Treatment of Colonic Diverticular Bleeding

No large studies have evaluated the effectiveness of treatment strategies for colonic diverticular bleeding (CDB), based on stigmata of recent hemorrhage (SRH). To identify the best strategy among combinations of SRH identification in endoscopic treatment strategies, 5823 CDB patients were analyzed who underwent colonoscopy at 49 hospitals throughout Japan (CODE-BLUE j-Study). Three strategies were compared: SRH (definitive CDB) found and treated endoscopically, found SRH (definitive CDB) and treated conservatively, and without the presence of finding SRH (presumptive CDB), treated conservatively.

With pair-wise comparison of outcomes in these groups, propensity score-matching analysis to balance baseline characteristics between the groups being compared was carried out.

Both early and late recurrent bleeding rates were significantly lower in patients with definitive CDB treated endoscopically than in those with presumptive CDB treated conservatively (less than 30 days - 19.6% vs. 26%; less than 365 days - 33.7% vs. 41.6%, respectively).

In patients with definitive CDB, the early recurrent bleeding rate was significantly lower in those treated endoscopically than in those treated conservatively (17.4% vs. 26.7%) for a single test or hypothesis; however, correction for multiple testing of data removed this significance. The recurrent bleeding rate was also lower, but not significantly in those treated endoscopically (32% vs. 36%).

Definitive CDB treated endoscopically showed significantly lower early and late recurrent bleeding rates than when treated conservatively in cases of SRH with active bleeding, non-active bleeding, and in the right side of the colon, but not the left side of the colon.

It was concluded that treating definitive CDB endoscopically was most effective in reducing recurrent bleeding over the short- and long-term, compared with not treating definitive CDB or presumptive CDB. An attempt should be made to find and treat SRH for suspected CDB.

Gobinet-Suguro, M., Nagata, N., Kobayashi, K., et al. "Treatment Strategies for Reducing Early and Late Recurrence of Colonic Diverticular Bleeding Based on Stigmata of Recent Hemorrhage: A Large, Multicenter Study." Gastrointestinal Endoscopy 2022; Vol. 95, pp. 1210-1222.

Pickle Brine in the Treatment of Cirrhotic Cramps

Since muscle cramps are common among persons with cirrhosis and have been associated with poor health-related quality of life and since treatment options are limited, an attempt was made to determine whether pickle juice can improve muscle cramp severity.

A total of 82 patients were enrolled with cirrhosis and a history of greater than 4/10 muscle cramps in the previous month from December 2020 to December 2021. They were randomized 1:1 sips of pickle juice vs. tap water at cramp onset. Primary outcome assessed at 28 days identified the change in cramp severity measured by the visual analog scale for cramps (VAS-cramps, scaled 0-10). Cramps were assessed 10 times over 28 days using interactive text messages. Secondary outcomes included the proportion of days with VAS-cramps <5, change in sleep quality and global health-related quality of life measured through the EQ-5D.

A total of 74 patients completed the trial, age 56.6 +/- 11.5 years, 54% male, 41% with ascites, 38% with encephalopathy and model for end-stage liver disease-sodium score 11.2 +/- 4.9. Many patients were receiving other cramp therapies at baseline. The baseline VAS for cramps was 4.2 +/- 3.4. The EQ-5D was 0.8 and 43% related sleep as poor. At trial completion, the respected value of the pickle juice and control arms were -2.25 +/- 3.61 points on the VAS for cramps, compared

with control 35% and the change in sleep quality was not different.

The end-of-trial EQ-5D was 0.78 vs. 0.80. No differences in weight change were observed in those with and without ascites.

In this randomized trial, sips of pickle brine consumed at cramp onset improve cramp severity without adverse events.

Tapper, E., Salim, N., Baki, J., et al. "Pickle Juice Intervention for Cirrhotic Cramps Reduction: The PICCLES Randomized Control Trial." American Journal of Gastroenterology, 2022; Vol. 117, pp. 895-901.

Functional Gastrointestinal Symptoms in Celiac Disease

In order to explain persisting gastrointestinal symptoms on celiac disease (CD), patients on a gluten-free diet (GFD) and considering functional gastrointestinal disorders (FGIDs), an online health questionnaire was completed by adult members of Celiac UK in October 2018 that included validated questions on Rome IV FGIDs, nongastrointestinal somatic symptoms, anxiety, depression, quality of life, health care use, GFD duration, and its adherence using the celiac dietary adherence test score (with a value ≤ 13 indicating optimal adherence). The prevalence of FGIDs and associated health impairment in the celiac cohort was compared against an age- and sex-matched, population-based controlled group.

Of the 863 individuals with CD (73% female; mean age 61 years), all were taking a GFD for at least 1 year, with 96% declaring that they had been on the diet for 2 or more years. The adherence to a GFD was deemed optimal in 61% (n = 523), with the remaining 39% (n = 340) nonadherent. Those adhering to a GFD fulfilled criteria for FGID in approximately one-half of cases, although this was significantly lower than nonadherent subjects (51% vs. 75%). The prevalence of FGIDs in GFD-adherent subjects was significantly higher than in matched population-based controls (35%, OR, 2.0). This was accounted for by functional bowel (46% vs. 31%; OR, 1.9), and anorectal disorders (14.5% vs. 9.3%; OR, 1.7), but not functional esophageal (7.6% vs. 6.1%) or gastroduodenal disorders (8.7% vs. 7.4%).

Finally, GFD-adherent subjects with FGIDs were significantly more likely than their counterparts without FGIDs to have abnormal levels of anxiety (5% vs. 2%; OR, 2.8), depression (7% vs. 2%; OR, 3.6), somatization (31% vs. 8%; OR, 5.1), and reduced quality of life.

It was concluded that one in 2 people with CD, despite having been on GFD for a number of years and demonstrating optimal adherence, have ongoing symptoms compatible with a Rome IV FGID. This is 2-fold the odds of FGIDs seen in an age- and sex-matched controls. The presence of FGIDs is associated with significant health impairment, including psychological comorbidity. Addressing disorders of gut-brain interaction might improve outcomes in this specific group of patients.

Parker, S., Palsson, O., Sanders, D., et al. "Functional Gastrointestinal Disorders and Associated Health Impairment in Individuals with Celiac Disease." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1315-1325.

Food Avoidance and Restriction in Irritable Bowel Syndrome

To evaluate and identify those patients and characterize the symptoms, quality of life and nutrient intake of patients with irritable bowel syndrome (IBS) with severe food avoidance and restriction, those patients who completed the IBS Quality of Life Instrument (IBS-QOL) at our secondary and tertiary centers were included. The 3 questions constituting the food domain were used to identify patients with reported severe food avoidance and restriction. The patients also completed validated questionnaires to assess stool form (Bristol Stool Form), gastrointestinal (GI) symptom severity (a score of IBS Severity

Scoring System and Gastrointestinal Symptom Rating Scale-IBS), psychological distress (Hospital Anxiety and Depression Scale), GI-specific anxiety (Visceral Sensitivity Index), and somatic symptom severity (score of Symptom Checklist–90-Revised and Patient Health Questionnaire–15). A 4-day food diary was used to analyze food intake in 246 patients.

A total of 955 IBS patients (75% women; mean age 38.3), were included. In total, 13.2% of the patients reported severe food avoidance and restriction, and in these patients, all aspects of quality of life were lower and psychological, GI, and somatic symptoms were more severe. Reported severe food avoidance and restriction was associated with lower total energy intake and lower intake of protein and carbohydrates. In a logistic regression analysis, loose stools were found to be independently associated with reported severe food avoidance and restriction.

It was concluded that IBS patients with severe food avoidance and restriction constitute a subgroup with more severe symptoms overall, reduced quality of life and reduced intake of nutrients requiring acknowledgement of same in the clinical management of these patients.

Melchior, C., Algera, J., Colomier, E., et al. "Food Avoidance and Restriction in Irritable Bowel Syndrome: Relevance for Symptoms, Quality of Life and Nutrient Intake." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1290-1298.

Vedolizumab Vs. Anti-Tumor Necrosis Factor Agents in Older Adults with IBD

To evaluate the safety and effectiveness of IBD treatments in older adults, a study was carried out to compare the safety and effectiveness of anti-tumor necrosis factor (TNF)-a agents and vedolizumab in older adults with IBD.

A retrospective cohort study was conducted using an active comparator, new-user design for adults age 65 years and older with IBD-initiating anti-TNF-a agents and vedolizumab in the Medicare Claims Database from 2014 to 2017.

The primary safety outcome was infection-related hospitalization (excluding intra-abdominal and perianal abscesses). Co-primary outcomes to estimate effectiveness were IBD-related hospitalization, IBD-related surgery, and new corticosteroid use 60 days or more after biologic initiation. Propensity scores were performed, weighting to control for confounding and estimated adjusted hazard ratios and 95% confidence intervals using standardized morbidity ratio-weighted variables.

A total of 1152 anti-TNF-a new users were identified and 480 vedolizumab new users with a median age of 71 years in both cohorts and 11% were age 80 or older. Crohn's disease patients comprised 54% of the anti-TNF-a cohort and 57% of the vedolizumab cohort. There were no significant differences in demographics, health care utilization or frailty in both cohorts. More than half of both cohorts had a Charlson comorbidity index of 2 or higher. Vedolizumab

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users had a decreased risk of infection-related hospitalization (adjusted hazard ratio 0.47). There was no significant difference in the outcomes approximating effectiveness.

It was concluded that older IBD patients treated with vedolizumab had a lower risk of infection-related hospitalization compared with those initiating anti-TNFs. There was no difference observed in effectiveness defined by hospitalizations, surgery or new corticosteroid use.

Kochar, B., Pate, V., Kappelman, M. "Vedolizumab is Associated with a Lower Risk of Serious Infections Than Anti-Tumor Necrosis Factor Agents in Older Adults." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1299-1305.

Perianal Fistula Treatment Improves with Higher Anti-TNF-a Levels

To evaluate the association between anti-TNF drug levels and radiologic outcomes in perianal fistulizing Crohn's disease, a cross-sectional, retrospective, multicenter study was undertaken. Patients with perianal fistulizing Crohn's disease on maintenance infliximab or adalimumab with drug levels within 6 months of perianal MRI studies were included. Patients receiving dose changes for fistula surgery between drug level and imaging were excluded. Radiologic disease activity was scored using the Van Assche Index, with an inflammatory subscore calculated using indices: T2-weighted imaging hyperintensity, collections >3 mm diameter, rectal wall involvement. Primary endpoint was radiologic healing (inflammatory subscore ≤6). Secondary end point was radiologic remission (inflammatory subscore =0).

Of 193 patients (infliximab, n = 117; adalimumab, n = 76) patients with radiologic healing had higher median drug levels compared with those with active disease (6.0 vs. 3.9 for infliximab, 9.1 vs. 6.2 for adalimumab). Patients with radiologic remission also had higher median drug levels compared with those with active disease (infliximab 7.4 vs. 3.9 ug/mL, adalimumab 9.8 vs. 6.2 ug/mL). There was a significant incremental reduction in median inflammatory subscores with higher anti-TNF drug level tertiles.

It was concluded that higher anti-TNF drug levels were associated with improved radiologic outcomes on magnetic resonance imaging in perianal fistulizing Crohn's disease, with an incremental improvement in higher drug level tertiles for both infliximab and adalimumab.

De Gregorio, M., Lee, T., Krishnaprasad, K., et al. "Higher Anti-Tumor Necrosis Factor-a Levels Correlate With Improved Radiologic Outcomes in Crohn's Perianal Fistulas." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1306-1314.

Avoidant Restrictive Food Intake Disorder in IBD

Patients with IBD alter their dietary behaviors to reduce disease-related symptoms, avoiding feared food triggers, and control inflammation. To estimate the prevalence of avoidant/restrictive food intake disorder (ARFID), evaluate risk factors and examine the association with risk of malnutrition in patients with IBD, a cross-sectional study recruiting adult patients with IBD from an ambulatory clinic was carried out. ARFID risk was measured using the Nine-Item ARFID screen. Nutritional risk was measured with the Patient Generated-Subjective Global Assessment. Logistic regression models were used to evaluate the association between clinical characteristics and a positive ARFID risk screen. Patient demographics, disease characteristics, and medical history were abstracted from medical records.

Of the 161 participants (Crohn's 45.3%, UC 51.6%, IBD-unclassified, 3.1%), 28 (17%) had a positive ARFID risk score (≥2.4). Most

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participants (92%), reported avoiding 1 or more foods having active symptoms, and 74% continued to avoid 1 or more foods, even in the absence of symptoms. Active symptoms (OR 5.35) and inflammation (OR 3.3), were significantly associated with positive ARFID risk. Patients with a positive ARFID risk screening were significantly more likely to be at risk for malnutrition (69.7% vs 15.8%).

It was concluded that avoidant eating behaviors are common in IBD patients, even when in clinical remission. Patients who exhibit active symptoms and/or inflammation should be screened for ARFID risk, with referrals to registered dietitians to help monitor and address disordered eating behaviors and malnutrition risk.

Yelencich, E., Truong, E., Widaman, A., et al. "Avoidant Restrictive Food Intake Disorder Prevalent Among Patients with Inflammatory Bowel Disease." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1282-1289.

Glucagon-Like Peptide-1 Receptor Agonist and Cirrhosis

To compare the effectiveness of glucagon-like peptide-1 receptor agonists (GLP-1RAs) with dipeptidyl peptidase-4 (DPP-4) inhibitors, sulfonylureas or sodium-glucose co-transporter-2 (SGLT-2) inhibitors in reducing decompensation events, among patients with cirrhosis and type 2 diabetes.

A population-based, retrospective cohort study included patients with type 2 diabetes and cirrhosis in a commercial healthcare database (IBM MarketScan).

A 3-pair wise 1:1 propensity score (PS)-matched cohorts of adults initiating GLP-1RAs or a comparator medication (ie, DPP-4 inhibitors), sulfonylureas or SGLT-2 inhibitors. Patients were followed in an as-treated approach for decompensation events (ie, ascites, SBP, hepatorenal syndrome, hepatic encephalopathy, or esophageal variceal hemorrhage). Within each PS-matched cohort, we estimated hazard ratios (HRs) and 95% confidence intervals for >90 baseline characteristics.

Over 132 days of median follow-up (interquartile range 73-290 days), PS-matched ratios of any decompensation were significantly lower among GLP-1RA initiators vs. DPP-4 inhibitor initiators (105.2 vs. 144 per 1000 person-years; HR 0.68; n = 1431 pairs), and vs. sulfonylureas (97.3 vs. 144 per 1000 PY; HR 0.64; 95%, n = 1246 pairs).

Similar, inverse associations were found for individual decompensation events, including ascites, SBP, or hepatorenal syndrome (HR 0.66; 95%; and HR 0.66, respectively; esophageal variceal hemorrhage (HR 0.62 and HR 0.59, respectively), hepatic encephalopathy (HR 0.76 and HR 0.60, respectively). Results persisted

in subgroups of patients with and without previously decompensated cirrhosis. In contrast, decompensation rates were similar with GLP-1RAs and SGLT-2 inhibitors were directly compared (103.5 vs 112.8 per 1000 PY; HR 0.89).

It was concluded that among cirrhotic patients with type 2 diabetes, there was a high rate of decompensation consistent with previous reports and those rates were substantially lower among GLP-1RA initiators, compared with DPP-4 inhibitors or sulfonylureas.

Simon, T., Patorno, E., Schneeweiss, S. "Glucagon-Like Peptide-1 Receptor Agonists and Hepatic Decompensation Events in Patients with Cirrhosis and Diabetes." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1382-1393.

HCC Risk with Positive HBeAg Positivity in Chronic Hepatitis B

Antiviral treatment from HBeAg-positive status may attenuate the integration of hepatitis B virus DNA into the host genome, causing hepatocellular carcinoma (HCC). An investigation was conducted in Korean patients who started entecavir or tenofovir in either HBeAg-positive or HBeAg-negative patients. The results in the cohort were validated in a Caucasian PAGE-B cohort.

A total of 9143 Korean patients (mean age 49.2 years), were included: 49.1% were HBeAg-positive and 49.2% had cirrhosis. During follow-up (median, 5.1 years), 916 patients (10%), developed HCC. Baseline HBeAg positivity was not associated with the risk of HCC in the entire cohort or cirrhotic cohort. However, in the noncirrhotic cohort, HBeAg positivity was independently associated with a lower risk of HCC in multivariable (adjusted hazard ratio [a-HR], 0.41; propensity score-matching (aHR 0.46), and inverse probability weighting analyses (aHR 0.44). In the Caucasian cohort (n = 719; mean age 51.8 years; HBeAg-positive, 20.3%; cirrhosis, 34.8%), HBeAg positivity was not associated with the risk of HCC either in the entire cohort or cirrhotic subcohort. In the non-cirrhotic subcohort, none of the HBeAg-positive group developed HCC, although the difference failed to reach statistical significance (aHR 0.21).

This multinational cohort study implies that HBeAg positivity at the onset of antiviral treatment seems to be an independent factor associated with lower risk of HCC in patients with chronic hepatitis B without cirrhosis, but not in those with cirrhosis.

Jang, H., Yoon, J., Park, S., et al. "Impact of HBeAg on Hepatocellular Carcinoma Risk Through an Oral Antiviral Treatment in Patients With Chronic Hepatitis B." Clinical Gastroenterology and Hepatology 2022; Vol. 20, pp. 1343-1353.

Vitamin E as a Preventative Approach for NAFLD

Vitamin E supplementation has been recommended for treatment of nonalcoholic fatty liver disease (NAFLD) for nondiabetic patients, but in order to evaluate its preventative effects, assessment of dietary vitamin E intake was carried out with disease phenotypes and vitamin E levels were evaluated with the development of NAFLD.

Data from greater than 210,000 participants demonstrated that increased dietary vitamin E associates with reduced rates of several gastrointestinal diseases and with reduced overall mortality. Diabetic and overweight subjects with increased vitamin E intake had fewer NAFLD diagnoses.

The findings revealed relevance of vitamin E consumption for several gastrointestinal diseases with recommendation for further mechanistic and therapeutic investigations.

Scorletti, E., Creasy, K., Vujkovic, M., et al. "Dietary Vitamin E Intake is Associated with a Reduced Risk of Developing Digestive Diseases and Nonalcoholic Fatty Liver Disease." American Journal of Gastroenterology 2022; Vol. 117, pp. 927-930.