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Courtesy Dr. Lisa A. Boardman

Dr. Lisa A. Boardman, of Mayo Clinic, Rochester, Minn., said that newly diagnosed patients should be counseled about genetic testing.

AGA Clinical Practice Update

Young adult–onset CRC diagnosis, management

BY AMY KARON
MDedge News

The rising incidence of colorectal cancer in adults younger than 50 years heightens the need to evaluate the colon and rectum of any patient, regardless of age, who presents with symptoms such as rectal bleeding, weight loss, abdominal pain, iron-deficiency anemia, or changes in bowel habits, according to a new American Gastroenterological Association clinical practice update.

In addition to receiving cancer staging or being referred to an oncologist, newly diagnosed patients should be counseled about both germline genetic testing and fertility preservation, wrote Lisa A. Boardman, MD, of Mayo Clinic in Rochester, Minn., with associates in Clinical Gastroenterology and Hepatology. "Clinicians should present the role of fertility preservation prior to [administering] cancer-directed therapy, including surgery, pelvic radiation, or chemotherapy."

It remains unclear why the incidence of young

See **CRC** · *page 18*

Pandemic worsens disparities in GI and liver disease

Screenings, procedures are down.

BY WILL PASS
MDedge News

FROM THE AGA FORWARD PROGRAM

Suspension of disease screening and nonurgent procedures because of the COVID-19 pandemic will negatively impact long-term outcomes of GI and liver disease, and people of color will be disproportionately affected, according to a leading expert.

Novel, multipronged approaches are needed to overcome widening disparities in gastroenterology and hepatology, said Rachel B. Issaka, MD, of Fred Hutchinson Cancer Research Center in Seattle.

"The COVID-19 pandemic has led to unprecedented drops in breast, colorectal, and cervical cancer screenings," Dr. Issaka said during an AGA FORWARD Program webinar. Screening rates for these diseases are down 83%-90%, she said.

"Certainly this creates a backlog of cancer screenings that need to occur, which poses very significant challenges for health systems as they're adapting to this new state of health care that we have to provide," Dr. Issaka said.

During her presentation, Dr. Issaka first addressed

See **Disparities** · *page 24*

Tools predict liver failure in cirrhosis

BY INGRID HEIN

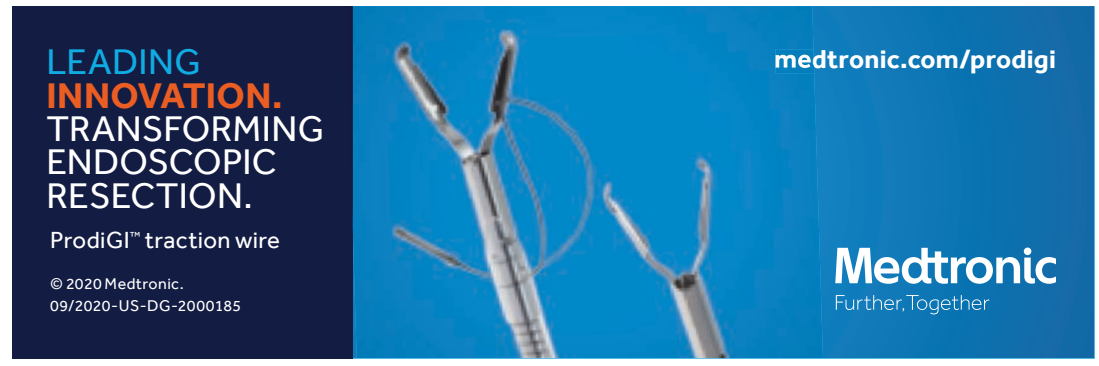
Systemic inflammation and portal hypertension are key predictors of acute-on-chronic liver failure (ACLF) in the 3 months after a hospital stay for acute decompensated cirrhosis and also of death after 12 months, a preliminary analysis of data from the PREDICT study shows.

"Before this, we never had any patient signatures to identify ACLF," said Jonel Trebicka, MD, PhD, from the University Hospital Frankfurt (Germany).

Now, Dr. Trebicka's team has "characterized the phenotypes in pre-ACLF that will progress within 3 months," he said in an interview. "Those with high levels of inflammatory proteins, white blood cell count, are more likely to develop ACLF."

See **Cirrhosis** · *page 20*

INSIDE



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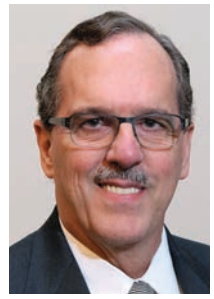
LETTER FROM THE EDITOR

Despite overall exhaustion, health care workers continue on

I write this editorial in mid-September. Fires (and ash) are devastating the West and multiple hurricanes are pummeling the Gulf Coast states. We are struggling to admit how our democracy has systematically failed so many people and learn how we might rectify past inequities and abuses so we can create a better future together. All this with the backdrop of COVID-19, as we pass 200,000 American deaths. We will figure this out and be stronger, but for now it is exhausting, and many people are suffering.


Dr. Allen

The year 2020 will change gastroenterology forever. The economic fallout already has accelerated the disappearance of traditional medical practices, whose finances were based on steady cash flow. Medicaid rolls will increase from 70 million to over 80 million next year, putting State budgets in deficit and likely altering enrollment requirements. Currently, only half of Baby Boomers are enrolled in Medicare, a statistic that will change with loss of employment and early retirements. Many Americans are losing their employer-based insurance and shifting to government-based insurance (or losing insurance entirely). Providers will face enormous financial headwinds for years no matter how rapidly our economy recovers.

But not all news is bad. We can still read how scientific knowledge continues to progress (our issue this month is rich with examples). Our responses to COVID-19 have been breath-taking in their speed. The death rate per hospitalized patient has fallen dramatically, we continue to learn how to mitigate the effects of COVID-19, and we anticipate a vaccine in record time compared with past epidemics. Physicians and other health care providers are demonstrating daily their dedication to patients despite physical, emotional, and mental exhaustion.

I have no glib answers or words of advice. But I continue to be optimistic. In a nonpartisan tone, I quote Bill Clinton's 1993 inaugural address: "There is nothing wrong with America that cannot be cured by what is right with America."

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

DDSEP 9
Digestive Diseases Self-Education Program

Quick quiz

Q1. A 19-year-old male with elevated liver enzymes is found to have a serum ceruloplasmin of 3 mg/L, and a urine copper excretion of 210 mcg/24 hours. He is started on trientine to treat his illness.

What level of urine copper is the goal of this therapy?
A. No urine copper should be found if therapy is effective
B. Urine copper should be 200-500 mcg/24 hours
C. Urine copper should be 500-1,000 mcg/24 hours
D. Urine copper should be 1000-1,500 mcg/24 hours
E. Urine copper should be more than 1,500 mcg/24 hours

Q2. A 65-year-old woman with primary biliary cholangitis is seen for a clinic visit. She reports increasing shortness of breath with her usual activities and can barely walk one flight of steps. She does not smoke. On examination her vitals and weight are stable. She has jaundice and no asterixis. She takes diuretics and lactulose.

What is the most likely diagnosis that would potentially preclude her from liver transplantation?
A. Hepatopulmonary syndrome
B. Large hepatic hydrothorax
C. Pulmonary embolism
D. Pneumonia
E. Portopulmonary hypertension

The answers are on page 16.

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References: 1. IQVIA. National Prescription Audit Report. September 2018. **2.** Rex DK, DiPalma JA, Rodriguez R, McGowan J, Cleveland M. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc.* 2010;72(2):328-336. **3.** SUPREP Bowel Prep Kit [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2017. **4.** Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc.* 2015;81(1):31-53.

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HH27314A September 2018

Bariatric surgery resolved NASH long term

BY AMY KARON
MDedge News

Bariatric surgery resolved nonalcoholic steatohepatitis (NASH) without worsening fibrosis in 84% of patients with follow-up biopsies, according to the findings of a prospective study.

The study included 180 severely or morbidly obese adults (body mass index > 35 kg/m^2) with NASH who underwent bariatric surgery at a center in France. Among 94 patients evaluated 5 years later, 68% had follow-up liver biopsies, of whom 84% (95% confidence interval, 73.1%-92.2%) met the primary endpoint of resolution of NASH without worsening of fibrosis. All histologic aspects of NASH had improved, median nonalcoholic fatty liver disease scores (NAS) fell from 5 (interquartile range, 4-5) to 1 (IQR, 0-2; $P < .001$), and 90% of patients achieved at least a 2-point NAS improvement. Hepatocellular ballooning also improved in 87.5% of patients. Baseline severity of NASH did not affect the chances of its resolving at 5 years. "The reduction of fibrosis [was] progressive, beginning during the first year and continuing through 5 years," Guillaume Lassailly, MD, and associates wrote in Gastroenterology.

NASH is a priority for clinical research because of the substantial risk for subsequent cirrhosis, added Dr. Lassailly of CHU Lille (France). For NASH to resolve, most patients need to lose at least 7%-10% of their body weight, but "only 10% of patients reach this objective with lifestyle therapy at 1 year, and less than half maintain the weight loss 5 years later." Despite ongoing drug development efforts, no medications have been approved for treating NASH. Although weight loss after bariatric surgery has been reported to resolve NASH in approximately 80% of patients at 1 year, longer-term data have been unavailable, and it has remained unclear whether bariatric surgery can slow or halt fibrosis progression.

All patients in this study had biopsy-confirmed NASH and at least a 5-year history of morbid obesity (BMI > 40) or severe obesity (BMI > 35) with at least one comorbidity, such as diabetes mellitus or arterial hypertension. Patients were not heavy drinkers, and none had detectable markers of chronic liver disease.

Bariatric surgery produced a median 12-kg/m^2 drop in body mass index. At 5-year follow-up, 93% of patients meeting or exceeding this threshold who had biopsies performed showed resolution of NASH without worsening of fibrosis. Furthermore, 56% of patients (95% CI, 42.4%-69.3%) had no histologic evidence of fibrosis, including 45.5% of patients who had bridging fibrosis at baseline.

Participants in this study received

Continued on following page

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SUPREP® Bowel Prep Kit (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution is an osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults. Most common adverse reactions (>2%) are overall discomfort, abdominal distention, abdominal pain, nausea, vomiting and headache.

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Lusutrombopag found safe, effective for severe thrombocytopenia in patients with HCC

BY AMY KARON
MDedge News

For patients with severe thrombocytopenia and chronic liver diseases, including hepatocellular carcinoma (HCC), treatment with lusutrombopag prior to invasive procedures significantly decreased the need for platelet transfusions without increasing the need for rescue treatment for bleeding or the rate of thromboembolic events.

In a post hoc analysis of data from 270 patients in two manufacturer-sponsored, multicenter, randomized, double-blind, placebo-controlled, phase 3 trials, significantly more lusutrombopag recipients met the primary efficacy endpoint, including patients with HCC (68.0% vs. 8.9% in the placebo group; $P < .0001$) and those without it (77.0% vs. 21.6%; $P < .0001$). Rates of treatment-emergent adverse events were similar between the lusutrombopag and placebo groups, and patients with HCC were not at increased risk for thrombosis, Naim Alkhouri, MD, of Texas Liver Institute in San Antonio, and associates wrote in Clinical Gastroenterology and Hepatology.

Platelet transfusion is the treatment mainstay for patients with thrombocytopenia related to cirrhosis who are undergoing invasive procedures, but its effects are short-lived, and at least one in five transfusions fails. Thrombopoietin agonists such as lusutrombopag are efficacious and approved in this setting, but they can be prothrombotic, particularly in patients with HCC, who already are at heightened risk for portal vein thrombosis.

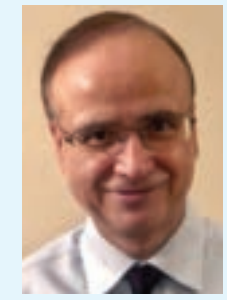
Dr. Alkhouri and associates performed an integrated analysis of the PLUS 1 trial (Japan, October 2013–May 2014) and the L-PLUS 2 (global, June 2015–April 2017). Participants were adults with Child-Pugh Class A or B chronic liver disease and baseline platelet counts under 50 x 10^9 per L who were scheduled for invasive procedures. Of the 270 patients, 95 had HCC. Patients were randomly assigned on a one-to-one basis to receive either lusutrombopag (3 mg) or placebo daily for up to 7 days before procedures. The primary endpoint was the percentage of patients in the per-protocol population who did not need a platelet transfusion before the invasive procedure or rescue therapy within 7 days afterward.

Continued on page 10

Thrombocytopenia is of clinical concern in patients with cirrhosis, as it complicates routine patient care and results in delayed or canceled procedures because of risk of bleeding. In the last few years, thrombopoietin (TPO) receptor agonists have facilitated the performance of elective invasive procedures in cirrhotic patients with severe thrombocytopenia.

These agents have reduced the risk of procedure related bleeding and need for platelet transfusions. However, thrombotic events remain a key safety concern with the use of TPO receptor agonists, particularly in patients with HCC, who are at increased risk for spontaneous thrombosis.

In this integrated analysis of data from two phase 3 studies, Alkhouri et al. demonstrated the efficacy of a novel TPO receptor agonist, lusutrombopag, in reducing bleeding events and need for platelet transfusion in cirrhotic patients undergoing invasive procedures. The risk for thrombosis-related adverse events was not increased in lusutrombopag recipients with or without HCC. Previous studies with another TPO, eltrombopag, resulted in high rate of symptomatic portal vein thrombosis. Avatrombopag, a recently approved TPO receptor agonist reported few thrombotic symptomatic events but no prospective imaging for evaluation of thrombotic events was included in the protocol. A unique strength of this study was inclusion of prospective imaging for evaluation of portal vein thrombosis. Lusutrombopag can be given orally in convenient daily doses and provides a 7-10-day procedural window for performing elective invasive procedures. However, because of several days of lag period for platelet production, these agents cannot be used for emergent cases.


Dr. Sood

Gagan K. Sood, MD, AGAF, is an associate professor of medicine and surgery, division of gastroenterology and hepatology and division of abdominal transplantation, Baylor College of Medicine, Houston. He has no conflicts of interest.

Continued from previous page

intensive preoperative support, including evaluations by numerous specialists, a nutrition plan, and a 6- to 12-month therapeutic education program. Bariatric surgery techniques included Roux-en-Y gastric bypass, gastric banding, and sleeve gastrectomy. A subgroup analysis linked gastric bypass to a significantly higher probability of meeting the primary endpoint, compared with gastric banding. Refusal was the most common reason for not having a follow-up biopsy, the researchers said. "Patients without liver biopsy after bariatric surgery were not significantly different from those with a histological follow-up except for a lower BMI at 1 year. Baseline fibrosis did not influence the probability of undergoing histological reevaluation at 5 years."

Two study participants died from surgical complications within 1 month after surgery, and one patient died from cardiac dysfunction 4 years later. No fatality was deemed liver related.

The study was funded by the French Ministry of Health, Conseil Régional Nord-Pas de Calais, National de la Recherche, and the European commission (FEDER). The researchers reported having no conflicts of interest.

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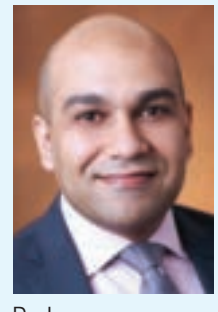
SOURCE: Lassailly G et al. Gastroenterology. 2020 Jun 15. doi: 10.1053/j.gastro.2020.06.006.

As obesity prevalence increases at an alarming pace, nonalcoholic steatohepatitis (NASH) has become the most common indication for liver transplantation in women and the second most common in men in the United States. Impeding the inflammation and reversing the resultant fibrosis prior to the development of end-stage liver disease and needing liver transplantation are essential goals in NASH management. The lack of Food and Drug Administration–approved pharmacotherapy triggered interest in the effect of weight loss on NASH and short-term benefits were noted. In this article, Lassailly et al. demonstrated long-term benefits of bariatric surgery in patients with NASH. They prospectively enrolled 180 patients and histologically followed 64 patients at 1 year and 5 years postoperatively. NASH resolved in 84% of patients and fibrosis regressed in >70%. Importantly, advanced fibrosis (F3) regressed in 15/19 patients. Cirrhosis regressed to F3 in two-thirds of patients. No liver-related mortality or decompensation was observed. These favorable outcomes embolden the practice of referring NASH patients with morbid obesity to bariatric surgery before liver disease severity becomes prohibitive of this approach. NASH pharmacotherapy may become available in the future. However, we must not forget that cardiovascular disease remains a common cause of morbidity and mortality in NASH patients. With these study findings and previously established benefits of bariatric surgery on mitigating cardiovascular risk and treating relevant metabolic derangements (e.g., diabetes mellitus), early consideration of bariatric surgery, when indicated, in obese NASH patients may have widespread later benefits including resolution of NASH, prevention of cardiovascular disease, metabolic optimization, and potentially longer and healthier life.


Dr. Izzy

Manhal J. Izzy, MD, is assistant professor of medicine, Vanderbilt Digestive Disease Center, Vanderbilt University, Nashville, Tenn. He has no conflicts of interest.

Scoring system identified patients with suspected small-bowel bleeding

BY AMY KARON
MDedge News

For patients with suspected small-bowel bleeding, a three-variable scoring system predicted the diagnostic outcomes of video capsule endoscopy, according to the findings of a multicenter study.

"Admission to the hospital with overt bleeding and having a hemoglobin [level] of less than 6.4 g/dL were two positive predictors of a diagnosis. Being younger than 54 years old at the time of the video capsule endoscopy (VCE) exam was a significant negative predictor of a diagnosis," Neil B. Marya, MD, of the University of California, Los Angeles, and associates wrote in Techniques and Innovations in Gastrointestinal Endoscopy.

To develop the scoring system, they analyzed retrospective data from 162 adults with suspected small-bowel bleeding who received VCEs at the University of Massachusetts or the University of California, Los Angeles, in 2016 or 2017. Most of these individuals were outpatients with occult gastrointestinal bleeding, but nearly one-third were inpatients with overt bleeding.

In all, 70 (43%) patients had a relevant finding on VCE, most frequently arteriovenous malformation (26%), blood (10.5%), or ulceration (10.5%). On multivariable analysis, the odds of positive VCE were significantly higher when patients had been admitted to the hospital with overt bleeding (adjusted odds ratio, 2.38; 95% confidence interval, 1.05-5.39) or had a baseline hemoglobin level less than or equal to 6.4 g/dL (aOR, 2.68; 95% CI, 1.11-6.48). In contrast, patients who were younger than 54 years were significantly less likely to have diagnostic lesions (aOR, 0.25; 95% CI, 0.11-0.58). After designating these variables as A, B, and C, respectively, the researchers derived the following equation to produce the score: (0.87 x A) + (0.99 x B) – (1.38 x C). Each variable was scored as 1 (present) or 0 (absent). Based on this equation, the highest score possible score was 1.86, and the lowest possible score was –1.38.

The researchers validated this scoring system by analyzing data from 152 adults with suspected small-bowel bleeding who were examined prospectively at the two centers. The development and validation cohorts resembled each other except that the validation cohort had lower mean hemoglobin levels (8.2 g/dL versus 9.0 g/dL in the development cohort; $P < .01$) and higher mean blood urea nitrogen levels (25.3 mg/dL vs. 19.9 mg per dL; $P = .03$). Receiver operating curves were similar between the two groups (respective C-statistics, 0.70 and 0.69; $P = .91$).

However, the scoring system's maximum specificity was only 30.6%, yielding a positive predictive value of only 48.6%. The associated cutoff score was greater than or equal to 0. At this cutoff, sensitivity was "at least 90%," and negative predictive value was 83.6%. Thus, the scoring system is best suited for identifying patients who are unlikely to have a diagnostic lesion found on VCE, the researchers said.

"Patients with scores of less than 0 could conceivably have capsule examinations deferred," they concluded. "Consider a clinician taking care of a hospitalized patient who meets criteria for undergoing [VCE] for the indication of suspected small intestinal bleeding, but finds that the patient has a ... diagnosis score of less than 0. The clinician could decide to have their patient undergo the [VCE] as an outpatient, since the likelihood of detecting an actionable lesion is low. This decision could have a [beneficial] financial impact."

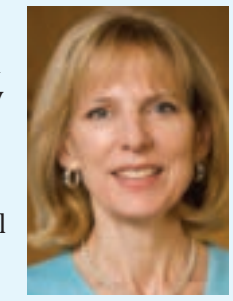
No external funding sources were reported. Dr. Marya disclosed a consulting for AnX Robotica. Two coinvestigators disclosed consulting with Medtronic and research support from Olympus and Medtronic.

ginews@gastro.org

SOURCE: Marya NB et al. Tech Innov Gastrointest Endosc. 2020 Jun 19. doi: 10.1016/j.tige.2020.06.001.

Over the last 20 years the use of video capsule endoscopy (VCE) for the evaluation of suspected small-bowel bleeding has increased logarithmically and has profoundly affected our ability to identify hemorrhagic lesions and manage GI bleeding. The current standard of care after negative bidirectional endoscopy is deployment of VCE, but recommendations about more discriminate use of this device are limited. This paper helps provide some guidance and direction. While the specific clinical predictors of small-bowel bleeding cited in this paper, such as overt hemorrhage, significant anemia, older age, and inpatient status, are not new revelations, what is unique is the creation of a simple, user-friendly scoring system for predicting a positive diagnosis. This is the first such scoring system for VCE management.

The benefits of utilizing a scoring system include refining clinical decision-making, minimizing low-yield testing, and possibly lowering health care costs for hospitalized patients, although this has not been specifically studied. Because this system is sensitive but not specific, it is most useful for identifying low-risk patients. Physicians need to be cautious, however in excluding patients from testing solely on the basis of a score. Pathology found in younger patients is often more sinister, and clinical judgment is critical in all decisions.


Dr. Fisher

This is an important step forward in more rational and precise utilization of VCE as a diagnostic tool. Refining a scoring system to reflect a high positive predictive value may be the next goal.

Laurel Fisher, MD, AGAF, is professor of clinical medicine and director of the small-bowel imaging program, division of gastroenterology, University of Pennsylvania, Philadelphia. She has participated in research trials with Medtronic.

Continued from page 5

The treatment and placebo arms were similar except that patients with HCC were about 10 years older on average. In patients with HCC, 60.5% more lusutrombopag recipients than placebo recipients met the primary endpoint, and rates of bleeding-related adverse events were 9.1% and 15.7%, respectively. In patients with other chronic liver diseases without HCC, 52.6% more lusutrombopag recipients met the primary endpoint. Rates of bleeding-related adverse events were 5% and 10.6%.

"Approximately 88% of patients with hepatocellular carcinoma underwent ablation or transcatheter chemoembolization, whereas patients without hepatocellular carcinoma underwent other procedures," the investigators wrote. "This is significant because ablations or transcatheter arterial chemoembolizations can be associated with serious bleeding complications. It is clinically important that in patients undergoing invasive liver-related procedures, the incidence of bleeding-related adverse events was lower in patients treated with lusutrombopag than placebo."

Imaging after the procedures confirmed low rates of thromboses in both groups and subgroups. Four patients developed portal vein thromboses, including two lusutrombopag recipients (one of whom had HCC) and two placebo recipients without HCC.

These trials excluded patients undergoing major surgical procedures and those with decompensated cirrhosis; portal vein thrombosis; hematopoietic tumors; aplastic anemia; myelodysplastic syndrome; myelofibrosis; liver transplantation; splenectomy; and thrombocytopenia that was congenital, autoimmune, or drug induced. "A limitation of this study was the high rate of protocol violations related to platelet transfusions," the researchers noted. "A number of patients [42 in all] were excluded from the per-protocol population owing to receipt of unnecessary platelet transfusions, or because they did not receive a needed platelet transfusion."

Shionogi makes lusutrombopag and sponsored the study. Dr. Alkhouri reported an advisory relationship with Shionogi and Dova Pharma. Two coinvestigators reported being employed by Shionogi. Three coinvestigators also disclosed ties to Shionogi and to several other pharmaceutical companies.

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SOURCE: Alkhouri N et al. Clin Gastroenterol Hepatol. 2020 Mar 20. doi: 10.1016/j.cgh.2020.03.032.

See *Gastroenterology's* curated colorectal cancer research collection

Gastroenterology is proud to announce the release of a special collection of colorectal cancer articles. This curated collection includes some of the top colorectal cancer research published over the last 3 years with new research being added to the collection as it's published.

View the special collection on *Gastroenterology's* website, which is designed to help you quickly scan recent colorectal cancer research and easily navigate to studies of interest. Recent articles include:

- Use of Artificial Intelligence-Based Analytics From Live Colonoscopies to Optimize the Quality of the Colonoscopy Examination in Real Time: Proof of Concept
- Risk Factors for Early-Onset Colorectal Cancer
- Causes of Post-Colonoscopy Colorectal Cancers Based on World Endoscopy Organization System of Analysis

To view all of *Gastroenterology's* curated article collections, please visit gastro.org/GastroCollections.

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Meet the recipients of AGA's COVID-19 research funding

When COVID-19 hit, the AGA Research Foundation quickly announced the AGA-Takeda COVID-19 Rapid Response Research Awards to provide funding to kick-start research into the virus' impact on the digestive tract. We're excited to share our three award recipients with you. Read about their research projects below.

David A. Drew, PhD, and Long H. Nguyen, MD, MS, from Massachusetts General Hospital and Harvard Medical School will test their hypothesis that gut microbial communities mediate the relationship between gastroenterology symptoms and the varied clinical presentations and outcomes in patients with COVID-19. To accomplish this goal, they will jointly develop and rapidly deploy a multinational digital infrastructure for large-scale epidemiologic studies during the current global pandemic. By characterizing the gastroenterology symptoms most predictive of COVID-19 infection risk and severity, their work will offer timely insights into the ongoing pandemic and offer a foundation for further study on the effects of COVID-19 on human gut microbial communities.

Congratulations to Drs. David A. Drew, Long H. Nguyen, and Jeffrey Wade Brown – recipients of our AGA-Takeda COVID-19 Rapid Response Research Awards from the AGA Research Foundation.

Jeffrey Wade Brown, MD, PhD, from Washington University is evaluating the infective potential of the metaplastic GI foregut. For this project Dr. Brown and his team will use a novel, unique, and unpublished organoid system that propagates the features of upper GI human metaplasia in vitro to study a potential role for metaplasia in the predisposition to COVID-19. Dr. Brown hopes this research will directly help by making a previously naive population know that they are potentially at higher risk. Further, the high-throughput screening technology they are developing will not only be useful here but also could quickly be adapted to other pandemics.

The AGA Research Foundation Awards Program recruits, retains and supports the most promising researchers in gastroenterology and hepatology. To view all of the AGA Research Foundation awardees, please visit Foundation.gastro.org.

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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:

- Patient case: Crohn's patient with three different strictures (https://community.gastro.org/posts/22491)
- Patient case: Alcoholic hepatitis and positive anti-smooth muscle antibody (https://community.gastro.org/posts/22407)
- COVID-19: The importance of preparedness in independent GI practices (https://community.gastro.org/posts/22340)
- Patient case: Crohn's patient with no tissue (https://community.gastro.org/posts/22472)

Roundtables (https://community.gastro.org/discussions/)
- Roadmap for the future of colorectal cancer screening in the U.S.
- Windows on Clinical GI lecture series: NAFLD, Crohn's disease and gastroparesis

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

AGA announces October GI Forging Forward virtual symposia

Join us for our new GI Forging Forward virtual symposia series, a practical educational training program covering timely topics for GIs through the lens of COVID-19. Experts in the field will present the latest COVID-19 findings, share proven strategies to communicate and manage disaster and crisis situations, and educate participants on evidence-based recommendations to meet today's evolving needs. Upcoming topics will cover keeping you, your staff and patients safe, new approaches and training in research, leading in times of crisis, and rapid-response guideline development.

Registration for this month's virtual webinars are now open:

- Meet NIH Leadership: Minorities health disparities, research and career development: Oct. 15, 2020, 5:30 p.m. EDT
- Effective leadership in times of crisis: Oct. 22, 2020, 5:30 p.m. EDT

For more information, visit www.gastro.org/GIForgingForward.

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AGA Clinical Practice Update

Diagnosis and treatment of SIBO

BY AMY KARON
MDedge News

Unexplained diarrhea may be the most reliable symptom of small-intestine bacterial overgrowth (SIBO) in at-risk patients, according to a new clinical practice update from the American Gastroenterological Association.

"In those predisposed to SIBO due to anatomical, pathological, pharmacological or other changes that promote stasis or recirculation of colonic contents and/or impaired resistance to bacteria, SIBO will lead to diarrhea and can progress to a full-blown malabsorption syndrome" marked by steatorrhea and vitamin deficiencies, wrote Eamonn M.M. Quigley, MD, of Houston Methodist Hospital and Weill Cornell Medical College in Houston together with his fellow experts in Gastroenterology. But malabsorption is uncommon in patients whose SIBO is not caused by structural abnormalities, and gastrointestinal symptoms are "weakly predictive at best" if patients lack clear risk factors for SIBO, the experts cautioned.

Recent progress in techniques to measure bacterial populations and their metabolic products "should provide much needed clarity," but for now, a SIBO diagnosis simply means that a patient's presenting symptoms or laboratory findings are attributed to bacterial changes in the small intestine, the experts wrote.

A SIBO diagnosis simply means that a patient's symptoms or lab findings are attributed to bacterial changes in the small intestine.

Detecting SIBO also remains challenging. Most patients have normal results on routine laboratory tests, and there is not enough evidence to support testing for inflammatory markers such as fecal calprotectin. Patients with SIBO may have increased folate levels because of bacterial production of folic acid. Vitamin B_{12} and other nutrient deficiencies also occur but are less common. The preferred diagnostic method is culture of a duodenal aspirate, and recent research supports a cutoff value of greater than 10^3 CFUs of coliform bacteria per mL.

Breath testing is less invasive but "more complex than simply measuring hydrogen," the experts stressed. Methane-producing microorganisms suppress hydrogen on a breath test (fortunately, standard breath tests measure methane). Furthermore, a positive methane breath test also has been linked to constipation-predominant irritable bowel syndrome (IBS). Recent studies also suggest that lactulose breath testing is more sensitive than glucose for identifying SIBO in patients with IBS.

Antibiotic therapy is the treatment mainstay but remains largely empiric. The goal is to improve SIBO symptoms, not eradicate bacteria from the small intestine. Ideally, the antimicrobial regimen should cover both aerobic and anaerobic bacteria, but clinicians should be mindful of the risks of chronic broad-spectrum antibiotic exposure. In studies, a single 7- to 10-day antibiotic course improved symptoms in 45%-90% of patients with SIBO (rates of breath test response were lower). For patients with IBS and SIBO, rifaximin (which is poorly absorbed) produced encouraging results in two phase 3 studies, but most patients were not breath tested.

Patients with recurrent SIBO symptoms may need multiple courses of antibiotics with specific regimens rotated to help prevent resistance.

"Decisions on management should be individualized and also [should factor in] such risks as diarrhea, *Clostridiodes difficile* infection, intolerance, and cost," the experts wrote.

Dr. Quigley disclosed financial ties to 4D Pharma, Alimentary Health, Allergan, Biocodex, Biomerica, Ironwood, Salix, Takeda, Vibrant, and Zealand. He also disclosed patents with and equity in Alimentary Health. Both coauthors also disclosed ties to various pharmaceutical companies.

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SOURCE: Quigley EMM et al. Gastroenterology. 2020 Jun 1. doi: 10.1053/j.gastro.2020.06.090.

DDSEP 9
Digestive Diseases Self-Education Program

Quick quiz answers

Q1. Correct answer: B

Rationale

A serum ceruloplasmin less than 5 mg/L and a 24-hour urine copper excretion greater than 100 mcg/24 hours are both highly suggestive of Wilson's disease, a disorder of copper metabolism caused by a mutation in a P-type ATP-ase that mediates the excretion of copper into the bile. Treatment of Wilson's disease consists of copper chelation therapy. Commonly used therapies include D-penicillamine, trientine, and zinc. Patients on therapy should have 24-hour urine copper determination every 6-12 months. Patients on maintenance trientine or D-penicillamine should have urine copper excretion of 200-500 mcg/24 hours. Patients on zinc therapy should have much lower copper excretion, in the range of 75 mcg/24 hours.

References

European Association for the Study of the Liver. J Hepatol. 2012;56:671-85.
Roberts EA, Schilsky ML. Hepatology. 2008;47:2089-111.

Q2. Correct answer: E

Rationale

Patients with advanced liver disease display a variety of pulmonary abnormalities including portopulmonary hypertension (PoPHT) and hepatopulmonary syndrome (HPS). The diagnosis of PoPHT requires elevated pulmonary arterial PAP > 25 mm Hg, pulmonary capillary wedge pressure < 15 mm Hg, and pulmonary vascular resistance > 240 dynes/s per cm^{-5} in addition to portal HT. Dyspnea is the most common symptom in patients with PoPHT. Treatment to decrease the elevated pulmonary pressure is essential before liver transplant listing. The goal of vasodilator therapy is a mean pulmonary pressure of <35 mm Hg, which is not always achievable even with the most aggressive therapy. Although oxygen management after transplant in the setting of HPS may be challenging, oxygen requirements steadily decline following successful transplant. All other listed conditions do not constitute contraindication to liver transplantation once treated.

Reference

Porres-Aguilar M et al. Ann Hepatol. 2008;7:321–30.

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Ferring is committed to exploring the crucial link between the gut microbiome and the threat of recurrent *Clostridioides difficile* infections. With the 2018 acquisition of Rebiotix and several other alliances, Ferring is rapidly advancing its microbiome research, developing novel therapies to address significant unmet needs in deadly and debilitating diseases, and helping people live better lives.

Germline mutation testing is crucial

CRC *from page 1*

adult–onset colorectal cancer is rising, but the trend is not limited to the United States. Implicated risk factors include inflammatory bowel disease, prior irradiation, harboring a pathogenic germline mutation for a known hereditary cancer syndrome, and having a first- or second-degree relative with colorectal cancer. Indeed, the odds of developing young adult–onset disease are nearly 4 times higher if a parent has colorectal cancer and nearly 12 times higher if a sibling is affected.

For newly diagnosed young adults, it is important to collect a family cancer history but vital, regardless of history, to discuss targeted or multiplex germline mutation testing. Detecting hereditary colorectal cancer syndromes is crucial because their nature informs surgical options for treatment. "Roughly one in five young adult–onset colorectal cancers will be caused by a germline mutation, and among those with a detectable hereditary condition, half of those patients with young adult–onset colorectal cancer will have Lynch syndrome," the experts noted. For these patients (who have mutations involving MSH2, EPCAM, MLH1, MSH6, and PMS2), ileorectostomy (IRA) for colorectal cancer should be considered.

For patients with the classic subtype of familial adenomatous polyposis, ileal pouch anal anastomosis is recommended after the polyp burden can no longer be managed endoscopically, although initial IRA with subsequent conversion to ileal pouch anal anastomosis is an option for women of child-bearing age, according to the clinical practice update. Patients with the attenuated subtype of familial adenomatous polyposis should consider IRA or colectomy if colorectal cancer develops or if the polyp burden exceeds endoscopic control. In contrast, colectomy is the only type of surgery recommended for patients with serrated polyposis syndrome requiring surgical treatment.

'Roughly one in five young adult–onset colorectal cancers will be caused by a germline mutation, and among those with a detectable hereditary condition, half of those patients with young adult–onset colorectal cancer will have Lynch syndrome.'

Finally, clinicians should offer screening for hereditary cancer syndromes only if young adults with cancer have been diagnosed with a hereditary colorectal cancer syndrome. "For patients with sporadic young adult–onset colorectal cancer, extracolonic screening and colorectal cancer surveillance intervals are the same as for patients with older adult–onset colorectal cancer," the experts wrote. For young patients without an apparent underlying genetic syndrome, molecular studies may eventually help tailor treatment options, "but at this point, more extensive surgery or more aggressive chemotherapy cannot be recommended. As cancer treatments evolve to use patient tumor specific therapeutics, our management of patients with young adult–onset colorectal cancer will improve."

Dr. Boardman and associates reported having no relevant conflicts of interest.

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SOURCE: Boardman LA et al. Clin Gastroenterol Hepatol. 2020 Jun 7. doi: 10.1016/j.cgh.2020.05.058.

Aspirin may accelerate cancer progression in older adults

BY SARA FREEMAN
MDedge News

Aspirin may accelerate the progression of advanced cancers and lead to an earlier death as a result, new data from the ASPREE study suggest.

The results showed that patients 65 years and older who started taking daily low-dose aspirin had a 19% higher chance of being diagnosed with metastatic cancer, a 22% higher chance of being diagnosed with a stage 4 tumor, and a 31% increased risk of death from stage 4 cancer, when compared with patients who took a placebo. John J. McNeil, MBBS, PhD, of Monash University in Melbourne, and colleagues, detailed these findings in the Journal of the National Cancer Institute.

"If confirmed, the clinical implications of these findings could be important for the use of aspirin in an older population," the authors wrote.

When results of the ASPREE study were first reported in 2018 (N Engl J Med. 2018;379:1519-28), they "raised important concerns," Ernest Hawk, MD, and Karen Colbert Maresso wrote in an editorial related to the current publication (J Natl Cancer Inst. 2020 Aug 11. doi: 10.1093/jnci/djaa115).

"Unlike ARRIVE, ASCEND, and nearly all prior primary prevention CVD [cardiovascular disease] trials of aspirin, ASPREE surprisingly demonstrated increased all-cause mortality in the aspirin group, which appeared to be driven largely by an increase in cancer-related deaths," wrote the editorialists, who are both from the University of Texas MD Anderson Cancer Center in Houston.

Even though the ASPREE investigators have now taken a deeper dive into their data, the findings "neither explain nor alleviate the concerns raised by the initial ASPREE report," the editorialists noted.

What were the ASPREE design and results?

ASPREE is a multicenter, double-blind trial of 19,114 older adults living in Australia (n = 16,703) or the United States (n = 2,411). Most patients were 70 years or older at baseline. However, the U.S. group also included patients 65 years and older who were racial/ethnic minorities (n = 564).

'Unlike ARRIVE, ASCEND, and nearly all prior primary prevention CVD trials of aspirin, ASPREE surprisingly demonstrated increased all-cause mortality in the aspirin group, which appeared to be driven largely by an increase in cancer-related deaths.'

Patients were randomized to receive 100 mg of enteric-coated aspirin daily (n = 9,525) or matching placebo (n = 9,589) from March 2010 through December 2014.

At inclusion, all participants were free from cardiovascular disease, dementia, or physical disability. A previous history of cancer was not used to exclude participants, and 19.1% of patients had cancer at randomization. Most patients (89%) had not used aspirin regularly before entering the trial.

At a median follow-up of 4.7 years, there were 981 incident cancer events in the aspirin-treated group and 952 in the placebo-treated group, with an overall incident cancer rate of 10.1%. Of the 1,933 patients with newly diagnosed cancer, 65.7% had a localized cancer, 18.8% had a new metastatic cancer, 5.8% had metastatic disease from an existing cancer, and 9.7% had a new hematologic or lymphatic cancer. A quarter of cancer patients (n = 495) died as a result of their malignancy, with 52 dying from a cancer they already had at randomization.

Aspirin was not associated with the risk of first incident cancer diagnosis or incident localized cancer diagnosis. The hazard ratios were 1.04 for all incident cancers (95% confidence interval, 0.95-1.14) and 0.99 for incident localized cancers (95% CI, 0.89-1.11). However, aspirin was associated with an increased risk of metastatic cancer and cancer presenting at stage 4. The HR for metastatic cancer was 1.19 (95% CI, 1.00-1.43), and the HR for newly diagnosed stage 4 cancer was 1.22 (95% CI, 1.02-1.45).

Furthermore, "an increased progression to death was observed amongst those randomized to aspirin, regardless of whether the initial cancer presentation had been localized or metastatic," the investigators wrote.

The HRs for death were 1.35 for all cancers (95% CI, 1.13-1.61), 1.47 for localized cancers (95% CI, 1.07-2.02), and 1.30 for metastatic cancers (95% CI, 1.03-1.63).

"Deaths were particularly high among those on aspirin who were diagnosed with advanced

Continued on following page

Continued from previous page

solid cancers," study author Andrew Chan, MD, AGAF, of Massachusetts General Hospital in Boston, said in a press statement. Indeed, HRs for death in patients with solid tumors presenting at stage 3 and 4 were a respective 2.11 (95% CI, 1.03-4.33) and 1.31 (95% CI, 1.04-1.64). This suggests a possible adverse effect of aspirin on the growth of cancers once they have already developed in older adults, Dr. Chan said.

Sage Ross/Wikimedia Commons

Where does that leave aspirin for cancer prevention?

"Although these results suggest that we should be cautious about starting aspirin therapy in otherwise healthy older adults, this does not mean that individuals who are already taking aspirin – particularly if they began taking it at a younger age – should stop their aspirin regimen," Dr. Chan said.

There are decades of data supporting the use of daily aspirin to prevent multiple cancer types, particularly colorectal cancer, in individuals under the age of 70 years. In a recent meta-analysis, for example, regular aspirin use was linked to a 27% reduced risk for colorectal cancer, a 33% reduced risk for squamous cell esophageal cancer, a 39% decreased risk for adenocarcinoma of the esophagus and gastric cardia, a 36% decreased risk for stomach cancer, a 38% decreased risk for hepatobiliary tract cancer, and a 22% decreased risk for pancreatic cancer (Ann Oncol. 2020 May;31[5]:558-68).

While these figures are mostly based on observational and case-control studies, it "reaffirms the fact that, overall, when you look at all of the ages, that there is still a benefit of aspirin for cancer," John Cuzick, PhD, of Queen Mary University of London, said in an interview.

In fact, the meta-analysis goes as far as suggesting that perhaps the dose of aspirin being used is too low, with the authors noting that there was a 35% risk reduction in colorectal cancer with a dose of 325 mg daily. That's a new finding, Dr. Cuzick said.

He noted that the ASPREE study largely consists of patients 70 years of age or older, and the authors "draw some conclusions which we can't ignore about potential safety."

One of the safety concerns is the increased risk for gastrointestinal bleeding, which is why Dr. Cuzick and colleagues previously recommended caution in the use of aspirin to prevent cancer in elderly patients. The group published a study in 2015 that suggested a benefit of taking aspirin daily for 5-10 years in patients aged 50-65 years, but the risk/benefit ratio was unclear for patients 70 years and older (Ann Oncol. 2015 Jan;26[1]:47-57).

Dr. Cuzick noted that the ASPREE study largely consists of patients 70 years of age or older, and the authors 'draw some conclusions which we can't ignore about potential safety.'

The ASPREE data now add to those uncertainties and suggest "there may be some side effects that we do not understand," Dr. Cuzick said.

"I'm still optimistic that aspirin is going to be important for cancer prevention, but probably focusing on ages 50-70," he added. "[The ASPREE data] reinforce the caution that we have to take in terms of trying to understand what the side effects are and what's going on at these older ages."

Dr. Cuzick is currently leading the AsCaP project, an international effort to better understand why aspirin might work in preventing some cancer types but not others. AsCaP is supported by Cancer Research UK and also includes Dr. Chan among the researchers attempting to find out which patients may benefit the most from aspirin and which may be at greater risk of adverse effects.

The ASPREE trial was funded by grants from the National Institute on Aging, the National Cancer Institute, the National Health and Medical Research Council of Australia, Monash University, and the Victorian Cancer Agency. Several ASPREE investigators disclosed financial relationships with Bayer Pharma. The editorialists had no conflicts of interest. Dr. Cuzick has been an advisory board member for Bayer in the past.

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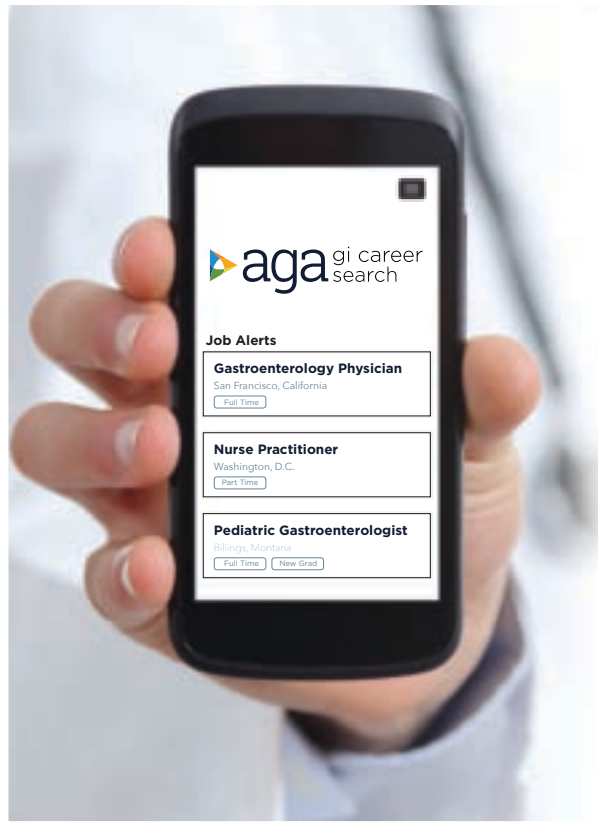
SOURCE: McNeil JJ et al. J Natl Cancer Inst. 2020 Aug 11. doi: 10.1093/jnci/djaa114.



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Fecal transplant may reduce alcohol craving

BY INGRID HEIN

Fecal microbiota transplantation results in a short-term reduction in alcohol craving in patients with alcohol-induced cirrhosis who can't stop drinking, results from a new study show.

And that reduction could lead to a better psychosocial quality of life for patients with cirrhosis and alcohol use disorder, said investigator Jasmohan Bajaj, MD, AGAF, from Virginia Commonwealth University, Richmond.

"This is the most common addiction disorder worldwide, but we have nothing to treat these patients with," he said.

Cirrhosis is associated with an altered gut-brain axis. It leads to organ damage in several parts of the body, including the brain, gut, pancreas, and liver. This makes changing the gut microbes "an attractive target," Dr. Bajaj said at the Digital International Liver Congress 2020.

For their phase 1, double-blind study, he and his colleagues assessed 20 men from a Virginia veteran's hospital with untreatable alcohol use disorder who were not eligible for liver transplantation.

All had failed behavioral or pharmacologic therapy and were unwilling to try again. "That's what made them good candidates to try something new," Dr. Bajaj said during a press briefing.

Mean age in the study cohort was 65 years, mean Model for End-Stage Liver Disease score was 8.9, and demographic characteristics were similar between the 10 men randomly assigned to fecal transplantation and the 10 assigned to placebo. One man in each group dropped out of the study.

The investigators evaluated cravings, microbiota, and quality of life during the 30-day study period.

At day 15, significantly more men in the transplant group than in the placebo group experienced a reduction in alcohol cravings (90% vs. 30%).

At 30 days, levels of creatinine, serum interleukin-6, and lipopolysaccharide-binding protein were lower in the transplant group than in the placebo group. In addition, levels of butyrate and isobutyrate increased, as did cognition and quality of life scores.

There was also a decrease in urinary ethyl glucuronide in the transplant group, which "is the objective criteria for alcohol intake," Dr. Bajaj reported, noting that there was no change in ethyl glucuronide in the placebo group.

The increase in microbiota diversity was significant in the transplant group but not in the placebo group. *Alistipes*, *Odoribacter*, and *Roseburia* were more abundant in the transplant group than in the placebo group.

During the 30-day study period, two men in the placebo group required medical attention, one for hyponatremia and the other for atrial fibrillation. However, no adverse events were seen in any men in the transplant group. "This was the No. 1 result," Dr. Bajaj said.

Liver disease and the microbiome

"Understanding of interactions between the human and microbiome genome [metagenome] in health and disease has represented one of the major areas of progress in the last few years," said Luca Valenti, MD, from the University of Milan, who is a member of the scientific committee of the European Association the Study of the Liver, which organized the congress.

"These studies lay the groundwork for the exploitation of this new knowledge for the treatment of liver disease," he said.

"We are [now] diagnosing liver disease and the stages of liver disease based on microbiome changes," said Jonel Trebicka, MD, PhD, from University Hospital Frankfurt (Germany), who chaired a session at the congress on the role of the microbiome in liver disease.

The current study also "shows clearly that the microbiome plays a role in craving. FMT reduces the desire for alcohol," said Dr. Trebicka.

"The way to the brain is through the gut," Dr. Bajaj said.

Dr. Bajaj, Dr. Trebicka, and Dr. Valenti disclosed no relevant financial relationships.

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

AGA Resource

Visit the AGA Center for Gut Microbiome Research and Education to learn more about AGA activities, research, news, and policy updates related to the gut microbiome, one of the most exciting and promising areas of science today at http://ow.ly/e3hQ30raoGZ.

Two main mechanisms involved

Cirrhosis *from page 1*

ACLF is a highly complex disorder that can lead liver, cardiovascular, renal, cerebral, pulmonary, intestinal, adrenal, and immune systems to fail, Dr. Trebicka explained when he discussed the analysis – published online in the Journal of Hepatology – during the virtual International Liver Congress 2020.

The chance of survival after the onset of ACLF is low – the 28-day survival rate is 30% – and "the only treatment we have is liver transplant," he said.

For their prospective observational study, Dr. Trebicka and his colleagues assessed 1,071 participants from 48 European hospitals in 14 countries who were admitted for an episode of acute decompensation, defined as the development of ascites, hepatic encephalopathy, gastrointestinal hemorrhage, infection, or a combination thereof.

The researchers identified three distinct clinical courses for a patient hospitalized with acute decompensated cirrhosis that will help clinicians predict the development of ACLF.

At study enrollment, more than half of the patients at highest risk for ACLF had pre-ACLF and high-grade systemic inflammation. The patients at intermediate risk had unstable decompensated cirrhosis with low-grade systemic inflammation and complications related to severe portal hypertension. And those at lowest risk for ACLF had stable decompensated cirrhosis and no severe systemic inflammation or portal hypertension complications, and did not develop ACLF or another episode of acute decompensation in the subsequent 3 months.

"There have been hints of possible phenotypes before – for stable and unstable ACLF – but we never had anything specific to diagnose," Dr. Trebicka reported.

"We found that there are two main mechanisms in the development of ACLF that are most important," he said. The first is systemic inflammation with high levels of proteins, which "leads to organ failure. This is the most striking acute mechanism."

The second is the development of portal hypertension. "This is slower, but also very important, causing increased pressure in the portal vein, and leading to bleeding if the pressure is too great," he said.

More tools emerging to help predict ACLF

The albumin functionality test (AFT), which uses serum albumin levels to evaluate liver and kidney function, might also be useful in the prediction of ACLF and 12-month survival, according to a separate study an Italian group presented at the virtual ILC.

"Our main results are that parameters from albumin predict the development of ACLF in acute decompensated patients with the same diagnostic performance as the CLIF-AD score," said Katja Waterstradt, PhD, from the University of Bologna (Italy).

And when the two tests are combined, diagnostic performance is increased, she added.

Dr. Trebicka has disclosed no relevant financial relationships. Dr. Waterstrand is a researcher for MedInnovation GmbH.

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

Mortality after hospitalization for acute decompensated cirrhosis

Risk group	3 months	12 months
High	53.7%	67.4%
Intermediate	21.0%	35.6%
Low	0.0%	9.5%

MDedge News

Note: The prospective observational study involved 1,071 participants who were admitted for an episode of acute decompensation.

Source: Dr. Trebicka

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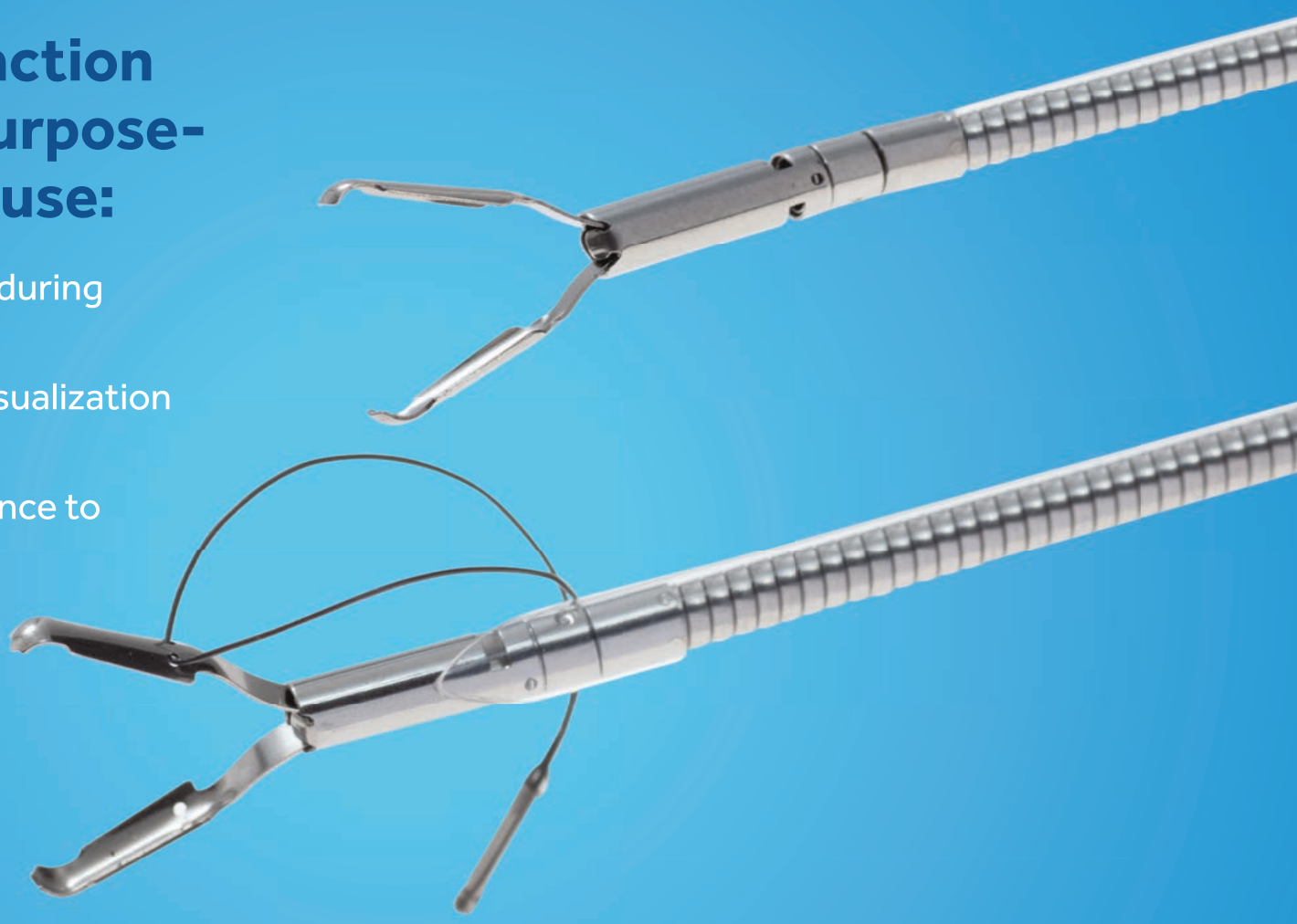

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References

1. RE00221182 (A) ProdiGI™ Traction Wire Design Validation Report.

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GERD: Endoscopic therapies alternative to PPIs?

BY WILL PASS
MDedge News

For patients with gastroesophageal reflux disease (GERD), endoscopic and minimally invasive surgical techniques may be viable alternatives to proton pump inhibitor (PPI) therapy, according to investigators.

Still, their exact role in the treatment process remains undetermined, reported Michael F. Vaezi, MD, PhD, of Vanderbilt University Medical Center in Nashville, Tenn., and colleagues.

"The frequent incomplete response to PPI therapy, in addition to recent studies suggesting chronic complications with PPI therapy, have fueled discussion of alternative strategies for treating patients with GERD," the investigators wrote in Gastroenterology. "For a substantial number of patients and providers with the above concerns who are unwilling to pursue the traditional surgical gastric fundoplication, endoscopic or less invasive surgical strategies have gained some traction."

Dr. Vaezi and colleagues noted that they conducted the scoping review with intentions of being more descriptive than prescriptive.

"Our goal is not to recommend the utility of any of the discussed techniques in specific clinical scenarios," they wrote. "Rather, it is to summarize the currently available evidence and identify where more research may be helpful."

Across 22 randomized, controlled trials and observational studies, objective and symptomatic improvement varied between modalities. Measured outcomes also varied; most studies reported symptoms, health-related quality of life, and PPI use; fewer studies (but still a majority) reported intraesophageal acid exposure and/or lower esophageal sphincter (LES) pressure. Conclusions drawn by Dr. Vaezi and colleagues are summarized below.

Magnetic sphincter augmentation of the LES

In multiple trials, magnetic sphincter augmentation demonstrated a "high degree of efficacy" in the short or midterm, and a favorable safety profile. Dr. Vaezi and colleagues highlighted significant improvements in disease-related quality of life, with "a substantial proportion" of patients achieving normalization or at least 50% improvement in acid exposure. While some patients required esophageal dilation after the procedure, this was not needed any more frequently than after surgical fundoplication.

> **The place of some endoscopic and minimally invasive approaches to GERD in the treatment algorithm will 'be better defined when important clinical parameters, especially the durability of their effect, are understood.'**

Radiofrequency ablation

Across five trials, radiofrequency ablation, which involves delivery of energy to the LES and gastric cardia, improved GERD-related quality of life, and reduced, but did not normalize, acid exposure. The technique lessened short-term need for PPIs, but long-term relief was not observed. Compared with observational studies, efficacy signals were weaker in randomized, controlled trials. The procedure was generally safe.

Surgical implantation of LES pacemaker

Limited data were available for LES sphincter stimulation among patients with GERD, and the most recent study, involving a comparison of device placement with or without stimulation, was terminated early. Still, available data suggest that the technique is generally well tolerated, with reduced need for PPIs, improved symptoms, and lessened acid exposure. Dr. Vaezi and colleagues noted that the manufacturing company, EndoStim, is in receivership, putting U.S. availability in question.

Full-thickness fundoplication

Endoscopic full-thickness fundoplication was associated with improvement of symptoms and quality of life, and a favorable safety profile. Although the procedure generally reduced PPI use, most patients still needed PPIs long-term. Reflux improved after the procedure, but not to the same degree as laparoscopic plication.

Transoral incisionless fundoplication

Based on a number of studies, including five randomized, controlled trials, transoral incisionless fundoplication appears safe and effective, with reduced need for PPIs up to 5 years. According to Dr. Vaezi and colleagues, variable results across studies are likely explained by variations in the technique over time and heterogeneous patient populations. Recent studies in which the "TIF 2.0 technique" has been performed on patients with hiatal hernias less than 2 cm have met objective efficacy outcomes.

Incisionless fundoplication with magnetic ultrasonic surgical endostapler

The magnetic ultrasonic surgical endostapler, which allows for incisionless fundoplication, had more limited data. Only two studies have been conducted, and neither had sham-controlled nor comparative-trial data. Furthermore, multiple safety signals have been encountered, with "substantial" complication rates and serious adverse events that were "noticeable and concerning," according to Dr. Vaezi and colleagues.

Concluding their discussion, the investigators suggested that some endoscopic and minimally invasive approaches to GERD are "promising" alternatives to PPI therapy.

"However, their place in the treatment algorithm for GERD will be better defined when important clinical parameters, especially the durability of their effect, are understood," they wrote.

The investigators reported no conflicts of interest.

ginews@gastro.org

SOURCE: Vaezi MF et al. Gastroenterology. 2020 Jul 1. doi: 10.1053/j.gastro.2020.05.097.

Gastric screening cancer cost effective in Asian Americans

BY JIM KLING
MDedge News

A new model of gastric cancer screening suggests that, for Asian Americans, endoscopic screening alongside colonoscopy and follow-up surveillance of gastric preneoplasia is a cost-effective strategy. Incremental cost-effectiveness ratios (ICERs) were lowest for Chinese, Japanese, and Korean Americans. The model simulated results for asymptomatic 50-year-old subjects.

Gastric cancer risk is highest in Asian Pacific, Latin American, and Eastern European countries. Asia Pacific countries alone represent about half of all new cases. *Helicobacter pylori*–related gastritis is the strongest known risk factor for intestinal-type noncardia gastric adenocarcinoma (NCGA), which is the most common gastric cancer, and this chronic inflammation can lead to gastric intestinal metaplasia (GIM). Individuals with GIM have a 0.16% increased annual risk of NCGA, which makes them good candidates for endoscopic screening that could catch new cancers at an early stage.

In a previous study (Gastroenterology. 2018 May 17;155[3]:648-60), researchers at Vanderbilt University Medical Center in Nashville, Tenn., at Boston University School of Medicine, and at the University of Pennsylvania in Philadelphia showed that, in asymptomatic 50-year-old Asian Americans, Hispanic patients, and non-Hispanic Black patients, performing a single esophagogastroduodenoscopy (EGD) concomitantly with a colonoscopy, followed by screening EGDs if indicated (such as for a GIM diagnosis), is a cost-effective strategy. They found ongoing screening was not cost effective if the original results were normal.

In the new study published in Clinical Gastroenterology and Hepatology, the researchers followed up this finding with an attempt to tease out the cost-effectiveness of screening in different subgroups, as well as by sex. They built a Markov decision model focusing on the six most common Asian groups in the United States: Chinese, Filipino, Southeast Asian, Vietnamese, Korean, and Japanese Americans.

Model inputs were based on the published literature, and the outputs were compared with data

Continued on following page

Continued from previous page

from the Surveillance, Epidemiology, and End Results (SEER) data for disaggregated Asian Americans between 2001 and 2014 and separately with the California Cancer Registry (2011-2015). The model produced a good fit to the epidemiological data.

The model then compared cost-effectiveness of three hypothetical screening strategies in asymptomatic 50-year-old Asian Americans: one-time upper EGD with biopsies conducted at the time of colonoscopies for colorectal cancer screening, followed by EGDs every 3 years if GIM was detected (or other appropriate management of higher-grade pathology); EGD with biopsy at a colonoscopy for CRC screening followed by EGD biennially regardless of initial findings; and no endoscopy screening.

The one-time EGD strategy was the most cost effective, regardless of sex, with an ICER of $75,959 per quality-adjusted life-year (QALY) in males and $74,329/QALY in females. The lowest ICER was found for Chinese Americans (males and females, $68,256/QALY), followed by Japanese Americans (males, $69,011/QALY; females, $73,748/QALY), and Korean Americans (males, $70,739/ QALY; females, $70,236/QALY). The highest ICERs were among Filipino American males and females, but the strategy was still cost effective at the predetermined willingness-to-pay threshold of $100,000 ($83,732/QALY).

In all ethnic groups, the biennial screening strategy produced more harm than good and was costlier.

The authors believe that the strategy could be applied to other ethnic groups that come from countries with populations at higher relative risk of gastric cancer, such as Central and Latin American countries.

Asked to comment on the study, Mimi Tan, MD, an assistant professor of gastroenterology at Baylor College of Medicine in Houston, suggested that the estimates of precancerous lesions used in the Markov model were quite high because they were based on pathology databases. These sources tend to be biased toward symptomatic individuals since these are the patients typically referred for upper endoscopy biopsies. "Therefore, these probabilities may not represent true probability of these precancerous lesions among asymptomatic screening populations," Dr. Tan said in an interview. She also questioned whether the study represented the true risk in female populations since the literature for women is sparse.

Dr. Tan suggested that a more cost-effective screening strategy might be one-time *H. pylori* immunoglobulin G testing in Asian Americans. The Houston Consensus Conference on Testing for *H. pylori* Infection already recommends testing for first-generation immigrants from high-prevalence areas and Latino and African American racial or ethnic groups (Clin Gastroenterol Hepatol. 2018 Jul;16[7]:992-1002). "Future studies should compare cost-effectiveness of one-time upper endoscopy, which is more costly but able to detect premalignant lesions, to one-time *H. pylori* testing," said Dr. Tan.

The study was supported by the Agency for Healthcare Research and Quality, Patient-Centered Outcomes Research Institute, the American Gastroenterological Association, and the Department of Veteran Affairs.

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SOURCE: Shah SC et al. Clin Gastroenterol Hepatol. 2020 Jul 21. doi: 10.1016/j.cgh.2020.07.031.

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[1] Cash BD, Epstein MS, Shah SM. Patient satisfaction with IBS symptom relief using a novel peppermint oil delivery system in a randomized clinical trial and in the general population. After peer review, published in *Int J Dig. Dis.* 2016;2(2). **doi:10.4172/2472-1891.100027**.
[2] Cash BD, Epstein MS, Shah SM. IBgard: a novel small intestine targeted delivery system of peppermint oil results in significant improvement in severe and unbearable IBS symptom intensity. Results from the U.S.-based, 4-week, randomized, placebo-controlled, multi-center **IBSREST**™ trial. Approved after peer review and then presented at DDW, May 2015.
[3] Cash BD, Epstein MS, Shah SM. A novel delivery system of peppermint oil is an effective therapy for irritable bowel syndrome symptoms. After peer review, published in *Dig Dis Sci.* 2016;61(2):560-571.
[4] Ford AC, Moayyedi P, Chey WD et al. American College of Gastroenterology Monograph on Management of Irritable Bowel Syndrome. *Am J Gastroenterol.* 2018 Jun;113(Suppl 2):1-18.
[5] Chey WD, Lacy BE, Cash BD, et al. A novel, duodenal-release formulation of a combination of caraway oil and l-Menthol for the treatment of FD: a RCT. After peer review, published in *Clinical and Translational Gastroenterology* 2019;00:e-00021. **doi.org/10.14309 ctg.0000000000000021 (FDREST**™, **F**unctional **D**yspepsia **R**esponse **E**valuation and **S**afety **T**rial).
[6] Chey W. Rapid relief of functional dyspepsia symptoms with a novel formulation of caraway oil and l-Menthol: outcomes from a self-reported patient outcomes study. Presented at American College of Gastroenterology Annual Conference; 2017; Orlando, FL.
[7] **FDACT**™, **F**unctional **D**yspepsia **A**dherence and **C**ompliance **T**rial. After peer review, presented at the American College of Gastroenterology (ACG) Annual Meeting, 2017.
[8] Micka A, et al. Effect of consumption of chicory inulin on bowel function in healthy subjects with constipation: a randomized, double-blind, placebo-controlled trial. After peer review, published in *International Journal of Food Sciences and Nutrition.* Aug 2017 68:1, 82-89.
[9] Lacy B, Epstein M, Shah S, Corsino P. Improved regularity with a chewable inulin fiber (CIF): results from a Patient Reported Outcomes (PRO) study. Approved after peer review and then presented at American College of Gastroenterology Annual Conference - Philadelphia, PA.; 2018.
† Among gastroenterologists who recommended peppermint oil for IBS. IQVIA ProVoice (2015-2020 surveys). Among gastroenterologists who recommended herbal products for Functional Dyspepsia. IQVIA ProVoice survey (June 2019). Among gastroenterologists who recommended a chewable fiber brand (tablets and gummies). IQVIA ProVoice survey (June 2019).

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Local solutions may improve care

Disparities *from page 1*

pandemic-related issues in colorectal cancer (CRC).

The sudden decrease in colonoscopies has already affected diagnoses, she said, as 32% fewer cases of CRC were diagnosed in April 2020 compared with April 2019, a finding that is "obviously very concerning." All downstream effects remain to be seen; however, one estimate suggests that over the next decade delayed screening may lead to an additional 4,500 deaths from CRC.

Dr. Issaka called for universal health insurance not associated with employment, research funding for health disparities, sustainable employment wages, climate justice, and desegregation of housing.

"These effects are particularly noticeable in medically underserved communities where CRC morbidity and mortality are highest," Dr. Issaka wrote, as coauthor of a study published in Gastrointestinal Endoscopy.

Dr. Issaka and colleagues predict that the pandemic will likely worsen "persistent CRC disparities" in African American and Hispanic communities, including relatively decreased screening participation, delayed follow-up of abnormal stool results, limited community-based research and partnerships, and limited community engagement and advocacy.

"COVID-19 related pauses in medical care, as well as shifts in resource allocation and workforce deployment, threaten decades worth of work to improve CRC disparities in medically underserved populations," wrote Dr. Issaka and colleagues.

Dr. Issaka described similar issues in hepatology. She referred to a recent opinion article by Tapper and colleagues, which predicted that the COVID-19 pandemic will impact patients with liver disease in three waves: first, by delaying liver transplants, elective procedures, imaging, and routine patient follow-up; second, by increasing emergent decompensations, transplant waitlist dropouts, and care deferrals; and third, by losing patients to follow-up, resulting in missed diagnoses, incomplete cancer screening, and progressive disease.

"This could disproportionately impact Black, Hispanic, and Native American populations, who may have already had difficulty accessing [liver care]," Dr. Issaka said.

To mitigate growing disparities, Dr. Issaka proposed a variety of strategies for CRC and liver disease.

Fred Hutchinson Cancer Research Center

Dr. Rachel B. Issaka of Fred Hutchinson Cancer Research Center in Seattle suggested multipronged approaches such as telehealth, mailed FIT, and advocacy to address disparities.

For CRC screening, Dr. Issaka suggested noninvasive modalities, including mailed fecal immunochemical tests (FIT), with focused follow-up on patients with highest FIT values. For those conducting CRC research, Dr. Issaka recommended using accessible technology, engaging with community partners, providing incentives where appropriate, and using other methods. For cirrhosis care, Dr. Issaka suggested that practitioners turn to telehealth and remote care, including weight monitoring, cognitive function testing, home medication delivery, and online education.

More broadly, Dr. Issaka called for universal health insurance not associated with employment, research funding for health disparities, sustainable employment wages, climate justice, desegregation of housing, and universal broadband Internet.

"The solutions to these problems are multipronged," Dr. Issaka said. "Some will happen locally; for instance, well-executed planning around telehealth. Some will happen at the state level through opportunities like advocacy or even just reaching out to your own [congressional representative]. And then some will also happen programmatically – How can we as a health system begin to leverage something like mailed FIT?"

Finally, Dr. Issaka suggested that tools from another branch of science can help improve screening rates.

"We don't, in medicine, tap into the benefits of behavioral psychology enough," she said. "That's a great discipline with really great tools that we can all use."

Dr. Issaka described the power of community, in that people are more likely to undergo screening if they know how many others in their community are also being screened.

"I think as much as we can gather those kinds of data and share those with individuals to provide reassurance about the safety and importance of screening, I think [that] will help," she said.

AGA FORWARD program is funded by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (DK118761). Dr. Issaka has no conflicts of interest.

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SOURCES: Issaka RB. AGA FORWARD Program Webinar. 2020 Aug 27; Balzora et al. Gastrointest Endosc. 2020 Jun 20. doi: 10.1016/j.gie.2020.06.042; Tapper et al. J Hepatology. 2020 Apr 13. doi: 10.1016/j.jhep.2020.04.005.

FDA approves new saliva test, COVID-19 can persist

BY LUCAS FRANKI
MDedge News

FDA approves new COVID-19 saliva test

The Food and Drug Administration granted an emergency use authorization to SalivaDirect, a new type of coronavirus test that could cut down on testing costs and the time it takes to process results.

The test, manufactured by Yale University, New Haven, Conn., does not require a special type of swab or collection tube, just a sterile container; the test also does not require a special type of extractor.

Yale University will provide the instructions to labs as an "open source" protocol. The test does not require proprietary equipment, so any lab can manufacture it. This test could cost about $10.

Mounting data support COVID-19 acute pancreatitis

A chart review of nearly 50,000 patients indicates that acute pancreatitis is a possible complication of COVID-19 (Gastroenterology. 2020 Aug 26. doi: 10.1053/j.gastro.2020.08.044).

Of 48,000 patients, 11,883 were positive for SARS-CoV-2. A total of 189 patients had pancreatitis in the entire study population, 32 of whom had COVID-19. The most common etiologies for pancreatitis were gallstones (34%) and alcohol (37%), compared with just 16% and 6% of SARS-CoV2–positive cases of pancreatitis.

Avinash Ketwaroo, MD, of Baylor College of Medicine, Houston, noted that more research is required, but that "there appears to be enough circumstantial evidence to consider a COVID-19 diagnosis in patients presenting with acute pancreatitis."

Infectious COVID-19 can persist in gut

SARS-CoV-2 infection in the GI tract of people with confirmed COVID-19 can persist well after nasopharyngeal swabs yield negative results, and can be present in people without GI symptoms (Gut. 2020 Jul 20. doi: 10.1136/gutjnl-2020-322294).

In a small study, stool samples had genomic evidence of active infection in 7 of 15 people. Positive test results were found up to 6 days after nasopharyngeal swabs returned a negative result, and none of the seven had GI symptoms when they were admitted for COVID-19.

David A. Johnson, MD, chief of gastroenterology at Eastern Virginia Medical School, Norfolk, said that the study has serious implications for people who test negative after COVID-19 infection, as they may be cleared per Centers for Disease Control and Prevention guidelines but still be infectious.

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

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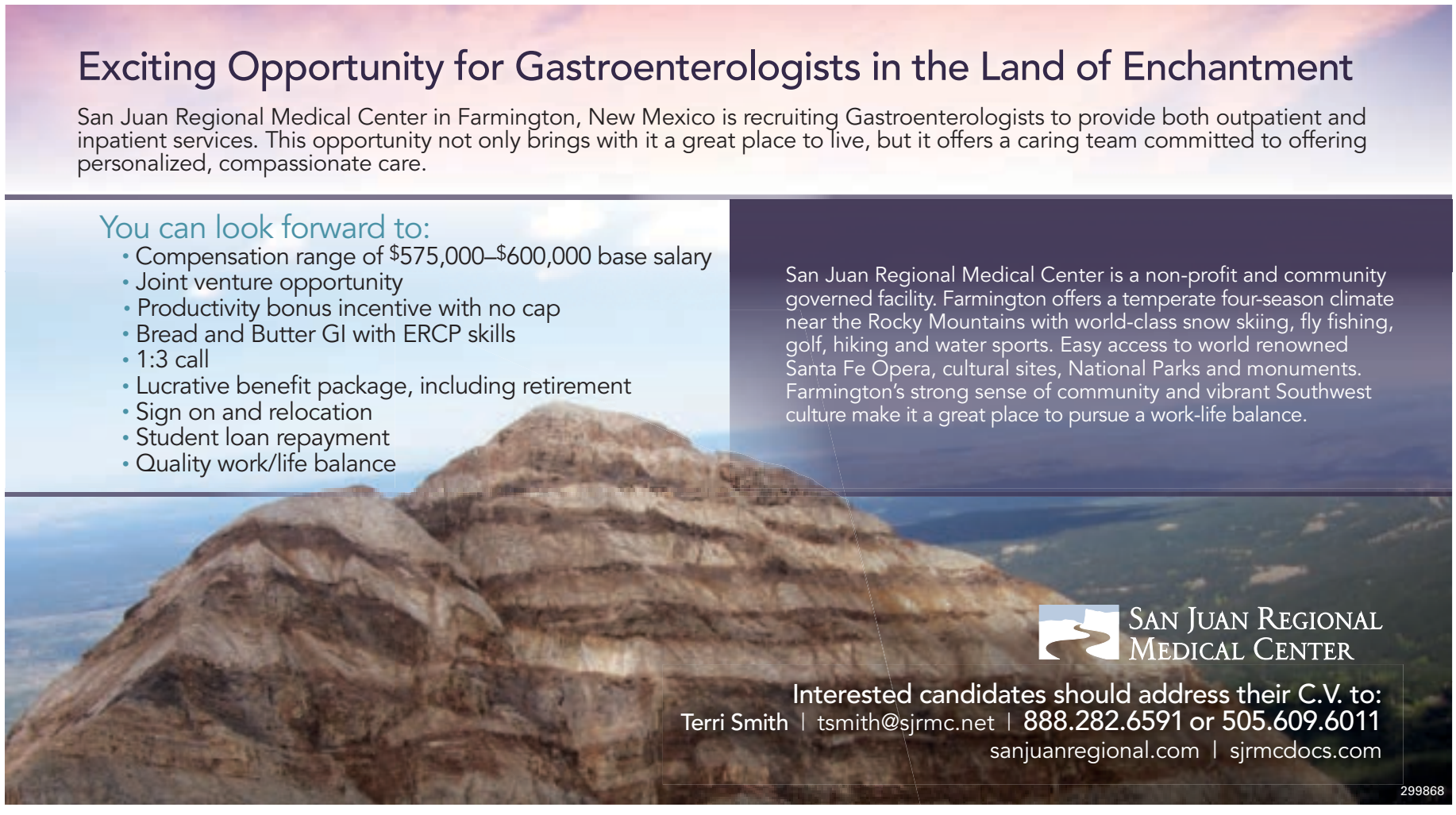

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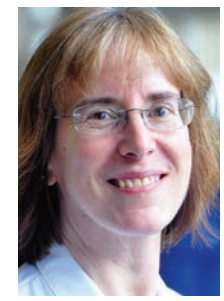
The 2021 proposed Medicare fee schedule: Can the payment cuts be avoided?

BY LISA M. GANGAROSA, MD, AGAF, AND SHIVAN J. MEHTA, MD, MBA

Payment cuts to nearly all of medicine, including gastroenterology, could be in store beginning Jan. 1, 2021. Physicians may also face elimination of some services the Centers for Medicare & Medicaid Services granted temporary access to during the coronavirus (COVID-19) pandemic according CMS's recently released policy and payment recommendations. These proposals could be implemented as physician practices are still recovering financially from states' temporary ban on elective surgeries from March through May 2020 in response to the public health emergency (PHE) and continuing to deal with the clinical and financial challenges of the pandemic.

Dr. Mehta



Dr. Gangarosa

In early August, CMS proposed a number of changes for 2021 that affect physicians. There's plenty of good, bad, and ugly in this proposed rule.

Let's start with two positives (The good):

Medicare proposes to maintain the current values for colonoscopy with biopsy (45385) and esophagogastroduodenoscopy (EGD) with biopsy (43239). Despite a recent reevaluation of these codes in 2016 and 2014, respectively, Medicare conceded to Anthem's suggestion that the procedures were not overvalued and needed another evaluation. The AGA and our sister societies' data affirmed the current values and Medicare proposed to maintain them in 2021.

Medicare proposes to increase the price for scope video system equipment (ES031) from $36,306 to $70,673.38 and the suction machine (Gomco) (EQ235) from $1,981.66 to $3,195.85, phased in over 2 years. This will provide a small increase in the practice expense value for all GI endoscopy procedures. Since CMS began conducting a review of scope systems in 2017, the AGA and our sister societies have successfully worked to convince the Agency to increase its payment for GI endoscopes and associated equipment by providing invoices. We are pleased Medicare is updating these items to reflect more accurate costs.

Now onto items that could negatively affect the practice of gastroenterology.

The bad

Medicare proposes to stop covering and paying for telephone evaluation and management (E/M) visits as soon as the COVID-19 PHE expires. After originally denying that Medicare beneficiaries had trouble accessing video E/M visits and refusing to cover existing telephone (audio only) E/M codes 99441-99443, the agency responded to enormous pressure from AGA and other specialties and added the codes to its covered telehealth services list, setting the payment equal to office/outpatient established patient E/M codes 99212-99214 during the PHE. Telephone E/M has been a vital lifeline, allowing Medicare beneficiaries who don't have a smart phone or reliable internet connection to access needed E/M services, while allowing them to stay safe at home during the PHE. There is evidence that our most vulnerable patients have the greatest need for telephone visits to advance their care.[1]

Medicare's proposal to stop covering and paying for telephone E/M visits as soon as the COVID-19 PHE expires, while disappointing, is not surprising because of the agency's reluctance to admit they were needed in the first place. The agency believes that creating a new code for audio-only patient interactions similar to the virtual check-in code G2012 but for a longer unit of time and with an accordingly higher value will suffice. Physicians

appreciate that E/M delivered via telephone is not the same as a check-in call to a patient, and the care provided requires similar time, effort, and cognitive load as video visits. The AGA and our sister societies plan to object to Medicare's proposal to treat these services as "check-ins" with slightly higher payment and will continue to advocate for permanent coverage of the telephone E/M CPT codes and payment parity with in-person E/M visits.

The ugly

The Medicare Physician Fee Schedule (MPFS) conversion factor, the basis of Medicare payments, is proposed to be cut almost 11% percent from $36.09 in 2020 to $32.26 in 2021.

How it happened

Medicare agreed to implement coding and valuation changes to office and outpatient E/M codes (99202-99205, 99211-99215) in 2021 as recommended by the American Medical Association and widely supported by specialty societies. E/M services account for about 40% of all Medicare spending annually, which magnifies the impact of any changes to their relative value units (RVUs). By law, payment increases that occur from new work RVUs must be offset by a reduction, referred to as a budget-neutral adjustment, applied to offset the increase in total spending on the MPFS.[2]

CMS explained in the 2021 MPFS proposed rule, "If revisions to the RVUs cause expenditures for the year to change by more than $20 million, we make adjustments to ensure that expenditures do not increase or decrease by more than $20 million." Medicare calculated that the corresponding adjustment to the conversion factor for 2021 needed to fall by nearly 11% to achieve budget neutrality. Because gastroenterologists report a significant portion of E/M in addition to performing procedures, the overall estimated impact is –5% of all reimbursement from Medicare.

What you can do

Visit the AGA Advocacy Action Center at https://gastro.quorum.us/AGAactioncenter/ and select "Fight back against CMS's cuts to specialty care payments" to tell your lawmakers to stop these cuts and preserve care for patients by waiving Medicare's budget neutrality requirements for E/M adjustments.

You can also use the AGA's Medicare Physician Fee Schedule Calculator tool to determine the effect of the proposed cuts.[3] By contacting AGA staff, Leslie Narramore, at Lnarramore@gastro.org with the overall effect on your practice, you can help AGA use these data as we work with the physician community to urge Congress to prevent these payment cuts.

What AGA is doing

The AGA and our sister societies have joined the AMA and others in urging Congress and CMS to waive budget-neutrality rules for the implementation of the changes in E/M services effective 2021. We also joined with AMA and over 100 specialty societies in a letter asking Secretary of Health & Human Services Alex Azar that the agency use its authority under the public health emergency declaration to waive budget neutrality for the changes, given these difficult times for practices across the country.

What next steps to take

The AGA and our sister societies are developing comment letters in response to the proposals in the 2021 MPFS proposed rule. Medicare plans to publish its final decisions for 2021 in December. Please do your part by visiting the AGA Advocacy Action Center at https://gastro.quorum.us/AGAactioncenter/ to tell your lawmakers to stop the proposed 2021 payment cuts and preserve care for patients by waiving Medicare's budget-neutrality requirements for E/M adjustments.

References

1. Serper M et al. Positive early patient and clinician experience with telemedicine in an academic gastroenterology practice during the COVID-19 pandemic [published online ahead of print, 2020 Jun 18]. Gastroenterology. 2020;S0016-5085(20)34834-4. doi: 10.1053/j.gastro.2020.06.034.

2. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/MACRA-MIPS-and-APMs/MACRA-MIPS-and-APMs.

3. https://gastro.org/news/prepare-for-and-help-prevent-2021-medicare-cuts-to-gi/.

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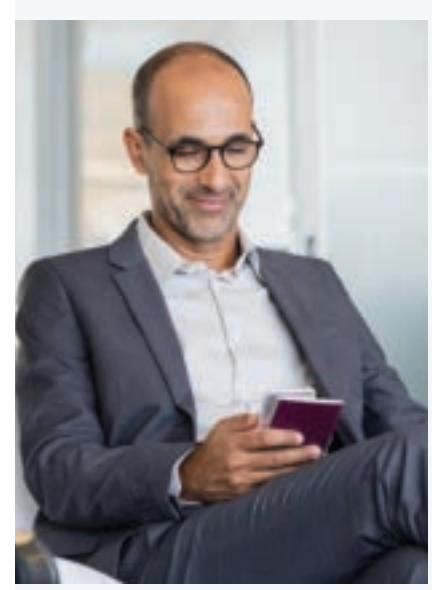

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