.7% and 27.7% of vedolizumab and adalimumab patients, respectively (difference 11.9%, 95% CI 5.3% to 18.5%, $p<0.001$). However, corticosteroid-free remission was observed in a lower percentage of vedolizumab than adalimumab patients (12.6% vs 21.8%).

The inconsistency between superior clinical remission and endoscopic improvement versus poorer corticosteroid-free remission with vedolizumab remained elusive to the study authors. In an era of rapidly increasing options for biologic therapy in inflammatory bowel disease, more head-to-head trials against existing standard treatments are essential to guide clinicians in the timing and selection of treatment escalation.

Irritable bowel syndrome after *Campylobacter* infection

This retrospective cohort study, published in the *American Journal of Gastroenterology*, investigated the incidence of post-*Campylobacter* irritable bowel syndrome (IBS) in the USA.⁴

Four thousand one hundred and forty-three *Campylobacter* cases and 20491 controls were identified. The 1-year incidence rate of IBS was 33.1 and 5.9 per 1000 in cases and controls, respectively. Risk ratio (RR) was 5.6 (95% CI: 4.3 to 7.3). Hospitalised patients had a higher incidence than outpatients (39.0 vs 29.8 per 1000, respectively). Using the definition of 'persisting gastrointestinal symptoms', 1-year incidence rate was 118.8 and 24.3 per 1000 in cases and controls, respectively (RR 4.9; 95% CI: 4.3 to 5.6).

Overall, the risk of developing IBS was 5.6 times higher in post-*Campylobacter* patients than controls and higher in those hospitalised than outpatients, supporting an association between illness severity and IBS risk.

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