GASTRO-HEP News

By Samantha Alleman

First-Degree Relatives of Individuals With Celiac Disease at Higher Risk of Diagnosis

First-degree relatives (FDRs) of individuals diagnosed with celiac disease (CD) have an increased risk of developing the condition themselves, regardless of whether they have symptoms, and could benefit from screening, according to results of a retrospective cohort study published online on August 22, 2019 ahead of print publication in *Mayo Clinic Proceedings*. A diagnosis of CD is based on elevated serologic markers such as anti–tissue transglutaminase (anti-TTG) antibodies as well as endoscopy to examine and biopsy the small intestine lining.

Dr Shilpa S. Nellikkal and colleagues assessed the prevalence of FDRs with CD detected at screening and the diagnostic significance of anti-TTG antibodies using data from Mayo Clinic electronic records and a CD registry spanning from December 1983 to May 2017. Data included demographics, presenting symptoms, indication for testing, family history, number of other family members screened for CD, biopsy reports, and serologic test results. A total of 104 patients diagnosed with CD and their FDRs (n=477) were identified.

Of the 477 FDRs, 360 had been screened for CD, of whom 160 (44.4%) were diagnosed with the condition and tested positive for anti-TTG antibody titers. Clinical features were reported in 148 diagnosed FDRs, including 9 (6%) with classic symptoms and 97 (66%) with nonclassic symptoms. Forty-two FDRs (28%) reported no symptoms. Mean age at diagnosis was 31.9±21.6 years, and 62% of the FDRs with CD were female. A level of anti-TTG antibodies greater than or equal to 2.75 of the upper limit of normal identified FDRs with villous atrophy with 87% sensitivity, 82% specificity, and a positive predictive value of 95%. Histology reports from 155 FDRs showed that 12 (8%) had Marsh 1 classification, 77 (50%) had Marsh 3a classification, and 66 (43%) had Marsh 3b classification.

The authors noted that their study was limited by the retrospective design, referral bias from a tertiary care center, and limited follow-up of patients.

Combination of Glecaprevir/Pibrentasvir Effective in Patients With Hepatitis C Virus Genotype 1 Infection With Previous Treatment Failure

The direct-acting antiviral combination of glecaprevir and pibrentasvir (Mavyret, AbbVie) for 16 weeks is effective in patients with chronic hepatitis C virus (HCV) genotype 1 infection who previously failed treatment with sofosbuvir (Sovaldi, Gilead) and a nonstructural (NS) 5A inhibitor, according to results of a phase 3b, open-label study published online on August 8, 2019 ahead of print publication in *Gastroenterology*.

Dr Anna S. Lok and colleagues conducted a multicenter, randomized trial to assess the safety and efficacy of 12 and 16 weeks of glecaprevir/pibrentasvir, with or without ribavirin. A total of 177 patients with chronic HCV genotype 1 infection who received previous treatment with sofosbuvir and an NS5A inhibitor were included and randomized into 4 groups. Patients without cirrhosis received glecaprevir/pibrentasvir for either 12 weeks (n=78, group A) or 16 weeks (n=49, group B), and patients with compensated cirrhosis received glecaprevir/pibrentasvir plus ribavirin for either 12 weeks (n=21, group C) or glecaprevir/pibrentasvir alone for 16 weeks (n=29, group D). The primary endpoint was sustained virologic response at 12 weeks following treatment (SVR12). Samples collected at baseline and at time of treatment failure were sequenced for resistance-associated substitutions (RASs) in NS3 and NS5A.

SVR12 was achieved by 90%, 94%, 86%, and 97% of patients in groups A, B, C, and D, respectively. Baseline NS5A RASs were present in 76% of patients, and treatment-emergent NS3 and NS5A RASs were reported in 9 and 10 patients with treatment failure, respectively. Thirteen patients (7.3%) failed treatment overall, including 6 (7.7%) from group A, 3 each from groups B (6.1%) and C (14.3%), and 1 from group D (3.4%). Overall, glecaprevir/pibrentasvir was well tolerated. The most commonly reported adverse events were fatigue, nausea, and headache. The inclusion of ribavirin increased adverse events but did not increase efficacy. No patient discontinued treatment due to adverse events or laboratory abnormalities.

Oral Antibiotic Use Associated With Increase in Colon Cancer Risk, Decrease in Rectal Cancer Risk

The use of oral antibiotics is associated with an increased risk of colon cancer but a reduced risk of rectal cancer, suggesting differences in gut microbiota and carcinogenesis mechanisms along the lower intestinal tract, according to results of a matched case-control study published online on August 20, 2019 ahead of print publication in *Gut*.

Using the Clinical Practice Research Datalink in the United Kingdom, Dr Jiajia Zhang and colleagues identified 28,980 cases of incident colorectal cancer (CRC) from 1989 to 2012 and matched them with 137,077 controls. Various risk factors of CRC, including the use of oral antibiotics, a history of smoking, and alcohol use, were compared between the 2 groups.

The use of oral antibiotics increased the risk of colon cancer in a dose-dependent manner. Oral exposure to anti-anaerobic antibiotics produced the most significant effect in the proximal colon. However, an inverse association was detected between the use of antibiotics and the development of rectal cancer, especially when exposed to antibiotics for more than 60 days vs no antibiotic exposure. Penicillins, ampicillin/amoxicillin in particular, increased the risk of colon cancer, whereas tetracyclines reduced the risk of rectal cancer. The association between antibiotic use and development of cancer was found in individuals who had been exposed to antibiotic use more than a decade before diagnosis. Individuals who developed CRC were also more likely than those in the control group to have a history of smoking (49.9% vs 46.9%), to have moderate to heavy alcohol use (13.8% vs 11.4%), to have a history of diabetes (8.8% vs 7.7%), to be overweight (35.2% vs 33.8%) and obese (18.6% vs 16.4%), and to undergo colonoscopy (3.5% vs 2.9%). However, individuals with CRC were less likely than controls to have chronic nonsteroidal anti-inflammatory drug use (7.2% vs 9.0%).

Bariatric Surgery Linked to High Risk of Late Adverse Events

Bariatric surgery, including gastric bypass and sleeve gastrectomy, reduces long-term mortality in obese patients but is associated with a significantly high risk of late adverse events, according to results of a nationwide, observational, population-based, cohort study published online on August 2, 2019 ahead of print publication in *The Lancet Diabetes and Endocrinology*.

For the study, Dr Jérémie Thereaux and colleagues reviewed French National Health Insurance data of 8966 patients who underwent gastric bypass (n=4955; 55%) or sleeve gastrectomy (n=4011; 45%) in 2009 and matched them with 8966 control patients with obesity in terms of age, sex, body mass index category, and baseline antidiabetic and insulin therapies. Patients were excluded from the control group if they were pregnant; had cancer, chronic infectious disease, serious acute or chronic disease between 2005 to 2009; or were planning to undergo bariatric surgery in 2010 or 2011. Follow-up lasted a mean of 6.8 years. The incidence rate for each type of adverse event leading to inpatient hospital admission was calculated over a 7-year period. Incidence rate ratios were calculated to compare the rate of complications between the 2 groups. Risks of complications during follow-up were compared using Cox proportional-hazard regression analyses. Data were analyzed according to the intention-to-treat methodology.

Mortality was significantly lower in the bariatric surgery group compared to the control group. However, bariatric surgery patients had an increased risk for invasive gastrointestinal surgery or endoscopy, for gastrointestinal disorders not requiring invasive treatment, and for nutritional disorders. Neither bariatric procedure was significantly associated with any long-term psychiatric disorders aside from gastric bypass with alcohol dependence. The most common adverse events were gallstone disorders.

Connection Between Symptomatic Gastroesophageal Reflux Disease and Temporomandibular Disorder

Symptomatic gastroesophageal reflux disease (GERD) is associated with an almost 3-fold increased risk of chronic temporomandibular disorder (TMD), according to results of a study published online on August 19, 2019 ahead of print publication in *CMAJ*. Somatization, anxiety, and undermined sleep somewhat mediate the connection.

Dr Yuanyuan Li and colleagues conducted a case-control study that included 1522 consecutive patients with chronic TMD and 1522 matched controls, all between the ages of 18 and 70 years and recruited between July 2017 and April 2018. Trained dentists diagnosed chronic TMD using criteria from the Orofacial Pain Prospective Evaluation and Risk Assessment Study, and trained gastroenterologists made blind diagnoses of GERD using the Montreal definition and classification of at least 2 days of mild symptoms or 1 day of moderate or severe symptoms per week. Psychologic status and sleep quality were evaluated using validated questionnaires.

Overall, 132 patients in the TMD group were diagnosed with GERD vs 61 patients in the control group. GERD was considered a risk factor for TMD according to conditional logistic regression analysis (odds ratio, 2.74; 95% CI, 1.88-3.98). Mediation analyses demonstrated that somatization, anxiety, and undermined sleep, respectively, mediated 14%, 11%, and 10% of the association between TMD and GERD. The authors noted that teeth grinding or clenching, which are associated with GERD, could also contribute to jaw pain in TMD.

The authors concluded that proper consideration should be given to the evaluation and management of mental disorders and gastrointestinal symptoms when treating TMD.