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Courtesy Dr. Colleen Kelly, Brown University

Dr. Colleen Kelly, AGAF, of Brown University, Providence, R.I., pointed to Registry results that show safety, efficacy of fecal transplant.

Real-world safety, efficacy found for fecal transplant

BY LAIRD HARRISON

Fecal microbiota transplantation (FMT) appears safe and effective as a treatment for most *Clostridioides difficile* infections as it is currently being administered, researchers say.

"We actually didn't see any infections that were definitely transmissible via fecal transplant," Colleen Kelly, MD, AGAF, an associate professor of medicine at Brown University, Providence, R.I., said in an interview.

The findings, published online Oct. 1 in the journal Gastroenterology (doi: 10.1053/j.gastro.2020.09.038) come from the American Gastroenterological Association (AGA) National Institutes of Health–funded FMT National Registry and could allay concerns about a treatment that has yet to gain full approval by the Food and Drug Administration, despite successful clinical trials.

C. diff. infections are common and increasing in the United States, often can't

See **Transplant** · *page 29*

Test for coronavirus before endoscopy, AGA recommends

BY WILL PASS

MDedge News

The American Gastroenterological Association (AGA) has issued guidance for pre-endoscopy coronavirus testing based on a review of existing literature and a survey of endoscopist risk tolerance.

While serologic antibody testing is not recommended for any patients, use of nucleic acid amplification testing (NAAT) for viral RNA should be informed by local prevalence of asymptomatic individuals, reported lead guideline panelist Shahnaz Sultan, MD, AGAF, of the University of Minnesota in Minneapolis and colleagues.

"The two main concerns with a pretesting strategy are the false positives and false negatives," the panelists wrote in Gastroenterology. When performing endoscopy in a false-negative patient, health care providers who wear a surgical mask instead of an N95/N99 respirator may have an increased risk of infection, and the patient undergoing the procedure may be falsely reassured that they are not contagious, the panelists wrote.

Among false-positive individuals, "implications for the patient include cancellation of the procedure, self-quarantine for 14 days, apprehension, and loss of work."

Because of these con-

See **Test** · *page 32*

Identifying pancreatitis etiology may help prevent progression

BY HEIDI SPLETE

MDedge News

Pancreatitis remains the third most common gastroenterological cause of hospital admission. Staying on top of the latest quality indicators is important for the care and safety of patients, said Jamie S. Barkin, MD, AGAF, professor of medicine in the division of gastroenterology at the University of Miami, in a virtual presentation at the annual Digestive Diseases: New Advances conference jointly provided by Rutgers and Global Academy for Medical Education.

The basics of treatment have changed, said Dr. Bar-

See **Pancreatitis** · *page 12*

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LETTER FROM THE EDITOR

The disruption of our postpandemic world will precipitate innovation

When this editorial is published, we will know the results of the national election (hopefully) and whether there will be a smooth transition of power. We should know whether the Affordable Care Act will remain intact, and we will have indications about the impact of a COVID/flu combination. Health care will never be the same.


Dr. Allen

According to a recent Medscape survey, 62% of U.S. physicians saw a reduction of monthly income (12% saw a reduction of over 70%) in the first 6 months of this year. Almost a third of the physician workforce is contemplating retirement earlier than anticipated. As worrisome, according to a JAMA article (2020 Aug 4;324:510-3), the United States saw a 35% increase in excess deaths because of non-COVID etiologies, an indication of health care deferral and avoidance. We all are scrambling to catch up and accommodate an enormous demand.

According to a JAMA article, the United States saw a 35% increase in excess deaths because of non-COVID etiologies, an indication of health care deferral and avoidance.

We are witnessing a "K" shaped recovery for both individuals and GI practices. If your health care is covered by Medicare, you own a mortgage-free home and your wealth is based on a balanced equity/bond portfolio, then all of your assets increased in value compared to last year's peak valuations. For the other 90% of Americans, the recovery is modest, neutral, or more often nonexistent. Gastroenterologists who work in academic centers or large health systems were relatively protected from income loss by billion-dollar credit lines and robust days-cash-on-hand accounts available to these entities.

Independent practices (critically dependent on monthly cash flow) were decimated, furthering the trend toward consolidation, retirement, and acquisitions. With the new CMS E/M valuations we will see further reduction in procedural reimbursement.

Our postpandemic world will be dramatically different from pre-COVID times. However, disruption always precipitates innovation. Challenges are great but opportunities are clearly evident for those willing to risk.

John I. Allen, MD, MBA, AGAF
Editor in Chief

Top AGA Community patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community (https://community.gastro.org) to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses. The upgraded networking platform now features a newsfeed for difficult patient scenarios and regularly scheduled Roundtable discussions with experts in the field.

In case you missed it, here are some clinical discussions and Roundtables in the newsfeed this month:

- Initial results from the FMT National Registry (https://community.gastro.org/posts/22693)
- Practice update: Reducing rates of post endoscopy esophageal adenocarcinoma (https://community.gastro.org/posts/22805)
- Patient case: Eosinophilic gastrointestinal disease (https://community.gastro.org/posts/22743)
- Patient case: Repeat colonoscopy following splenic injury (https://community.gastro.org/posts/22739)
- Windows on Clinical GI Roundtables: Crohn's disease and gastroparesis

View upcoming Roundtables in the community at https://community.gastro.org/discussions.

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Diarrhea prevalent among COVID-19 patients with IBD

BY AMY KARON
MDedge News

Diarrhea affected one in every five patients with inflammatory bowel disease (IBD) and COVID-19, compared with only 7%-10% of all patients with COVID-19 in prior studies, researchers reported in Clinical Gastroenterology and Hepatology.

In a systematic review and meta-analysis of 23 studies incorporating data from 449 patients with IBD and COVID-19, their most common symptoms were fever (affecting 48.3% of patients), cough (46.5%), and diarrhea (20.5%). Diarrhea was approximately twice as prevalent as dyspnea, nausea, abdominal pain, and fatigue, wrote Ferdinando D'Amico, MD, of Humanitas University in Milan and his associates. "[S]ymptoms experienced by IBD patients with COVID-19 are similar to those occurring in the general population, except for a higher percentage of diarrhea," they wrote. This increased prevalence might result from IBD itself or from inflammatory effects of viral gut tropism, they noted. "Currently, the diagnostic–therapeutic approach does not differ between IBD and non-IBD patients, but further studies are needed to evaluate whether fecal research of viral RNA and treatment with IBD drugs may play a role in the management of COVID-19 patients."

To characterize the clinical presentation and course of patients with IBD and COVID-19, the researchers searched PubMed, Embase, Web of Science, and MedRxiv through July 29, 2020, for keywords related to COVID-19, Crohn's disease, ulcerative colitis (UC), and IBD. They identified 23 studies presenting clinical data from adults or children with a confirmed IBD diagnosis and least one case of COVID-19. Among 243,760 patients with IBD, 1,028 patients had COVID-19 infection, including 509 patients with Crohn's disease, 428 patients with UC, 49 patients with indeterminate colitis, and 42 patients for whom the IBD subtype was not recorded.

In all, 0.4% of patients with IBD had COVID-19. Nearly all had been diagnosed by polymerase chain reaction of nasopharyngeal swabs, and approximately 40% also had received chest CT scans. Most were male (56.5%), and 43.5% were older than 65 years. Patients were receiving a wide range of IBD therapies, most commonly anti–tumor necrosis factor agents, mesalamine, thiopurine), vedolizumab, ustekinumab, steroids, methotrexate, and tofacitinib. Results from six studies indicated that patients with IBD were significantly more likely to be diagnosed with COVID-19 if they were older than 66 years (odds ratio, 21.3) or had other comorbidities (OR, 1.24). The most commonly used drugs for managing COVID-19 were hydroxychloroquine, lopinavir/ritonavir, steroids, antibiotics, chloroquine, tofacitinib, and infliximab.

A total of 30.6% of patients with IBD and COVID-19 were hospitalized, 11.4% stayed in the ICU, 3.7% required mechanical ventilation, and 3.8% died from COVID-19. Significant risk factors for death from COVID-19 included older age, active IBD, and a Charlson Comorbidity Index score above 1. Similarly, risk factors for severe COVID-19 included older age, having two or more comorbidities, receiving systemic steroids, and receiving mesalamine/sulfasalazine. In one study, a recent (3-month) history of corticosteroid treatment was associated with a 60% increase in the risk for severe COVID-19. Other immune-mediated therapies did not show this association. Patients with UC were significantly more likely to be seen in the ED or hospitalized, compared with patients with other forms of IBD (adjusted OR, 12.7).

No funding sources were disclosed. Dr. D'Amico reported having no conflicts of interest. Two coinvestigators disclosed ties to AbbVie, MSD, Schering-Plough, UCB Pharma, and several other pharmaceutical companies.

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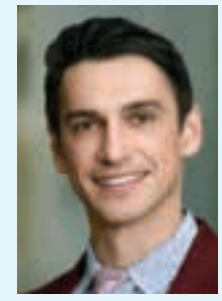
SOURCE: D'Amico F et al. Clin Gastroenterol Hepatol. 2020 Aug 7. doi: 10.1016/j.cgh.2020.08.003.


Dr. Kwapisz

Diarrhea is one of the hallmark features in inflammatory bowel disease (IBD). The systematic review and meta-analysis by D'Amico and colleagues highlights an increased prevalence of diarrhea in IBD patients with COVID-19. We have learned that SARS-CoV-2 enters the gastrointestinal tract through angiotensin-converting enzyme 2, which has been found in absorptive enterocytes of the ileum and colon. The subsequent invasion can cause a change in intestinal microbiota (dysbiosis) and trigger diarrhea. Prior studies also reported SARS-CoV-2 being isolated in the duodenum and rectum while showing RNA shedding in approximately 40% of patients. Clinicians may now face the diagnostic challenge of distinguishing the cause of diarrhea as an exacerbation from underlying IBD versus viral superinfection. The authors astutely hypothesized that having access to fecal polymerase chain reaction tests may be particularly useful to guiding clinical treatment decisions.

The study further showed that the mortality rate in IBD patients with COVID-19 (3.8%) was lower, compared with the general population (approximately 10%). This is a similar trend observed in the international SECURE-IBD database, which now includes more than 2,500 patients worldwide. Importantly, IBD patients who are elderly, have multiple comorbidities, or are on high-dose corticosteroids were most at risk of severe COVID outcomes, including intensive care admission and death. Ultimately, this meta-analysis along with expert consensus statements from organizations like the International Organization For the Study of Inflammatory Bowel Disease and the American Gastroenterology Association, demonstrate that IBD patients (including those on biologic treatments) were not at higher risk of contracting COVID-19, compared with the non-IBD population. These findings should encourage IBD patients and clinicians to continue maintenance biologic and immunosuppressant treatments.

Lukasz Kwapisz, MD, FRCPC, is assistant professor of medicine and gastroenterology at Baylor College of Medicine, Houston. He has no conflicts of interest.

Budesonide orodispersible tablets maintained remissions in EoE

BY AMY KARON
MDedge News

Budesonide orodispersible tablets maintained remissions of eosinophilic esophagitis (EoE) for 48 weeks in approximately 75% of patients and did not increase the risk for most adverse events, compared with placebo, according to the findings of a multicenter, randomized, double-blind trial.

While prior studies have shown that swallowed topical corticosteroids such as budesonide or fluticasone induce remission in EoE, this is the first multicenter phase 3 study of budesonide orodispersible tablets (BOTs) for maintaining remissions over the long term, wrote Alex Straumann, MD, of the Swiss EoE Research Group and University Hospital Zurich, and associates in Gastroenterology.

Eosinophilic esophagitis is the most common cause of esophageal dysphagia and food impaction. Swallowed topical corticosteroids improve symptoms and inflammation, but the off-label use of formulations developed for airway administration in asthma shows "suboptimal esophageal targeting and efficacy," the researchers wrote. In the phase 3 EOS-2 trial, twice-daily treatment with 1.0 mg BOTs had induced clinicohistologic remissions in 58% of adults with EoE at 6 weeks and in 85% at 12 weeks.

To study long-term maintenance BOT therapy, the researchers randomly assigned 204 of the remitted patients to 48 weeks of twice-daily BOT 0.5 mg, BOT 1.0 mg, or placebo. There were 68 patients per group. A total of 141 patients completed this double-blind phase, but all 204 were evaluable for the primary analysis. The primary outcome was remission at week 48, defined as freedom from relapse (dysphagia or odynophagia rated as 4 or higher on a 10-point numeric rating scale), histologic

Continued on following page

IL-23 has key roles in antimicrobial macrophage activity

BY AMY KARON
MDedge News

Interleukin-23 optimizes antimicrobial macrophage activity, which is reduced among persons harboring an IL-23 receptor variant that helps protect against inflammatory bowel disease (IBD), recent research has found.

"These [findings] highlight that the susceptibility to infections with therapeutic blockade of the IL-23/IL-12 pathways may be owing in part to the essential role for IL-23 in mediating antimicrobial functions in macrophages. They further highlight that carriers of the IL-23R–Q381 variant, who are relatively protected from IBD and other immune-mediated diseases, may be at increased risk for bacterial infection," Rui Sun and Clara Abraham, MD, of Yale University, New Haven, Conn., wrote in Cellular and Molecular Gastroenterology and Hepatology.

IL-23 is key to the pathogenesis of IBD and is being studied as a therapeutic target, both alone and in combination with IL-12 blocking. Although human macrophages express low levels of IL-23 receptor, recent research reveals that IL-23R is up-regulated "within minutes of exposure to IL-23," which promotes signaling and cytokine secretion, the investigators wrote. However, the extent to which IL-23 supports macrophage antimicrobial activity was unknown. To characterize protein expression, signaling, and bacterial uptake and clearance of bacteria by human macrophages derived from monocytes, the investigators tested these cells with Western blot, flow cytometry, and gentamicin protection, which involved coculturing human macrophages with bacteria, adding gentamicin solution, and then lysing and plating the cells onto agar to assess the extent to which

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Both genetic studies in humans and functional studies in mice have pinpointed interleukin-23 and its receptor as a key pathway in the pathogenesis of inflammatory bowel disease (IBD). IL-23 is released from myeloid cells in response to sensing of invading pathogens or danger-associated molecular patterns, where it drives induction of Th17, innate lymphoid cell responses, and inflammation.

Sun and Abraham describe a new function for IL-23 acting in a paracrine manner on macrophages to accelerate uptake and destruction of incoming bacteria via reactive oxygen, reactive nitrogen, and autophagic routes. The authors then explore how expression of IBD-protective IL23 receptor–susceptibility variants located in the IL-23R cytoplasmic tail might affect this pathway. They find the IBD-protective IL-23R–R381Q variant reduces uptake and degradation of bacteria, in addition to its role in reducing amplitude of inflammatory responses. Whether possession of the common IL-23R–R381Q variant predisposes to adverse sequelae during infections or whether blocking IL-23 in IBD may predispose to specific infections remains to be seen. In which case, it will be important to further dissect the mechanism of IL-23R signaling to ensure therapies selectively target inflammatory drivers while retaining protective effects.


Dr. Simmons

Alison Simmons, FRCP, PhD, is professor of gastroenterology, honorary consultant gastroenterologist, MRC human immunology unit, Weatherall Institute of Molecular Medicine, University of Oxford (England), and translational gastroenterology unit, Oxford University Hospitals NHS Trust. She has consultancies from AbbVie, Bristol-Myers Squibb, and Janssen, and is a cofounder and equity holder in TRexBio.

Continued from previous page

relapse (≥48 eosinophils per mm^2 high-power field), food impaction requiring endoscopic intervention, and dilation.

After 48 weeks, 51 patients in the 1-mg group (75%) and 50 patients in the 0.5-mg group (73.5%) remained in remission, compared with only 3 patients in the placebo group (4.4%; both *P* less than .0001). Patients in the placebo group relapsed after a median of 87 days off BOTs. Overall, BOT therapy was similarly efficacious regardless of factors such as history of allergic diseases, location of inflammation at the start of induction, or concomitant use of proton pump inhibitors. However, patients with inflammation of all three esophageal segments achieved "clinically relevant" greater rates of remission with twice-daily 1.0-mg BOT, compared with twice-daily 0.5-mg BOT (80% vs. 68%). In secondary analyses, rates of histologic relapse were 13.2% with 0.5-mg BOT twice daily, 10.3% with 1.0-mg BOT twice daily, and 90% with placebo, and rates of clinical relapse were 10.3%, 7.4%, and 60.3%, respectively. "Histological remission in the BOT 0.5 and 1.0 mg twice daily group was independently maintained in all esophageal segments," the researchers reported.

Rates of most adverse events were similar across treatment groups, and no serious treatment-emergent adverse events were reported. Average morning serum cortisol levels were similar among groups and did not change after treatment ended, but four patients on BOT therapy developed asymptomatic subnormal levels of morning cortisol. "Clinically manifested candidiasis was suspected in 16.2% of patients in the BOT 0.5 mg group and in 11.8% of patients in the BOT 1.0 mg group; all infections resolved with treatment," the researchers wrote.

The study and editorial support were funded by Dr. Falk Pharma GmbH, a pharmaceutical company in Germany. Dr. Falk Pharma was involved in the study design and data collection, analysis, and interpretation. Dr. Straumann disclosed fees from several pharmaceutical companies, including Dr. Falk Pharma and AstraZeneca, which makes budesonide. Several other coinvestigators also disclosed ties to Dr. Falk Pharma, AstraZeneca, and other pharmaceutical companies.

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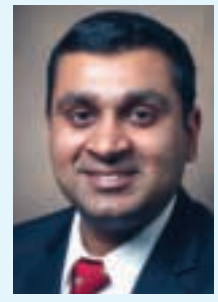
SOURCE: Straumann A et al. Gastroenterology. 2020 Jul 25. doi: 10.1053/j.gastro.2020.07.039.

Eosinophilic esophagitis (EoE) continues to rise in prevalence and prescription steroid therapy is limited to off-label use leading to a call for action for directed therapy for EoE and understanding long-term remission rates. In this phase 3 study, Straumann and colleagues studied budesonide orodispersible tablets (BOTs) and their ability to maintain remission, compared with placebo, at two doses specifically designed for EoE in adults with proton pump inhibitor–refractory EoE. Regardless of dose, at either 1.0 mg twice a day or 0.5 mg twice a day, there was an improvement in maintaining remission (73.5% for low dose and 75% for high dose, compared with 4.4% with placebo) at 48 weeks of therapy. Common side effects studied include an increase in candidiasis (12%-16% of patients), but there was no statistical change in morning cortisol.


Dr. Naik

Given the need for maintenance therapy for EoE, this study proves long-term efficacy and safety for the treatment of this chronic condition with a targeted esophageal formulation. We now have evidence of maintaining remission for EoE with a safe side-effect profile. Future research will be needed to look at long-term steroid use on bone health and immune dysregulation, especially in the pediatric population, which was not studied in this cohort. Moreover, future studies are needed to determine a minimally effective dose to help prevent potential side effects that can maintain remission while allowing discontinuation of all stable proton pump inhibitor doses to ensure no confounding effect.

Rishi D. Naik, MD, MSCI, is an assistant professor, department of medicine, section of gastroenterology & hepatology, Esophageal Center at Vanderbilt University Medical Center, Nashville, Tenn. He has no conflicts.

Continued from page 5

the macrophages had taken up the bacteria.

After 48 hours of exposure to IL-23 or IL-12, macrophages increased their intracellular clearance of clinically relevant bacteria, including *Enterococcus faecalis*, adherent invasive *Escherichia coli*, and *Salmonella typhimurium*. Notably, this did not occur when the investigators reduced ("knocked down") macrophage expression of either IL-23R or IL-12 receptor alpha-2. Additional investigations showed that in macrophages IL-23 promotes bacterial uptake, clearance, and autophagy by inducing a pyruvate dehydrogenase kinase 1 (PDK1)–dependent pathway mediated by Janus kinase 2/tyrosine kinase 2 and by inducing reactive oxygen species (ROS) and reactive nitrogen species (RNS) pathways. IL-23 also activates two key proteins involved in autophagy (ATG5 and ATG16L1), the researchers reported. "ROS, RNS, and autophagy cooperate to mediate IL-23-induced bacterial clearance. Reduction of each ROS, RNS, and autophagy pathway partially reversed the enhanced bacterial clearance observed with chronic IL-23 treatment."

Further tests found that IL-23 mediates antimicrobial pathways through the Janus kinase 2, tyrosine kinase 2, and STAT3 pathways, which "cooperate to mediate optimal IL-23-induced intracellular bacterial clearance in human macrophages." Importantly, human macrophages showed less antimicrobial activity when transfected with the IL-23R–Q381 variant than with IL-23R–R381. The IL-23R-Q381 variant, which reduces susceptibility to IBD, "decreased IL-23-induced and NOD2-induced antimicrobial pathways and intracellular bacterial clearance in monocyte-derived macrophages," the researchers explained. Evaluating actual carriers of these variants showed the same results – macrophages harboring IBD-protective IL-23R–R381/Q381 exhibited lower antimicrobial activity and less intracellular bacterial clearance compared with macrophages from carriers of IL-23R–R381/R381.

"Taken together, IL-23 promotes increased bacterial uptake and then induces a more rapid and effective clearance of these intracellular bacteria in human monocyte-derived macrophages," the researchers wrote. "The reduced inflammatory responses observed in IL-23R Q381 carriers are associated with protection from multiple immune-mediated diseases. This would imply that loss-of-function observed with the common IL-23R–R381Q variant may lead to a disadvantage in select infectious diseases, including through [this variant's] now identified role in promoting antimicrobial pathways in macrophages."

The National Institutes of Health provided funding. The investigators reported having no conflicts of interest.

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SOURCE: Sun R; Abraham C. Cell Molec Gastro Hepatol. 2020 May 28. doi: 10.1016/j.jcmgh.2020.05.007.

Delayed cancer screening could cause increase in deaths

BY CAROLYN CRIST

Delays in colorectal cancer screening because of the COVID-19 pandemic could lead to higher rates of advanced-stage cancer and death, according to a new study.

When compared with a delay of less than 3 months, the longer delay seen this year may result in an 11.9% increase in death rates.

"Across the globe, health care systems are facing serious difficulties while dealing with COVID-19, and it is imperative that support is given to the public and patients throughout the crisis, including for high-impact diseases such as colorectal cancer," Luigi Ricciardiello, MD, the lead study author and a professor at the University of Bologna (Italy), said in a statement.

Dr. Ricciardiello and colleagues presented their research at UEG Week Virtual 2020, an international conference for gastroenterologists. The study will be published in the UEG Journal.

The researchers created a model to forecast the effects of delayed cancer screening during 2020. A "moderate" delay of 7-12 months caused a 3% increase in advanced-stage colon cancer, and a long delay of more than 12 months caused a 7% increase in advanced cancer.

Based on a survival rate of 5 years for stage 3 or stage 4 colorectal cancer, the death rate would increase nearly 12% when screening is delayed for more than a year, as compared with less than 3 months of delay.

In a paper published in Clinical Gastroenterology and Hepatology in early September, they projected that deaths could increase 12% if screening is delayed for more than a year.

Throughout the pandemic, screening programs have been delayed in many countries, particularly across Europe.

United European Gastroenterology, a professional medical organization for digestive health specialists, has called for policymakers to implement colon cancer screening programs across the European Union. Annually, more than 375,000 new cases are diagnosed across the EU, and more than 170,000 people die from colorectal cancer, according to a UEG report.

"It is therefore essential that vital diagnosis tools, like screening programs, continue and help to prevent mortality rates from rising even further," said Dr. Ricciardiello.

At press time, Dr. Ricciardiello had no conflicts of interest.

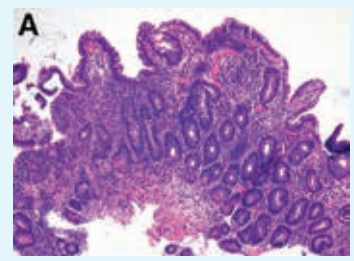
A version of this article originally appeared on Medscape.com.

CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Shria Kumar, MD, and Stacey Prenner, MD. Published previously in Gastroenterology (2019;157[1]:27-8).

A 24-year-old White man with depression and anxiety disorder is referred for an isolated alanine aminotransferase elevation found by his primary medical doctor on routine blood work. He denies a family history of liver disease, although he does report a family history of lupus. He denies risk factors for viral hepatitis. He drinks about three alcoholic beverages per week. His family is originally from Germany and Ireland. He denies use of over-the-counter medications or supplements beyond a rare use of ibuprofen. His only medication is daily escitalopram. On further questioning he also reports abdominal pain. The abdominal pain is described as dull, constant, right upper–quadrant pain near his rib cage. The pain occasionally becomes worse if he eats fast foods. He also notes a 3-month history of bloating and alternating bowel habits between diarrhea and constipation.



Physical examination is notable for unremarkable vital signs and a normal body mass index. He has no stigmata of chronic liver disease or hepatomegaly. He has normal bowel sounds without any tenderness to palpation. An in-office FibroScan is normal with a value of 3 kPa. Aspartate aminotransferase is 33 U/L (normal, 10-40 U/L). Viral serologies are notable for nonreactive hepatitis B surface antigen, surface antibody, and core antibody. Hepatitis

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C virus RNA is undetectable. Ferritin, iron, and creatine kinase are normal. Thyroid-stimulating hormone, antimitochondrial antibody, and antinuclear antibody are negative. Ceruloplasmin is normal and alpha-1 antitrypsin showed MZ phenotype. An abdominal ultrasound scan shows a normal size liver, normal echotexture, and sludge in the gallbladder, without any intrahepatic or extrahepatic bile duct dilation. The extrahepatic bile duct diameter is 0.3 cm.

Antismooth muscle and quantitative immunoglobulin tests were ordered. An endoscopy is performed for abdominal pain, and duodenal endoscopic and histologic images are provided (Figures A and B).

The diagnosis is on page 13.

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Medications may cause flares

Pancreatitis *from page 1*

kin. "A large volume of ringers lactate intravenous fluids given within the first 24 hours of admission, as opposed to normal saline, may decrease the inflammatory response in patients with acute pancreatitis." The preferred diagnostic method remains clinical evaluation along with use of serum lipase, which is more sensitive than serum amylase (97%) but with similar specificity (99%); current wisdom does not support CT for diagnosis unless there is a diagnostic dilemma.

Early establishment of disease etiology and its therapy is imperative to attempt to prevent recurrent episodes and progression to chronic pancreatitis, Dr. Barkin said. Genetic testing studies suggest that approximately 10% of acute pancreatitis cases are the result of genetic factors, and Dr. Barkin recommended performing genetic testing after a first attack of idiopathic acute pancreatitis, especially in younger patients.

There is an extensive list of medications that may cause acute pancreatitis, according to a recent study published in PLOS One, the most common of which include acetaminophen, amiodarone, azathioprine, and angiotensin-converting enzyme inhibitors, Dr. Barkin said (PLOS One. 2020 Apr 17 doi: 10.1371/journal.pone.0231883).

Current recommendations for hospital treatment of acute pancreatitis include early large-volume fluid replacement and initiation of per-oral nutrition as soon as tolerated, as well as pain control, Dr. Barkin said. In addition, management includes strict glycemic and triglyceride control and performance of cholecystectomy for mild and or moderate biliary pancreatitis or endoscopic retrograde cholangiopancreatography if the patient is not an operative candidate during the same hospital stay. "In patients who cannot undergo surgery, endoscopic sphincterotomy should be performed to allow spontaneous passage of any stones still in the gallbladder."

Current recommendations to prevent acute pancreatitis include avoiding irritants such as alcohol, nicotine, and drugs known to cause acute pancreatitis, including marijuana, said Dr. Barkin. Also, controlling metabolic factors such as obesity, diabetes, and triglycerides can help reduce risk of recurrence. Several of these factors are also linked to increased risk for progression to chronic pancreatitis.

In addition, acute pancreatitis patients should be screened long-term for development of pancreatic exocrine insufficiency, which may be present in approximately one-quarter of patients following an acute pancreatitis episode, and diabetes, he said.

Finally, at the time of discharge, it is essential to evaluate for risk of readmission, Dr. Barkin said. In addition to severe disease and systemic inflammatory response syndrome at the time of patient discharge, several factors increase the likelihood of readmission including ongoing abdominal pain requiring pain medicine, obesity, and inability to tolerate solid food, he noted.

Global Academy for Medical Education and this news organization are owned by the same parent company.

Dr. Barkin had no conflicts of interest.

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AGA Resource
Share AGA GI Patient Center education on pancreatitis to help your patients understand testing and treatment options and possible complications at http://ow.ly/nsdn30rcz5A.

Answer to "What is your diagnosis?" on page 10: Celiac hepatitis

The diagnosis

Endoscopic biopsy of this severely scalloped duodenal mucosa demonstrated characteristic findings of gluten-sensitive enteropathy, or celiac disease. Celiac disease involvement of the liver is a common extraintestinal manifestation of this immune-mediated disorder, termed celiac hepatitis. Celiac hepatitis affects 40% of adults with celiac disease.[1] The pathogenesis is poorly understood, but posited to be related to autoimmunity or toxin-mediated liver injury

The pathogenesis is poorly understood, but posited to be related to autoimmunity or toxin-mediated liver injury in the setting of gluten exposure.

in the setting of gluten exposure, gut permeability, chronic inflammation, and host susceptibility, among other mechanisms.[1-3]

Clinical manifestations of celiac hepatitis range from unexplained enzyme elevations in the absence of known liver disease to autoimmune hepatitis to hepatic steatosis, and even cirrhosis.[1] The initial presentation can also be elevated liver enzymes in the setting of known celiac disease, without known hepatic disease. Histology of the liver is similarly variable, from a mild or a chronic hepatitis to steatohepatitis and even fibrosis.[2] Elevated transaminases less than five times the upper limit of normal when found at celiac diagnosis suggest celiac hepatitis, and do not require further work-up.[1] For these individuals, response to a gluten-free diet should be monitored and liver chemistries should be repeated at 6-12 months. Persistently elevated aminotransferases should prompt further work-up.[1] Generally, enzyme elevation and even the histologic appearance of the liver improve after implementation of a gluten-free diet, although not for all.[2] In celiac hepatitis associated with autoimmune liver disease, immunosuppression may be required in addition to abstaining from gluten.[3] Our patient was found to have a tissue transglutaminase level >100 U/mL (normal, <4 U/mL). He began a gluten-free diet guided by a nutritionist, with rapid improvement in abdominal symptoms at 4 weeks, and will be followed to ensure normalization of liver enzymes, which can take up to 1 year.

References

1. Rubio-Tapia A; Murray JA. Liver involvement in celiac disease. Minerva Med. 2008;99:595-604.

2. Majumdar K et al. Coeliac disease and the liver: Spectrum of liver histology, serology and treatment response at a tertiary referral centre. J Clin Pathol. 2018;71:412-9.

3. Marciano F et al. Celiac disease-related hepatic injury: Insights into associated conditions and underlying pathomechanisms. Dig Liver Dis. 2016;48:112-9.

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Time to screen for liver disease in type 2 diabetes?

BY SARA FREEMAN
MDedge News

With high rates of fatty liver disease known to occur among people with type 2 diabetes, is it time to introduce routine liver screening into daily diabetes practice? The answer depends on whom you ask, and then there are still some important caveats.

From the hepatologist's perspective, there is no excuse not to consider liver surveillance now that noninvasive screening methods are available, suggested Michael Trauner, MD, AGAF, of the Medical University of Vienna.

"From a practical standpoint, I think every type 2 diabetic over 50 years of age is at high risk," and consequently should be screened at diagnosis, Dr. Trauner said during a debate at the virtual annual meeting of the European Association for the Study of Diabetes. "I would screen at diagnosis and then decide on recall depending on noninvasive fibrosis markers."

"It's a rising problem that we are facing these days," observed Michael Roden, MD, chair and professor of internal medicine, endocrinology and metabolic diseases at Heinrich-Heine University in Düsseldorf, Germany, who co-chaired the session. Not only do people with type 2 diabetes have an increased risk for developing liver diseases, but also there's a higher risk for those with fatty liver diseases developing type 2 diabetes.

A meta-analysis published in Gut illustrates just how big a problem this is – nonalcoholic fatty liver disease (NAFLD) "doubled the risk of type 2 diabetes," said Dr Rosen, who is also the director of the division of endocrinology and diabetology at University Clinics Düsseldorf. That analysis was based on more than 500,000 people, almost 28,000 of whom had incident diabetes over a 5-year period (Gut. 2020 Sep 16. doi: 10.1136/gutjnl-2020-322572).

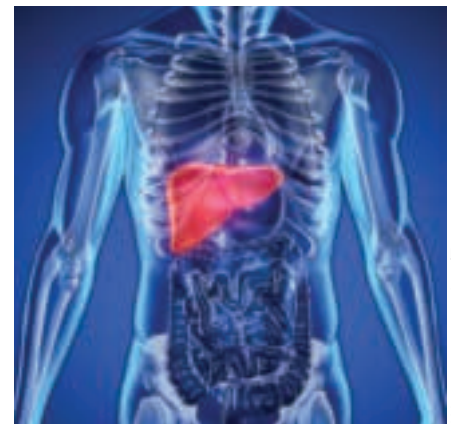
Screening tools scarce

This makes liver screening in type 2 diabetes patients "a formidable challenge," cautioned Gianluca Perseghin, MD, professor of endocrinology at the Monza (Italy) Polyclinic and the University of Milano-Bicocca in Milan.

"Hepatologists generally see only the most severe cases," Dr. Perseghin said. Diabetologists and endocrinologists would be likely to see huge numbers of patients that could potentially be at risk for liver disease and following the recommendations set out in the joint European Association for the Study of the Liver/EASD/European Association for the Study of Obesity guidelines would result in a huge number of patients being identified and potentially needing referral, he argued.

"At this stage, we need to build a friendly, reliable and cost-effective screening process to be applied in the health systems," Dr. Perseghin suggested. He proposed that liver surveillance would need to be not only personalized on a patient level, but also at the infrastructure level. Measuring liver enzymes, for example, was going to be less accurate in picking up liver disease but blood tests were widely available, whereas imaging methods were not going to be something all diabetes clinics would have immediate access to.

"There are clearly a lot of provocative decisions still to be made," acknowledged Philip Newsome, PhD, FRCPE, an honorary consultant hepatologist at the University of Birmingham (England), who co-chaired the debate.



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"We need to demonstrate that looking for the presence of liver disease in this cohort changes their outcomes in a way that is cost effective," said Dr. Newsome, who is also the secretary general of EASL.

"Tests are evolving, but more importantly, treatments are evolving. So, the decision around cost-effectiveness will clearly change," he added.

NAFLD therapies unclear

"There are still a lot of questions," Dr. Newsome said during a Novo Nordisk–sponsored "Meet the Expert" session discussing EASL-EASD-EASO guidelines. "We don't have any licensed therapies at the moment. But there's been a huge amount of investment, looking at all sorts of different approaches."

Dr. Newsome added: "We also don't know how to monitor these patients. Most of the noninvasive [methods] are very useful for staging patients, but we don't really understand how useful they are for monitoring changes in fibrosis."

Diabetologist Hannele Yki-Järvinen, MD, PhD, of the University of Helsinki, gave her thoughts on the topic during the same session.

"We should add FIB-4 [Fibrosis-4 index] to the annual exam and ask the lab to calculate FIB-4 automatically," Dr. Yki-Järvinen said. FIB-4 is calculated using the patient's age and the results of readily available blood tests that measure the AST/ALT ratio and the platelet count.

Dr. Trauner has received advisory fees and grant support from various companies with an interest in developing liver-directed therapies, and is also a coinventor of 24-norursodeoxycholic acid under development for cholestatic liver disease and potentially NAFLD. Dr. Perseghin has received honoraria and grant support from various pharmaceutical companies with an interest in diabetes care. Dr. Roden did not provide any disclosures. Dr. Newsome has received research grants from Boehringer Ingelheim and Novo Nordisk and acted as a consultant to many pharmaceutical companies. Dr. Yki-Järvinen disclosed receiving consultancy fees from Eli Lilly, MSD, and Novo Nordisk.

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SOURCE: Trauner M; Persghin G. EASD 2020. Session S27.

INR fails to predict bleeding in patients with cirrhosis

BY WILL PASS
MDedge News

International normalized ratio (INR) does not predict periprocedural bleeding in patients with cirrhosis, according to a meta-analysis of 29 studies.

This finding should deter the common practice of delivering blood products to cirrhotic patients with an elevated INR, reported lead author Alexander J. Kovalic, MD, of Novant Forsyth Medical Center in Winston Salem, N.C., and colleagues.

"INR measurement among cirrhotic patients is important in MELD [Model for End-Stage Liver Disease] prognostication and assessment of underlying hepatic synthetic function, however the INR alone does not capture the complicated interplay of anticoagulant and procoagulant deficiencies present in cirrhotic coagulopathy," Dr. Kovalic and colleagues wrote in Alimentary Pharmacology & Therapeutics. "Yet, the 'correction' of these aberrancies among peripheral coagulation tests remains common ... even in modern practice, and not uncommonly occurs in the periprocedural setting."

According to investigators, addressing INR with blood transfusion can have a litany of negative effects. Beyond the risks faced by all patient populations, increasing blood volume in those with cirrhosis can increase portal venous pressure, thereby raising risks of portal gastropathy or variceal hemorrhage. In addition, giving plasma products to patients with cirrhotic coagulopathy may further disrupt the balance between anticoagulants and procoagulants, potentially triggering disseminated intravascular coagulation.

Dr. Kovalic and colleagues noted that the lack of correlation between peripheral coagulation tests and bleeding risk has been a longstanding subject of investigation, citing studies from as early as 1981.

To add further weight to this body of evidence, the investigators conducted a systematic review and meta-analysis involving 13,276 patients with cirrhosis who underwent various procedures between 1999 and 2019. Primary out-

Continued on following page

Bariatric surgery linked to longer life

BY JIM KLING
MDedge News

A new analysis of the Swedish Obese Subjects (SOS) study shows that bariatric surgery is associated with about a 3-year increase in lifespan, compared with obese patients who do not undergo surgery. Still, surgery did not restore normal lifespan: Surgical patients' lifespan remained less than that of a sample from the general Swedish population. The study follows other reports suggesting reduced mortality after bariatric surgery, but with a longer follow-up.

"These data add even more evidence to the growing literature showing that patients who undergo bariatric surgery experience a reduction in all-cause long-term mortality. In making decisions around bariatric surgical procedures and care, patients and their health care providers need to understand the trade-offs between improved weight, health, and longer-term survival versus the surgical risks and problems over time," Anita P. Courcoulas, MD, MPH, chief of minimally invasive bariatric and general surgery at the University of Pittsburgh Medical Center, said in an interview. Dr. Courcoulas was not involved in the study.

The results appeared in the New England Journal of Medicine.

The SOS study drew from 25 surgical departments and 480 primary health care centers in Sweden. The researchers examined data from 2,007 patients who underwent bariatric surgery between 1987 and 2001, and compared their outcomes to 2,040 matched controls. All were between age 37 and 60 years, with a body mass index (BMI) of at least 34 kg/m^2 for men and 38 for women. They also compared outcomes with 1,135 individuals randomly sampled from the Swedish population registry.

'These data add even more evidence to the growing literature showing that patients who undergo bariatric surgery experience a reduction in all-cause long-term mortality.'

Procedures included banding (18%), vertical banded gastroplasty (69%), and gastric bypass (13%). After an initial BMI reduction of about 11, the surgery group stabilized by year 8 at a BMI about 7 lower than baseline, and there was little change in BMI among controls.

After a mean follow-up of 24 years (interquartile range, 22-27 years), there were 10.7 deaths per 1,000 person-years in the surgery group, 13.2 among obese controls, and 5.2 in the general population (hazard ratio, 0.77 for surgery versus no surgery; $P < .001$). The general population had a lower mortality than nonsurgical controls (HR, 0.44; $P < .001$).

The surgery group had a higher median life expectancy than controls (median, 2.4 years; adjusted difference, 3.0 years; $P < .001$). The general population group had a median life expectancy that was 7.4 years higher than the control group (adjusted difference, 8.5 years; $P < .001$). The surgery group's median life expectancy was still shorter than the general population reference (adjusted difference, 5.5 years; $P < .001$).

Cardiovascular disease risk was lower in the surgery group (HR, 0.70; 95% confidence interval, 0.57-0.85), as was risk of MI (HR, 0.51; 95% CI, 0.33-0.79), heart failure (HR, 0.52; 95% CI, 0.31-0.88), and stroke (HR, 0.45; 95% CI, 0.24-0.84). Cancer mortality was also lower (HR, 0.77; 95% CI, 0.61-0.96).

In the surgery group, causes of death that were elevated over the general population included cardiovascular causes (HR, 2.64; 95% CI, 1.78-3.91) and noncardiovascular causes, mainly infections; postsurgical complications; and factors such as alcoholism, suicide, or trauma (HR, 1.50; 95% CI, 1.18-1.91).

The study is limited by its retrospective nature and because the surgical techniques used at the time are less effective than those used today and could lead to weight gain over time. As a result, many patients who underwent surgery remained heavier than the general population. It's also possible that negative health effects accumulated before surgery and persisted afterwards, according to Dr. Courcoulas.

The findings are likely generalizable to people with obesity, many of whom choose not to undergo bariatric surgery despite the potential benefits. "The population studied in SOS had a similar profile of underlying medical diseases to those groups who undergo bariatric surgery today and in the U.S. and around the world," said Dr. Courcoulas.

The study was funded by the Swedish Research Council and others. Dr. Courcoulas has no relevant financial disclosures

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SOURCE: Carlsson L et al. N Engl J Med. 2020 Oct 15. doi: 10.1056/NEJMoa2002449.

Continued from previous page

comes included periprocedural bleeding events and the association between preprocedural INR and periprocedural bleeding events. Secondary outcomes included mortality, quantity of blood and/or plasma products used, and relationship between preprocedural platelet count and periprocedural bleeding events.

The analysis showed that preprocedural INR was not significantly associated with periprocedural bleeding events (pooled odds ratio, 1.52; 95% confidence interval, 0.99-2.33; $P = .06$), a finding that held across INR threshold subgroups. Similarly, no significant difference was found between mean INR of patients who had bleeding events versus that of those who did not (pooled mean difference, 0.05; 95% CI, 0.03-0.13; $P = .23$).

Preprocedural platelet count was also a poor predictor of periprocedural bleeding, with a pooled odds ratio of 1.24 (95% CI, 0.55-2.77; $P = .60$), although the investigators noted that platelet count thresholds varied widely across studies, from 30 to 150 × 10^9/L. When studies were stratified by procedural bleeding risk or procedure type, subgroup effects were no longer significant. Other secondary endpoints were incalculable because of insufficient data.

"Hopefully, these findings will spark initiation of more large-scale, higher-quality studies ... to reinforce minimizing administration of fresh frozen plasma for inappropriate correction of INR, which carries a multitude of adverse effects among cirrhotic [patients]," the investigators concluded.


Dr. Caldwell

According to Stephen H. Caldwell, MD, of the University of Virginia in Charlottesville, "The present paper augments accumulating literature over the past 15 years that INR should be discarded as a measure of procedure-related bleeding risk."

Dr. Caldwell pointed out that "bleeding in cirrhosis is usually related to portal hypertension, not with impaired hemostasis, with the occasional exception of hyperfibrinolysis, which is very different from a prolonged INR."

He went on to suggest that the present findings should dissuade clinicians from a practice that, for some, is reflexive rather than evidence based.

"It's remarkable how many medical practices become entrenched based on hand-me-down teaching during our early training years, and remain so for many years beyond as we disperse into various medical and surgical fields," Dr. Caldwell said. "These learned approaches to common problems can clearly persist for generations despite overwhelming evidence to the contrary that usually evolves slowly and well-insulated within subspecialties or sub-subspecialties, and hence takes several generations of training to diffuse into the wider practice of medical care for common problems. These may become matters of expedience in decision-making, much like the old antibiotic conundrum of 'no-think-a-cillin,' as critics referred to overuse of broad-spectrum antibiotics. And so it has been with the INR."

The investigators disclosed relationships with AbbVie, Eisai, Gilead, and others. Dr. Caldwell disclosed research support from Daiichi concerning the potential role of anticoagulation therapy in preventing cirrhosis progression.

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SOURCE: Kovalic AJ et al. Aliment Pharmacol Ther. 2020 Sep 10. doi: 10.1111/apt.16078.

Role of GIs in the U.S. in the management of gastric cancer

BY YUTAKA TOMIZAWA, MD, MSC

Dr. Tomizawa is a clinical assistant professor of medicine in the division of gastroenterology, University of Washington, Seattle. He has no conflicts.

Introduction

Although gastric cancer is one of the most common causes of cancer death in the world, the burden of gastric cancer in the United States tends to be underestimated relative to that of other cancers of the digestive system. In fact, the 5-year survival rate from gastric cancer remains poor (~32%)[1] in the United States, and this is largely because gastric cancers are not diagnosed at an early stage when curative therapeutic options are available. Cumulative epidemiologic data consistently demonstrate that the incidence of gastric cancer in the United States varies according to ethnicity, immigrant status, and country of origin. It is important for practicing gastroenterologists in the United States to recognize individual risk profiles and identify people at higher risk for gastric cancer. Hereditary diffuse gastric cancer (HDGC) is an inherited form of diffuse-type gastric cancer and has pathogenic variants in the E-cadherin gene that are inherited in an autosomal dominant pattern. The lifetime risk of gastric cancer in individuals with HDGC is very high, and prophylactic total gastrectomy is usually advised. This article focuses on intestinal type cancer.

Epidemiology

Gastric cancer (proximal and distal gastric cancer combined) is the fifth most frequently diagnosed cancer and the third most common cause of cancer death worldwide, with 1,033,701 new cases and 782,685 deaths in 2018.[2] Gastric cancer is subcategorized based on location (proximal [i.e., esophagogastric junctional, gastric cardia] and distal) and histology (intestinal and diffuse type), and each subtype is considered to have a distinct pathogenesis. Distal intestinal–type gastric cancer is most commonly encountered in clinical practice. In this article, gastric cancer will signify distal intestinal–type gastric cancer unless it is otherwise noted.

In general, incidence rates are about twofold higher in men than in women. There is marked geographic variation in incidence rates, and the age-standardized incidence rates in eastern Asia (32.1 and 13.2, per 100,000) are approximately six times higher than those in northern America (5.6 and 2.8, per 100,000) in both men and women, respectively.[2] Recent studies evaluating global trends in the incidence and mortality of gastric cancer have demonstrated decreases worldwide.[3-5] However, the degree of decrease in the incidence and mortality of gastric cancer varies substantially across geographic regions, reflecting the heterogeneous distribution of risk profiles. A comprehensive analysis of a U.S. population registry demonstrated a linear decrease in the incidence of gastric cancer in the United States (0.94% decrease per year between 2001 and 2015),[6] though the annual percent change in the gastric cancer mortality in the United States was lower (around 2% decrease per year between 1980 and 2011) than in other countries.[3]

Several population-based studies conducted in the United States have demonstrated that the incidence of gastric cancer varied by ethnicity, immigrant status, and country of origin, and the highest incidence was observed among Asian immigrants.[7,8] A comprehensive meta-analysis examining the risk of gastric cancer in immigrants from high-incidence regions to low-incidence regions found a persistently higher risk of gastric cancer and related mortality among immigrants.[9] These results indicate that there are important risk factors such as environmental and dietary factors in addition to the traditionally considered risk factors including male gender, age, family history, and tobacco use. A survey conducted in an ethnically and culturally diverse U.S. city showed that gastroenterology providers demonstrated knowledge deficiencies in identifying and managing patients with increased risk of gastric cancer.[10] Recognizing individualized risk profiles in higher-risk groups (e.g., immigrants from higher-incidence/prevalence regions) is important for optimizing management of gastric cancer in the United States.

Assessment and management of modifiable risk factors

Helicobacter pylori, a group 1 carcinogen, is the most well-recognized risk factor for gastric cancer, particularly noncardia gastric cancer.[11] Since a landmark longitudinal follow-up study in Japan demonstrated that people with *H. pylori* infection are more likely to develop gastric cancer than those without *H. pylori* infection,[12] accumulating evidence largely from Asian countries has shown that eradication of *H. pylori* is associated with a reduced incidence of gastric cancer regardless of baseline risk.[13] There are also data on the protective effect for gastric cancer of *H. pylori* eradication in asymptomatic individuals. Another meta-analysis of six international randomized control trials demonstrated a 34% relative risk reduction of gastric cancer occurrence in asymptomatic people (relative risk of developing gastric cancer was 0.66 in those who received eradication therapy compared with those with placebo or no treatment, 95% confidence interval, 0.46-0.95).[14] A U.S. practice guideline published after these meta-analyses recommends that all patients with a positive test indicating active infection with *H. pylori* should be offered treatment and testing to prove eradication,[15] though the recommendation was not purely intended to reduce the gastric cancer risk in U.S. population. Subsequently, a Department of Veterans Affairs cohort study added valuable insights from a U.S. experience to the body of evidence from other countries with higher prevalence. In this study of more than 370,000 patients with a history of *H. pylori* infection, the detection and successful eradication of *H. pylori* was associated with a 76% lower incidence of gastric cancer compared with people without *H. pylori* treatment.[16] This study also provided insight into *H. pylori* treatment practice patterns. Of patients with a positive *H. pylori* test result (stool antigen, urea breath test, or pathology), approximately 75% were prescribed an eradication regimen and only 21% of those underwent eradication tests. A low rate (24%) of eradication testing was subsequently reported by the same group among U.S. patients regardless of gastric cancer risk profiles.[17] The lesson from the aforementioned study is that treatment and eradication of *H. pylori* even among asymptomatic U.S. patients reduces the risk of subsequent gastric cancer. However, it may be difficult to generalize the results of this study given the nature of the Veterans Affairs cohort, and more data are required to justify the implementation of nationwide preventive *H. pylori* screening in the general U.S. population.

Smoking has been recognized as the other important risk factor. A study from the European prospective multicenter cohort demonstrated a

For gastroenterologists, the timely diagnosis of malignancies of the gastrointestinal tract is of utmost importance. Gastric cancer often portends a relatively poor prognosis, because at the time of presentation, the malignancy is often already at an advanced stage with limited, if any, curative therapeutic options. Several risk factors for the development of gastric cancer exist – the ability to readily identify these factors and stratify patients accordingly is critical in the ethnically diverse population of the United States.

The In Focus article for this quarter, which is brought to you by *The New Gastroenterologist*, broaches the important topic of gastric cancer. Written by Dr. Yutaka Tomizawa (University of Washington), this in-depth piece reviews the types of gastric cancer, the approach to modifiable risk factors, and most importantly, how to recognize patients at highest risk. This comprehensive article provides practical advice on optimizing management of patients based on their individual risk profiles, leading to earlier diagnosis of gastric malignancies and more favorable patient outcomes.

Vijaya L. Rao, MD
Editor in Chief, The New Gastroenterologist

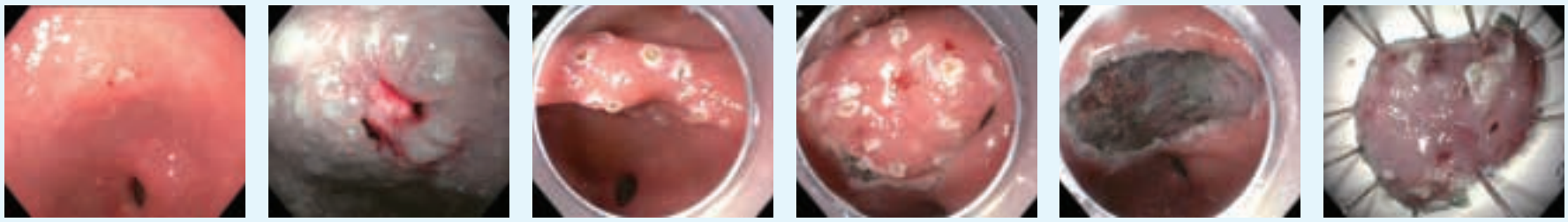

Figure 1. A 77-year-old woman who was found to have a 0-IIa+IIc lesion in the gastric antrum. Biopsy confirmed the presence of intramucosal adenocarcinoma. The lesion was resected en bloc by ESD. A: Initial inspection of the lesion under HDWL; B: NBI magnification (near focus function); C: Perimeter marking of the lesion; D: Submucosal dissection; E: En-bloc resection; F: Resected specimen.

significant association of cigarette smoking and gastric cancer risk (hazard ratio for ever-smokers, 1.45; 95% CI, 1.08-1.94; current-smokers in males, 1.73; 95% CI, 1.06-2.83; and current smokers in females, 1.87; 95% CI, 1.12-3.12, respectively) after adjustment for educational level, dietary consumption profiles, alcohol intake, and body mass index.[18] A subsequent meta-analysis provided solid evidence of smoking as the important behavioral risk factor for gastric cancer.[19] Smoking also predisposed to the development of proximal gastric cancer.[20] Along with other cancers in the digestive system such as in the esophagus, colon and rectum, liver, gallbladder, and pancreas, a significant association of BMI and the risk of proximal gastric cancer (relative risk of the highest BMI category compared with normal BMI, 1.8; 95% CI, 1.3-2.5) was reported, with positive dose-response relationships; however, the association was not sufficient for distal gastric cancer.[21]

There is also evidence to show a trend of greater alcohol consumption (>45 grams per day [about 3 drinks a day]) associated with the increased risk of gastric cancer.[21] It has been thought that salt and salt-preserved food increase the risk of gastric cancer. It should be noted that the observational studies showing the associations were published from Asian countries where such foods were a substantial part of traditional diets (e.g., salted vegetables in Japan) and the incidence of gastric cancer is high. There is also a speculation that preserved foods may have been eaten in more underserved, low-socioeconomic regions where refrigeration was not available and prevalence of *H. pylori* infection was higher. Except for documented inherited form of gastric cancer (e.g., HDGC or hereditary cancer syndromes), most gastric cancers are considered sporadic. A recent randomized study published from South Korea investigated a cohort of higher-risk asymptomatic patients with family history significant for gastric cancer. This study of 1,676 subjects with a median follow-up of 9.2 years showed that successful eradication of *H. pylori* in the first-degree relatives of those with gastric cancer significantly reduced the risk (HR, 0.45; 95% CI, 0.21-0.94) of developing gastric cancer.[22] As previously discussed, in the United States where the prevalence of *H. pylori* and the incidence of gastric cancer are both lower than in some Asian countries, routine screening of asymptomatic individuals for *H. pylori* is not justified yet. There may be a role for screening individuals who are first-generation immigrants from areas of high gastric cancer incidence and also have a first-degree relative with gastric cancer.

TABLE 1

Paris classification system of superficial gastric neoplastic lesions

Type	Subclass
0-I: Polypoid	0-Ip: Protruded, pedunculated 0-Is: Protruded, sessile
0-II: Nonpolypoid	0-IIa: Superficial, elevated 0-IIb: Flat 0-IIc: Superficial, depressed
0-III: Excavated	

Who should we consider high risk and offer screening EGD?

With available evidence to date, screening for gastric cancer in a general U.S. population is not recommended. However, it is important to acknowledge the aforementioned varying incidence of gastric cancer in the United States among ethnicity, immigrant status, and country of origin. Immigrants from high-incidence regions maintain a higher risk of gastric cancer and related mortality even after migration to lower-incidence regions. The latter comprehensive study estimated that as many as 12.7 million people (29.4% of total U.S. immigrant population) have emigrated from higher-incidence regions including East Asian and some Central American countries.[9] Indeed, an opportunistic nationwide gastric cancer screening program has been implemented in South Korea (beginning at age 40, biannually)[23] and Japan (beginning at age 50, biannually).[24]

Two decision-analytic simulation studies have provided insight into the uncertainty about the cost effectiveness for potential targeted gastric cancer screening in higher-risk populations in the United States. One study demonstrated that esophagogastroduodenoscopy (EGD) screening for otherwise asymptomatic Asian American people (as well as Hispanics and non-Hispanic Blacks) at the time of screening colonoscopy at 50 years of age with continued endoscopic surveillance every 3 years was cost effective, only if gastric intestinal metaplasia (GIM) or more advanced lesions were diagnosed at the index screening EGD.[25] Previous studies analyzing the cost-effectiveness for gastric cancer screening in the United States had the limitation of not stratifying according to race or ethnicity, or accounting for patients diagnosed with GIM. Subsequently, the same research group extended this model analysis and has published additional findings that this strategy is cost effective for each of the most prevalent Asian American ethnicities (Chinese, Filipino, Southeast Asian, Vietnamese, Korean, and Japanese Americans) in the United States irrespective of sex.[26] The authors raised a limitation that additional risk factors such as family history, tobacco use, or persistent *H. pylori* infection were not considered in the model because data regarding differentiated noncardia gastric cancer risk among Asian American ethnicities based on these risk factors are not available.

These two model analytic studies added valuable insights to the body of evidence that subsequent EGDs after the one-time bundled EGD is cost effective for higher-risk asymptomatic people in the United States, if the index screening EGD with gastric mucosal biopsies demonstrates at least GIM. Further population-based research to elucidate risk stratification among higher-risk people will provide a schema that could standardize management and resource allocation as well as increase the cost-effectiveness of a gastric cancer screening program in the United States. The degree of risk of developing gastric cancer in autoimmune gastritis varies among the reported studies.[27-29] Although the benefit of endoscopic screening in patients with autoimmune gastritis has not been established, a single endoscopic evaluation should be recommended soon after the diagnosis of autoimmune gastritis in order to identify prevalent neoplastic lesions.[30]

Practical consideration when we perform EGD for early gastric cancer screening

Identification of higher-risk patients should alert an endoscopist to observe mucosa with greater care with a lower threshold to biopsy any suspicious lesions. Preprocedural risk stratification for each individual before performing diagnostic EGD will improve early gastric cancer detection. While we perform EGD, detecting precursor lesions (atrophic gastritis and GIM) is as important as diagnosing an early gastric cancer. Screening and management of patients with precursor lesions (i.e., atrophic gastritis and GIM) is beyond the scope of this article, and this was published in a previous issue of the New Gastroenterologist. It is important to first grossly survey the entire gastric mucosa using high-definition white light (HDWL) endoscopy and screen for any focal irregular (raised or depressed) mucosal lesions. These lesions are often erythematous and should be examined carefully. Use of mucolytic and/or deforming agents (e.g., N-acetylcysteine or simethicone) is recommended for the improvement of visual clarity of gastric mucosa.[31] Simethicone is widely used in the United States for colonoscopy and should also be available at the time of EGD for better gastric mucosal visibility. If irregular mucosal lesions are noted, this area should also be examined under narrowband imaging (NBI) in addition to HDWL. According to a simplified classification consisting of mucosal and vascular irregularity, NBI provides better mu-

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Engage rather than react: A call for hepatologists

In the September issue of *Clinical Gastroenterology and Hepatology*, Meena B. Bansal, MD, FAASLD, from Icahn School of Medicine at Mount Sinai, New York, provides clinicians with practical guidance on their essential role in value-based health care. Read the article, which appears in CGH's Practice Management: The Road Ahead column: How Hepatologists Can Contribute to Value-Based Care.

Hepatologists can shift the cost curve while improving outcomes, and they can advocate for the additional resources needed.

Since hepatologists care for some of the sickest patients in the system, their role in documenting and managing chronic conditions is paramount to a system's success in value-based care. Hepatologists can expand their reach by:

- Advocating for improvement of coding specificity.
- Participating in quality improvement work.
- Supporting efforts to create a shift in the cost curve for their high-risk patients.

By highlighting how they can shift the cost curve while improving outcomes, they can advocate for the additional resources needed to care for this high-risk population and can have the opportunity to show the return on investment. With this outlook, hepatologists who "engage" rather than "react" can make a real impact on system leadership and play a key role in this dynamic health care landscape.

Read the full article in the September issue of Clinical Gastroenterology and Hepatology.

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AGA raises concerns about recent Executive Order

AGA is concerned by the Executive Order on Combating Race and Sex Stereotyping issued on Sept. 22, 2020. This order, while confirming that training of the federal workforce to create an inclusive workspace is beneficial, also leads to a misguided perception of the purpose and outcomes of this type of training. In addition, it may have unintended ramifications for institutions receiving federal research funding.

We believe it is critical and necessary to understand both the positive and negative realities of our nation's history, so that together we can forge forward into a brighter and more equitable future.

As highlighted in AGA's commentary published in Gastroenterology, AGA believes that equity is defined by fair treatment, access, opportunity, and advancement for all, acknowledging that there are historically underserved and underrepresented populations. Equity requires identifying and eliminating barriers that have created unbalanced conditions and prevented the full participation of some groups in order to provide equal opportunity for all groups.

By default, teaching and practicing equity, diversity, and inclusion aims not to place any group above or below any other group, or to create division. It rather seeks to achieve fairness and understanding, and to fully recognize the dignity of all groups, identities, and individuals.

AGA stands with the AAMC in our commitment to being a diverse, inclusive, equitable, and anti-racist organization.

Our commitment to this issue is manifest in the AGA Equity Project.

ginews@gastro.org

Be among the first to commit to AGA Giving Day

Our patients face racial health disparities daily, leading to inequalities in care and poorer health outcomes. AGA is bringing together the GI community to fund health disparities research with the goal of improving care for the patients who rely on us.

At this important moment in history, the AGA Research Foundation is uniquely qualified to push forward innovative research in health disparities in gastroenterology. With donations to our new initiative called AGA Giving Day, we can provide researchers with a secure source of funding that helps understand the causes of known health disparities, understand why the disparity exists, and develop interventions to reduce and eliminate health disparities.

The AGA Research Foundation invites you to support AGA Giving Day today through Dec. 3. Contributors will be recognized as supporters of our fight to achieve equity and eradicate disparities in digestive diseases.

Learn more at gastro.org/aga-givingday.

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cosal surface morphology for diagnosis of early gastric cancer compared with HDWL, and a thorough examination of the surface characteristics is a prerequisite.[32] This classification was further validated in a randomized control trial, and NBI increased sensitivity for the diagnosis of neoplasia compared with HDWL (92% vs. 74%).[33] The majority of institutions in the United States have a newer-generation NBI (Olympus America, EVIS EXERA III video system, GIF-HQ190), which provides brighter endoscopic images to better characterize gastric neoplastic lesions. Once we recognize an area suspicious for neoplasia, we should describe the macroscopic features according to a classification system.

The Paris classification, one of the most widely recognized classification systems among U.S. gastroenterologists, is recommended for gastric neoplastic lesions.[34] Gastric neoplastic lesions with a "superficial" endoscopic appearance are classified as subtypes of "type 0." The term "type 0" was chosen to distinguish the classification of "superficial" lesions from the Borrmann classification for "advanced" gastric tumors, which includes types 1-4. In the classification, a neoplastic lesion is called "superficial" when its endoscopic appearance suggests that the depth of penetration in the digestive wall is not more than into the submucosa (i.e., there is no infiltration of the muscularis propria). The distinctive characters of polypoid and nonpolypoid lesions are summarized in Table 1. Endoscopic submucosal dissection (ESD) has steadily gained acceptance for the treatment of early gastric cancer in the United States. The American Gastroenterological Association recommended in the 2019 institutional updated clinical practice guideline that ESD should be considered the first-line therapy for visible, endoscopically resectable, superficial gastric neoplasia.[35] This recommendation is further supported by the published data on efficacy and safety of ESD for early gastric neoplasia in a large multicenter cohort in the United States.[36] For all suspicious lesions, irrespective of pathological neoplastic confirmation, referral to an experienced center for further evaluation and endoscopic management should be considered. Lastly, all patients with early gastric cancer should be evaluated for *H. pylori* infection and treated if the test is positive. Eradication of *H. pylori* is associated with a lower rate of metachronous gastric cancer,[37] and treatment of *H. pylori* as secondary prevention is also recommended.

Conclusion

As summarized above, cumulative epidemiologic data consistently demonstrate that the incidence of gastric cancer in the United States varies according to ethnicity, immigrant status, and country of origin. New gastroenterologists will need to recognize individual risk profiles and identify people at higher risk for gastric cancer. Risk stratification before performing endoscopic evaluation will improve early gastric cancer detection and make noninvasive, effective therapies an option.

See references at MDedge.com/gihepnews/new-gastroenterologist.

Effective even with comorbidities

Transplant *from page 1*

be cured with conventional treatments such as antibiotics, and can be deadly.

Transplanting fecal matter from a donor to the patient appears to work by restoring beneficial microorganisms to the patient's gut. The procedure is also under investigation for a wide range of other ailments, from irritable bowel syndrome to mood disorders.

But much remains unknown. Researchers have counted a thousand bacterial species along with viruses, bacteriophages, archaea, and fungi in the human gut that interact in complex ways, not all of them beneficial.

Almost all participants received stool from an unknown donor, mostly from stool banks, with OpenBiome accounting for 67%.

The FDA has not enforced regulations that would prohibit the procedure, but in March, it warned about infections with enteropathogenic *Escherichia coli* and Shiga toxin–producing *E. coli* following fecal transplants.

As a result of these reports, and the theoretical risk of spreading SARS-CoV-2, OpenBiome, the largest stool bank in the United States, has suspended shipments except for emergency orders, and asked clinicians to quarantine any of its products they already have on hand.

In the meantime, long-term effects of the treatment have not been well documented. And clinical trials have excluded patients who might benefit, such as those who have been immunocompromised or have inflammatory bowel disease.

National registry follows patients outside clinical trials

To better understand how patients fare outside these trials, the AGA and other organizations developed a national registry, funded by a grant from the National Institute of Allergy and Infectious Diseases.

The current report summarizes results on 259 patients enrolled between Dec. 5, 2017, and Sept. 2, 2019, at 20 sites.

At baseline, 44% of these patients suffered moderate and 36% mild *C. diff.* infections. The duration of the diagnosis ranged from less than 1 week to 9 years, with a median duration of 20 weeks. They ranged from 1 to 15 episodes with a mean of 3.5.

Almost all had received vancomycin, and 62% had at least two courses. About 40% had received metronidazole and 28% had received fidaxomicin.

Almost all participants received stool from an unknown donor, mostly from stool banks, with OpenBiome accounting for 67%. About 85% of the transplants were administered through colonoscopy and 6% by upper endoscopy.

Out of 222 patients who returned for a 1-month follow-up, 90% met the investigators' definition of cure:

Continued on following page

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resolution of diarrhea without need for further anti–*C. diff.* therapy. About 98% received only one transplant. An intent-to-treat analysis produced a cure rate of 86%.

Results were good in patients with comorbidities, including 12% who had irritable bowel syndrome, 9% who had ulcerative colitis, and 7% who had Crohn's disease, Dr. Kelly said. "I hope everybody sees the importance of it. In these patients that are more complicated, who may have underlying comorbidities, who may not have been in the clinical trials, it looks effective in that group, and also incredibly safe."

She added that the risk of transmitting SARS-CoV-2 is minor. "I think it would be a very, very unlikely way for someone to get a respiratory pathogen."

Of the 112 participants who were cured at 1 month and returned for follow-up after 6 months, 4 developed recurrent *C. diff.* infection. Eleven patients who were not cured in the first month returned after 6 months. Of these, seven were reported cured at this later follow-up.

Three complications occurred as result of the procedure: one colonoscopic perforation and two episodes of gastrointestinal bleeding.

About 45% of participants reported at least one symptom, with diarrhea not related to *C. difficile* the most common, followed by abdominal pain, bloating, and constipation.

Eleven patients suffered infections, including two which the investigators thought might be related to the procedure: *Bacteroides fragilis* in one participant with severe diarrhea, and enteropathogenic *E. coli* in another with loose stools. Other infections included four urinary tract infections, three cases of pneumonia, one *E. coli* bacteremia, and one tooth infection.

Within a month of the procedure, 27 patients were hospitalized, with 3 of these cases considered possibly related to the procedure.

Findings may not apply to all clinical settings

Vincent B. Young, MD, PhD, a professor of medicine and infectious diseases at the University of Michigan, Ann Arbor, pointed out that the findings might not apply to all clinical settings. The participating clinicians were almost all gastroenterologists working in academic centers.

"Most of them are not Joe Doctor at the doctor's office," said Dr. Young, who was not involved with the study. Clinicians in other specialties, such as infectious diseases, might be more inclined to administer fecal transplants through capsules rather than colonoscopies.

'In no way, shape, or form does it mean you can use it for autism, depression, heart disease, or [irritable bowel syndrome].'

And he added that the study does not address effects of the transplant that might develop over years. "Some people talk about how changes in the microbiota lead to increased risk for long-term complications, things like cancer or heart disease. You're not going to see those in 6 months."

Also, the study didn't yield any findings on indications other than *C. diff*. "In no way, shape, or form does it mean you can use it for autism, depression, heart disease, or [irritable bowel syndrome]," he said.

Still, he said, the study "confirms the fact that fecal cell transplantation is an effective treatment for recurrent *C. diff.* infection when administered as they administered it."

The National Institute of Allergy and Infectious Diseases funded the registry. Dr. Kelly reported a relationship with Finch Therapeutics. Dr. Young reports financial relationships with Vedanta Biosciences and Bio-K+.

A version of this article originally appeared on Medscape.com.

Can IBD be treated with diet alone?

IBD can be treated with diet alone

BY ASHWIN N. ANANTHAKRISHNAN, MD, MPH

Inflammatory bowel diseases (IBD), comprising Crohn's disease and ulcerative colitis, have emerged as global diseases. One potential reason for the rapid increase in incidence over the past 2 decades is in changing diet. Prospective cohorts studies have demonstrated that preillness dietary patterns may modify risk of Crohn's disease and ulcerative colitis independent of other known environmental risk factors. Mechanistically, diet may influence the development of intestinal inflammation (or relapses of established disease) through modifying the microbiome or the direct effect of dietary ligands on the intestinal barrier and immune response. Exclusive enteral nutrition was the first dietary therapy to be robustly supported by randomized controlled trial evidence for use in inducing remission, particularly in pediatric Crohn's disease. More recently, less restrictive dietary approaches have shown considerable promise, either by mimicking the effect of an elemental diet on the microbiome or through combining a partial elemental diet with an exclusion diet minimizing exposure to processed foods and other inciting triggers, and enriched in potentially helpful components such as soluble fiber. Such dietary therapies, which are more likely to be sustainable, offer attractive, safe, effective, and inexpensive solutions for the management of these complex disabling diseases.


Dr. Ananthakrishnan

Read more!
Please find full-length versions of these debates online at MDedge.com/gihepnews/perspectives.

Dr. Ananthakrishnan is a gastroenterologist in the division of gastroenterology, Crohn's and Colitis Center, Massachusetts General Hospital and Harvard Medical School, Boston. He is supported by funding from the Crohn's and Colitis Foundation and the Chleck Family Foundation.

No, IBD cannot be treated with diet alone!

BY LAURA RAFFALS, MD, MS

How often do we hear phrases such as "You are what you eat" or "Food is fuel for your body"? It stands to reason that the food we put into our bodies would in turn affect the health of our gut. Our patients with inflammatory bowel diseases (IBDs) are eager to learn how they can use their diet to treat their underlying disease. While it is well recognized by gastroenterologists that proper nutrition is important for the body to restore itself to health, many gastroenterologists are hesitant to go so far as to prescribe a specific diet for treatment of IBD. However, the majority of our patients believe that diet is important for the treatment of their underlying disease. As a result, patients seek dietary advice on social media platforms or from friends and family and will experiment with various diets hoping to find a diet that will make a difference for their IBD. While diet plays an important role in the overall health of our IBD patients, we must acknowledge that IBD cannot be treated with diet alone; at least, not yet.


Dr. Raffals

Dr. Raffals is a gastroenterologist in the division of gastroenterology and hepatology, Mayo Clinic, Rochester, Minn. She has no financial conflicts of interest relevant to this study.

Dear colleagues and friends,

Thank you for your continued interest and support of the Perspectives debates.

In this edition, Dr. Ashwin N. Ananthakrishnan and Dr. Laura Raffals explore the controversial topic of diet-based therapy in inflammatory bowel diseases, highlighting the rationales for and against, and the current state of the evidence. All gastroenterologists frequently face questions pertaining to diet, and its purported effects on digestive health.

I found the discussion relevant to my own general practice, and I hope you will enjoy reading it as much as I did. As always, I welcome your comments and suggestions for future topics at ginews@gastro.org.

Charles J. Kahi, MD, MS, AGAF, professor of medicine, Indiana University School of Medicine, Indianapolis, is an Associate Editor for GI & Hepatology News.


Dr. Kahi

CDC guidance on rolling out vaccine, status of physician income

BY LUCAS FRANKI
MDedge News

CDC releases guidance for states' plans for potential future COVID-19 vaccine rollout

The Centers for Disease Control and Prevention has released a document, "COVID-19 Vaccination Program Interim Playbook for Jurisdiction Operations," to act as a guide for states to create a rollout plan for COVID-19 vaccines, should one be approved.

The CDC issued a deadline of Oct. 16 for states to submit their plan, a date that met with criticism with the Advisory Committee on Immunization Practices during a Sept. 22 meeting, as final storage requirements or optimal population would not be known by that time.

The CDC noted that states should use their best possible assumptions when making their plans, and that the guidance is a living document and will be updated as more information about potential vaccines is released.

Income for physicians drops, burnout grows

A survey of more than 7,500 physician across eight countries shows that the COVID-19 pandemic has had a significant effect on their personal and professional lives.

In the United States, 62% of physicians reported a drop in income; just over half of those who had salaries cut reported a drop of more than 25%, and nearly one-quarter reported a drop of more than 50%.

Burnout was also high among U.S. physicians, with 64% reporting that burnout had intensified over the course of the pandemic. Nearly half of U.S. physicians reported increased loneliness.

New billing code for added COVID-19 practice expense

There is a new billing code for extra practice expenses required to care for patients during the COVID-19 pandemic, according to an announcement from the American Medical Association.

The code, 99072, will cover supplies, materials, and clinical staff time over and above those usually included in an office visit when performed during a declared public health emergency, attributable to respiratory-transmitted infectious disease.

Frontline associate editor Lucas Franki compiled this column from reports first published on MDedge.com and Medscape.com.

Colonoscopy patients may get hit with a 'surprise' bill

BY ROXANNE NELSON, RN, BSN

A colonoscopy screening for colorectal cancer should be covered by commercial health insurance, but a new study reports that some patients receive a "surprise" bill.

The study was published online Oct. 13 as a research letter in Annals of Internal Medicine.

Nearly one in eight commercially insured patients who had an elective colonoscopy between 2012 and 2017 received an out-of-network bill, resulting in hundreds of dollars more than the typical insurance payment.

The median surprise bill was $418 (range $152-$981).

The findings are "disconcerting" say the authors, "because Section 2713 of the Patient Protection and Affordable Care Act eliminates consumer cost sharing for screening colonoscopy, and because a recent Federal Reserve study reported that 40% of Americans do not have $400 to cover unnecessary expenses."

Most of these surprise costs were incurred from the use of out-of network anesthesiologists and pathologists, the authors note.

"Doctors need to be aware of these out-of-network bills so that patients know what to expect when they undergo these screening procedures," said study author Karan R. Chhabra, MD, MSc, a resident in general surgery at Brigham and Women's Hospital, Boston. "Ideally, they should do their colonoscopies at facilities where all providers participate in the same major insurance plans."

"If gastroenterologists own their endoscopy facility, this is an obvious situation in which they should not be working with anesthesiologists or pathologists who are not in the same networks as them," he told this news organization. "And as we point out in our paper, anesthesiology and pathology review are not necessary in every single case – endoscopists can perform their own sedation, and in certain settings, lesions can be discarded without pathological examination."

But is it really that simple for physicians to make sure that all members of the team are in network?

It's not simple at all, and in fact it's a rather dif-

Continued on following page

Endoscopist risk tolerance has role

Test *from page 1*

cerns, the panelists concluded that pretesting strategies should be tailored to the local prevalence of asymptomatic infection because this rate is associated with likelihood of encountering false-positive and false-negative patients.

To determine appropriate prevalence thresholds, Dr. Sultan and colleagues first conducted a meta-analysis of 12 studies comparing the accuracy of various NAAT tests. This revealed a pooled sensitivity of 0.941 and a pooled specificity of 0.971. These figures remained consistent when only studies with low risk bias were considered; pooled sensitivity and specificity were 0.929 and 0.968, respectively.

"An important caveat of these studies is that tests were validated in samples from symptomatic individuals and it is likely that in asymptomatic individuals the tests may not perform as well and have lower sensitivity and specificity," the panelists noted.

Next, Dr. Sultan and colleagues conducted an online survey of U.S. endoscopists to determine their tolerance for risk of coronavirus transmission, with proposed risk thresholds ranging from 1/40,000 to 1/1,000. Out of 74 respondents, 28 (37.8%) said that they would be willing to accept a risk level of 1/40,000, whereas 27 (36.5%) would accept risks between 1/10,000 and 1/2,500, and 19 (25.7%) would accept a risk level of 1/1,000. Among clinicians expressing the highest risk tolerance (1/1,000), almost two-thirds (63.2%) were private practitioners.

Drawing on these findings, the panelists issued three tiered recommendations for pretesting based on local prevalence of asymptomatic infection.

- Low prevalence (less than 0.5%): Pretesting is not recommended.
- Intermediate prevalence (0.5-2%): Pretesting is recommended.
- High prevalence (greater than 2%): Pretesting is not recommended.

The panelists recommended against pretesting in low and high prevalence settings because of the likelihood of false positives and false negatives, respectively. For "hotspot" areas, in which hospital capacity is acutely burdened, the panelists noted that "resumption of outpatient endoscopy may depend on PPE [personal protective equipment] availability."

In areas of intermediate prevalence, the pretesting recommendation stands only if "testing is feasible and there is less perceived burden on patients, and when the benefits outweigh the downsides (e.g., false positives do not significantly outnumber the true positives)." According to the guidance, when upper and lower endoscopies are performed on negative patients in areas of intermediate prevalence, surgical masks are appropriate for endoscopists and staff, with the caveat that those unwilling to accept any increased risk may still wear an N95/N99 respirator or a powered air-purifying respirator.

The panelists recommended against pretesting in low and high prevalence settings because of the likelihood of false positives and false negatives, respectively.

Finally, the panelists made a recommendation against pretesting for antibodies in all areas, regardless of asymptomatic infection prevalence.

All recommendations were based on low- or very low–certainty evidence.

To help endoscopy centers determine an appropriate pretesting strategy, the AGA has created an online interactive tool that allows for input of diagnostic test accuracy and local prevalence rate. Instructions for using the tool, along with additional COVID-19 guidance, can be found on the AGA website: www.gastro.org/COVID.

The investigators reported no conflicts of interest.

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SOURCE: Sultan S et al. Gastroenterology. 2020 Jul 28. doi: 10.1053/j.gastro.2020.07.043.

Continued from previous page

ficult task, said Glenn Melnick, PhD, professor and chair in health care finance at the University of Southern California and director of USC's Center for Health Financing, Policy, and Management in Los Angeles.

"It would be really difficult for Dr. Smith to know that Dr. Jones is out of network, so it's really hard to hold the doctors responsible," Dr. Melnick said. "There are so many insurers and it may be difficult to know who is in network and who isn't."

In this study, anesthesiologists and pathologists were a source of surprise bills, and they are behind the scenes, he pointed out. "The patient doesn't select them directly and there is no opportunity to even find out who they are," said Dr. Melnick.

"The health plan could bear some responsibility here," Dr. Melnick commented, although he added that patients need to be informed. Patients who are undergoing an elective procedure should be told that other doctors may be involved, and then to ask if these doctors are in the network. "If enough patients do this, maybe then the gastroenterologist will use people in network," he commented.

Details of the surprise bills

Federal regulations eliminate consumer cost-sharing when screening colonoscopies are performed in network, but there are no stipulations regarding expenses when out-of-network providers are used, the authors note.

To investigate this issue, the authors used a claims database from a large national insurer and identified patients aged 18-64 years who had undergone colonoscopy between 2012 and 2017.

The analysis was limited to cases where both the facility and the endoscopist were in network, and the colonoscopies were stratified into those with visual inspection only and those during which an intervention was done, such as a biopsy. The primary outcome measure was the prevalence of out-of-network claims when the endoscopist and facility were in network, and the secondary outcome was the amount of the potential surprise bills, which were calculated as the total out-of-network charges less the typical in-network price.

A total of 1,118,769 elective colonoscopies with in-network endoscopists and facilities were identified and of these, 12.1% (n = 135,626) were involved with out-of-network claims. Out-of network anesthesiologists accounted for 64% of cases (median potential surprise bill, $488), while out-of-network pathologists were involved in 40% of cases (median potential surprise bill, $248). The likelihood of receiving an out-of-network claim was significantly higher if an intervention was performed during colonoscopy, as compared with those without intervention (13.9% vs. 8.2%; difference, 5.7%).

AGA Resource

AGA believes that patients should be incentivized, through the elimination of cost sharing, to use colonoscopy as a colorectal cancer screening mechanism. Learn more about how AGA advocates for patients at http://ow.ly/ULCZ30rf6J8.

The authors suggest that measures that can be taken to avoid surprise bills include having endoscopists and hospitals partner with anesthesia and pathology providers who are in network.

"Providers must realize many of our patients are at risk for considerable balance bills, and therefore they should provide resources that can provide reliable estimates for out-of-pocket costs relevant to site of service," said lead author James Scheiman, MD, AGAF, a professor of medicine at the University of Virginia School of Medicine in Charlottesville.

The study was funded by the University of Michigan. Dr. Chhabra reports personal fees from Blue Cross Blue Shield of Massachusetts. Dr. Scheiman and Dr. Melnick have no disclosures.

A version of this article originally appeared on Medscape.com.

GIs among the most likely to adopt telemedicine

BY JIM KLING
MDedge News

It's no secret that the COVID-19 pandemic has disrupted medical practice and led to a surge in telemedicine visits. A new report issued by the health care social network Doximity in September predicts that these changes will be permanent, and that the telehealth industry will more than triple from $29 billion at the end of this year to about $106 billion by 2023.

The report, titled "2020 State of Telemedicine," follows a similar 2019 publication and captures the changes created by the pandemic. "Obviously, telemedicine has been around for many years, but the pandemic around COVID-19 has really changed the game. Something that had been getting gradual adoption really rocketed to the forefront," said Peter Alparin, MD, who is an internist in San Francisco and vice president of product at Doximity, in an interview. The report predicts that 20% of medical visits will be conducted through telemedicine by the end of 2020.

Gastroenterology is one of the top specialties to adopt telemedicine, ranking third behind endocrinology and rheumatology, and that should come as no surprise. "Chronic disease patients lend themselves well to telemedicine because they have ongoing relationships with their physicians, so they can be seen more often and it's more convenient for them. The specialties that take care of patients with those sorts of illnesses were the ones that adopted it the most readily," said Dr. Alparin.

'Chronic disease patients lend themselves well to telemedicine because they have ongoing relationships with their physicians.'

That's probably in part because specialists dealing with chronic conditions have been triaging patients with telephone calls for years, which makes it easier to tell when a patient needs to come in for a physical visit. "It's a skill you learn, to tell when something is just a little bit different for a patient. It's really a clinical judgment that has been honed over years of experience," said Dr. Alparin. The report backs up that idea, as it found that the physician age groups that most often adopted telemedicine were those in their 40s, 50s, and 60s.

Telemedicine is popular with patients once they try it, and it can greatly expand a physician's reach, according to Dr. Alparin. "If you're a specialist, you can perhaps see patients in areas where that specialty is underrepresented, whether that's the inner city or a very rural area," he said. The most important barrier is high-speed Internet access, which remains a problem in many areas.

Doximity researchers surveyed more than 2,000 U.S. adults to get their opinions on telemedicine, and analyzed telemedicine adoption data from the platform's own set of telemedicine tools, and compared it to data from the 2019 report. They also reviewed studies looking at disparities in medicine and patient access to telemedicine.

Telemedicine use among patients grew from 14% before the pandemic to 35% who reported at least one telemedicine visit after COVID-19. A total of 23% said they planned to continue use of telemedicine after the pandemic ends, and 27% said they had become more comfortable using telemedicine. Among patients, 28% said telemedicine provides the same or better benefit as an in-person visit, and this rose to 53% among those with chronic illnesses.

Among physicians, telemedicine adoption rose by 20% between 2015 and 2018, but increased by 38% between 2019 and 2020. The highest percentage of physician telemedicine adopters were in large metro areas and East Coast states, led by Massachusetts, New Jersey, and North Carolina. None of the top 10 adopter states were west of Illinois.

Equity concerns remain: 64.3% of households with annual incomes of $25,000 or lower have access to broadband Internet, compared with 93.5% of those with incomes of $50,000 or lower. In nonmetropolitan areas, 78.1% of households have access, compared with 86.7% of metropolitan households. The good news is that many patients prefer cell phone use for telemedicine, and nearly as many Black and Hispanic Americans own cell phones as White Americans. "That has really democratized access," said Dr. Alperin.

A key to successful telemedicine appointments is to make sure that the patient is prepared, according to Dr. Alparin. Make sure the patient is in a relatively quiet, well-lit place, and that they have thought about the questions they want to ask. It's possible to replicate some aspects of a physical appointment with the right conditions. "You can visualize how they move their arms and legs; you can see how they're breathing. You can gain a lot of information by just watching somebody," said Dr. Alparin. A physician might also spot clues in the patient's surroundings. "If a patient is asthmatic and you see cats walking all over the place, or a patient is allergic to gluten and they have loaves of bread everywhere," he added.

A big concern for telemedicine has been reimbursement. In response to the pandemic, the Centers for Medicare & Medicaid Services created a number of waivers to requirements for billing for telemedicine services, and private insurers followed suit. In August, the agency announced it would make some of those waivers permanent, though others such as removal of restrictions on the site of care, eligible providers, and nonrural areas will likely require an act of Congress to enshrine, CMS administrator Seema Verma told reporters at an August press conference.

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SOURCE: 2020 State of Telemedicine Report.

The COVID-19 pandemic has emphasized the importance of social determinants of health. Historically underserved populations in the United States – particularly African American, Hispanic/Latino, and Native American – have been disproportionately affected, suffering from higher hospitalization rates and worsened morbidity/mortality related to the disease. Telemedicine feels like it should be the great equalizer of access in this time of national and personal stress, a technological solution that aspires for a universal reach. However, early lessons in the pandemic inform us that this is not inherently guaranteed. A review of access metrics in the Duke University Liver Clinic during the pandemic finds disparities in overall use and suboptimal use (phone versus video) for vulnerable populations, including older patients, underserved minorities, and those on Medicaid/Medicare insurance.


Dr. Patel

Though a phone visit is better than no visit, a video visit may be considered ideal for certain disease states such as cirrhosis, where exam findings such as jaundice, muscle wasting, and edema/ascites can be evaluated. Our experience underscores disparities in digital literacy or access that likely are at play throughout our country. As telemedicine becomes a staple of GI and liver chronic disease care, proactive methods are needed by health providers to ensure equitable access. This may include advocating for reduced-cost internet, education outreach for digital skills, ensuring adequate language interpreter access, and monitoring access metrics.

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Trump signs CR with Medicare loan relief

President Trump on Oct. 1 signed a bill to keep the federal government running through Dec. 11. This "continuing resolution" (CR), which was approved by the House by a 359-57 vote and the Senate by a 84-10 vote, includes provisions to delay repayment by physicians of pandemic-related Medicare loans and to reduce the loans' interest rate.

In an earlier news release, the American Medical Association reported that Congress and the White House had agreed to include the provisions on Medicare loans in the CR.

Under Medicare's Accelerated and Advance Payments (AAP) Program, the Centers for Medicare & Medicaid Services (CMS) advanced funds to physicians who were financially impacted by the pandemic. Revisions were made under the Coronavirus Aid, Relief, and Economic Security (CARES) Act to broaden the existing program to supply provider relief related to the public health emergency. The program was revised in March but suspended accepting new applications related to the pandemic in late April.

Physicians who received APP loans were required to begin repayment within 120 days after the loan disbursement. CMS planned to recoup the advances by offsetting them against Medicare claims payments due to physicians. Practices had up to 210 days (7 months) to repay the loans through this process before being asked to repay them directly with a 10.25 % interest rate.

For practices that received these advances, their Medicare cash flow was scheduled to dry up, starting in August. However, CMS quietly abstained from collecting these payments when they came due, according to Modern Healthcare.

New terms

Under the new loan repayment terms in the CR, repayment of the disbursed funds is postponed until 365 days after the date on which a practice received the money. The balance is due by September 2022.

The amount to be recouped from each claim is reduced from 100% to 25% of the claim for the first 11 months and to 50% of claims withheld for an additional 6 months. If the loan is not repaid in full by then, the provider must pay the balance with an interest rate of 4%.

More than 80% of the $100 billion that CMS loaned to health care providers through May 2 went to hospitals, Modern Healthcare calculated. Of the remainder, specialty or multispecialty practices received $3.5 billion, internal medicine specialists got $24 million, family physicians were loaned $15 million, and federally qualified health centers received $20 million.

In the AMA's news release, AMA President Susan Bailey, MD, who assumed the post in June, called the original loan repayment plan an "economic sword hanging over physician practices."

The American Gastroenterological Association has been advocating for more flexibility for the financial assistance programs, such as the Accelerated and Advanced Payment Program and the Paycheck Protection Program, that physicians have utilized. It is critical to give physicians leeway on these loans given that many practices are still not operating at full capacity.

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