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GI&Hepatology News

September 2024 Volume 18 / Number 9

Member SPOTLIGHT

Obesity Is Not a Moral Failing, GI Physician Says

Dr. Janese Laster

Courtesy Dr. Janese Laster

BY JENNIFER LUBELL

MDedge News

Stigma around obesity can have a crippling effect on patients. Janese Laster, MD, sees the impact of this problem every day.

It takes a long time for some patients with obesity to acknowledge that they need help, said Dr. Laster, a bariatric endoscopist who specializes in gastroenterology, nutrition, and obesity medicine at Gut Theory Total Digestive Care, and Georgetown University Hospital in Washington, DC. "If somebody has high blood pressure or has a cut or has chest pain, you don't wait for things. You would go seek help immediately. I wish more patients reached out sooner and didn't struggle."

Another big challenge is making sure patients have insurance coverage for things like medications, surgery, and bariatric endoscopy, she added.

Her response: education and advocacy. "I'm giving as many talks as I can to fellows, creating courses for residents and fellows and medical students" to change the way physicians talk about obesity and excess weight, she said. Patients need to understand that physicians care about them, that "we're not judging and we're changing that perspective."

See **Obesity** · *page 22*

Tirzepatide Shows Improvements in MASH Resolution, Fibrosis

BY BECKY MCCALL

FROM EASL 2024

MILAN — Tirzepatide, a glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor agonist, was more effective than was placebo in the resolution of metabolic dysfunction–associated steatohepatitis (MASH) and in the improvement of fibrosis, according to the results of the phase 2 SYNERGY-NASH trial.

Specifically, 44%-62% of participants with MASH and moderate or severe fibrosis treated with 5-15 mg of tirzepatide achieved MASH resolution without worsening of fibrosis compared with 10% on placebo; 51%-55% of those on tirzepatide achieved at least one stage of fibrosis improvement without worsening of MASH compared with 30% on placebo. Tirzepatide also led to weight loss.

The study (Abstract LBO-001) was presented at the European Association for the Study of the Liver (EASL) Congress 2024 by Rohit Loomba, MD, professor of medicine, NAFLD [nonalcoholic fatty liver disease] Research Center, University of California at San Diego in La Jolla, and published simultaneously in *The New England Journal of Medicine*.

"The results are clinically meaningful," Dr. Loomba said in an interview.

Both of the endpoints — improvements in MASH resolution and fibrosis — are considered approvable endpoints for MASH therapeutic development, and therefore, increase the likelihood of success of using

See **MASH** · *page 23*

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LETTER FROM THE EDITOR

A New Era of Obesity Medicine

Obesity has now reached epidemic proportions, with global prevalence of the condition increasing more than threefold between 1975 and 2022. In the United States alone, roughly two in five adults have obesity. As healthcare providers are intimately aware, obesity is linked to many serious health conditions, including type 2 diabetes, cardiovascular disease, and metabolic-associated steatotic liver disease, as well as some forms of cancer. As such, it presents a major challenge to chronic disease prevention and overall health.

Dr. Adams

For many years, management of obesity was considered within the purview of primary care as part of chronic disease management. However, as obesity has become more common, our understanding of the underlying causes of obesity has improved, and optimal strategies to manage and treat obesity have evolved. A new field of obesity medicine has arisen, attracting specialists such as gastroenterologists, surgeons, endocrinologists, and others. From glucagon-like peptide 1 agonists to an expanding armamentarium of bariatric procedures, emerging therapeutics have revolutionized treatment of patients with obesity and related health conditions.

As obesity has become more common, our understanding of the underlying causes of obesity has improved, and optimal strategies to manage and treat obesity have evolved.

In this month's Member Spotlight, we introduce you to gastroenterologist Janese Laster, who has built a successful career with a primary focus on obesity medicine. She shares her passionate perspective on why gastroenterologists should play a more prominent role in management of this complex, chronic disease. We also include a summary of obesity-related content presented as part of this spring's AGA Postgraduate Course, with helpful clinical pearls from experts Dr. Andres Acosta, Dr. Violeta Popov, Dr. Sonali Paul, and Dr. Pooja Singhal.

AGA

Dr. Andres Acosta (left) and Dr. Janese Laster spoke at a June 2024 AGA congressional briefing to educate and increase awareness about the obesity epidemic.

Also in our September issue, we highlight a recent, practice-changing randomized controlled trial from *Clinical Gastroenterology and Hepatology* supporting use of snare tip soft coagulation as the preferred thermal margin treatment to reduce recurrence rates following colorectal endoscopic mucosal resection. In our quarterly Perspectives column, Dr. Maggie Ham and Dr. Petr Protiva offer their insights into a pressing question on many of our minds — whether to take the 10-year "high-stakes" exam or opt for the Longitudinal Knowledge Assessment to maintain American Board of Internal Medicine certification. As always, thanks for reading and please don't hesitate to reach out with suggestions for future coverage. ■

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Editor in Chief

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AGA Clinical Guidelines

AGA Issues Guidance on Identifying, Treating Cyclic Vomiting Syndrome

BY CAROLYN CRIST
MDedge News

FROM GASTROENTEROLOGY

Clinicians and patients should become familiar with the signs and symptoms of cyclic vomiting syndrome (CVS), including sudden episodes of intense nausea, vomiting, and retching amid episode-free periods, according to a new clinical practice update (CPU) from the American Gastroenterological Association.


Dr. Levinthal

CVS affects up to 2% of US adults and is more common in women, young adults, and those with a personal or family history of migraine headaches. However, most patients don't receive a diagnosis or often experience years of delay in receiving effective treatment.

"A diagnosis is a powerful tool. Not only does it help patients make sense of debilitating symptoms, but it allows healthcare providers to create an effective treatment plan," said author David J. Levinthal, MD, AGAF, director of the Neurogastroenterology and Motility Center at the University of Pittsburgh Medical Center.

"Our goal with this clinical practice update is to increase awareness of cyclic vomiting syndrome to reduce the diagnostic delay and increase patients' access to treatment," he said. "We hope to reach primary care, ER, and urgent care providers who are on the frontlines interacting with CVS patients seeking care, especially during an attack."

The update was published online in *Gastroenterology* (2024 July. doi: 10.1053/j.gastro.2024.05.031).

Understanding CVS

CVS is a chronic disorder of gut-brain interaction (DGBI), which is characterized by acute episodes of nausea and vomiting, separated by time without symptoms. Patients can usually identify a pattern of symptoms that show up during and between episodes.

CVS can vary, ranging from mild — with less than four episodes per year and lasting less than 2 days — to moderate-severe — with more than four episodes per year, lasting more than 2 days, and requiring at least one emergency department (ED) visit or hospitalization.

The disorder has four distinct phases — inter-episodic, prodromal, emetic, and recovery — that align with distinct treatment and management strategies. Between episodes, patients typically don't experience repetitive vomiting but may experience symptoms such as mild nausea, indigestion, and occasional vomiting. Although CVS episodes can happen at any time, most tend to occur in the early morning.

For diagnosis, clinicians should consider CVS in adults presenting with episodic bouts of repetitive vomiting, following criteria established by the Rome Foundation. Rome IV criteria include acute-onset vomiting lasting less than 7 days, at least three discrete episodes in a year with two in the previous 6 months, and an absence of vomiting between episodes separated by at least 1 week of baseline health.

'Our goal … is to increase awareness of cyclic vomiting syndrome to reduce the diagnostic delay and increase patients' access to treatment. We hope to reach primary care, ER, and urgent care providers who are on the frontlines interacting with CVS patients seeking care.'

About 65% of patients with CVS experience prodromal symptoms, which last for about an hour before the onset of vomiting and may include panic, a sense of doom, and an inability to communicate effectively. During prodromal or emetic phases, patients have reported fatigue, brain fog, restlessness, anxiety, headache, bowel urgency, abdominal pain, flushing, or shakiness.

'Providing an individualized care plan for all patients could potentially address this problem and improve the physician-patient interaction. Efforts to raise awareness among the medical community and increase patient and provider engagement can optimize outcomes.'

As with migraines, CVS episodes may often be triggered by psychological and physiological factors, particularly stress. Episodes can stem from negative stress, such as a death or relationship conflicts, and positive stress, such as birthdays and vacations. Other triggers include sleep deprivation, hormonal fluctuations linked to the menstrual cycle, motion sickness, or acute infections.

Adult CVS is associated with several conditions, particularly mood disorders, including anxiety, depression, and panic disorder. Patients may also experience migraines, seizure disorders, or autonomic imbalances, such as postural orthostatic tachycardia syndrome, which may indicate pathophysiological mechanisms and routes for management.

The American Neurogastroenterology and Motility Society recommends testing to rule out similar or overlapping conditions, such as Addison's disease, hypothyroidism, and hepatic porphyria. Diagnostic workup should include blood work, urinalysis, and one-time esophagogastroduodenoscopy or upper gastrointestinal imaging. Repeated imaging and gastric emptying scans should be avoided.

Providing Treatment and Prevention

For treatment, knowing the CVS phase is "essential," the authors wrote. During the prodromal phase, abortive therapies can halt the transition to the emetic phase, and early intervention is associated with a higher probability of stopping an episode. Intranasal sumatriptan, ondansetron, antihistamines, and sedatives are recommended.

During the emetic phase, supportive therapy can help terminate the episode. This may include continuing the abortive regimen and going to the ED for hydration and antiemetic medications. Patients may also find relief in a quiet, darker room in the ED, along with IV benzodiazepines, with the goal of inducing sedation.

During the recovery phase, patients should rest and focus on rehydration and nutrition to return to the well phase.

During the well or inter-episodic phase, patients can follow lifestyle measures to identify and avoid triggers, such as taking prophylactic medication (tricyclic antidepressants, anticonvulsants, and neurokinin-1 receptor antagonists such as aprepitant), reducing stress, and implementing a good sleep routine.


Dr. Frazier

As part of patient education, clinicians can discuss the four phases and rehearse the actions to take to prevent or stop an episode.

"The unpredictable and disruptive nature of episodes can result in reduced health-related quality of life, job loss precipitated by work absenteeism, and even divorce," said Rosita Frazier, MD, a gastroenterologist at Mayo Clinic Arizona in Scottsdale who specializes in DGBI and CVS. Dr. Frazier, who wasn't involved with the CPU, has written about CVS diagnosis and management.

Patients often report negative interactions with physicians, particularly in the ED, where they may request specific treatments based on past experiences but are labeled as "drug seeking" and denied standard medical treatment.

"Providing an individualized care plan for all patients could potentially address this problem and improve the physician-patient interaction," she said. "Efforts to raise awareness among the medical community and increase patient and provider engagement can optimize outcomes."

The authors received no specific funding for this update. Dr. Levinthal is a consultant for Takeda Pharmaceuticals and Mahana. Dr. Frazier reported no relevant financial disclosures. ■

Late ERCP Is Incurring More Adverse Events

BY WILL PASS
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

First-time endoscopic retrograde cholangiopancreatography (ERCP) is increasingly being performed more than 1 year after cholecystectomy, leading to a rise in morbidity and adverse outcomes, according to investigators.

These findings suggest a need for more careful patient selection with ERCP, and greater reliance upon noninvasive imaging prior to considering the procedure, reported lead author Nikhil R. Thiruvengadam, MD, of Loma Linda University Health, Loma Linda, California, and colleagues.

"It is assumed that cholecystectomy is a definitive procedure for symptomatic gallstone disease in patients without concomitant choledocholithiasis," the investigators wrote in *Clinical Gastroenterology and Hepatology* (2024 Apr 9. doi: 10.1016/j.cgh.2024.03.027). "This is because the development of primary choledocholithiasis is rare. Despite this, many patients have persistent or new gastrointestinal symptoms post cholecystectomy."

Symptoms such as a dilated bile duct or abnormal liver function tests may suggest choledocholithiasis or sphincter of Oddi disorders (SOD), they noted, but recent data supporting ERCP for SOD show no significant benefit for patients with normal-sized ducts.


Dr. Thiruvengadam

"Guidelines advocate for confirming the presence of choledocholithiasis using magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) given the substantial risks associated with ERCP," Dr. Thiruvengadam and colleagues wrote.

Real-world implementation of this and associated strategies, however, remain unclear, prompting the present study.

The dataset, drawn from the Optum Clinformatics Data Mart, included 583,712 adults who had undergone cholecystectomy from 2004 to 2019, focusing on 4274 individuals who had their first ERCP more than 1 year post surgery. The investigators assessed the incidence, characteristics, and outcomes of these late ERCP procedures, exploring their association with patient comorbidities and the use of biliary imaging techniques such as MRCP and EUS.

From 2004 to 2021, use of noninvasive biliary imaging approximately doubled from 35.9% to 65.5% ($P < .001$). Yet incidence of first-time ERCP more than 1 year after cholecystectomy increased much more — by eightfold — from 0.5 to 4.2 per 1000 person-years ($P < .001$). Less than half (44%) of these late ERCP procedures involved gallstone removal.

Patients undergoing late ERCP were more likely to have higher baseline comorbidities, including disorders of gut-brain interaction (DGBI) and metabolic dysfunction–associated steatotic liver disease. They were also more likely to be taking an antispasmodic, anxiolytic, or chronic opioid medication.

"Late ERCP is more common and associated with worse outcomes, presumably because of higher baseline comorbidities that overlap with DGBI and mimickers of choledocholithiasis," the investigators noted. "These highly symptomatic individuals are more likely to undergo noninvasive biliary imaging, which seems to be prompting more late ERCP."

In turn, late ERCP is incurring more adverse events, including post-ERCP pancreatitis (7.1%), hospitalization (13.1%), and new chronic opioid use (9.7%).

"Given the known risks of ERCP, especially in this context, there remains a need to be more restrictive with offering ERCP in this setting," Dr. Thiruvengadam and colleagues concluded. "ERCP should be used sparingly for patients who do not have confirmed choledocholithiasis until future studies ... can define which patients with a remote history of cholecystectomy respond to ERCP interventions."

The investigators disclosed relationships with Olympus, Medtronic, ACI, and others. ■

Automated ERCP Report Card Offers High Accuracy, Minimal Work

BY WILL PASS
MDedge News

FROM TECHNIQUES AND INNOVATIONS IN GASTROINTESTINAL ENDOSCOPY

A new endoscopic retrograde cholangiopancreatography (ERCP) report card automatically imports and analyzes performance metrics from endoscopy records, offering a real-time gauge of both individual- and institutional-level quality indicators, according to the developers.

The tool boasts an accuracy level exceeding 96%, integrates with multiple electronic health records (EHRs), and requires minimal additional work time, reported Anmol Singh, MD, of TriStar Centennial Medical Center, Nashville, Tennessee, and colleagues.

"Implementation of quality indicator tracking remains difficult due to the complexity of ERCP as compared with other endoscopic procedures, resulting in significant limitations in the extraction and synthesis of these data," the investigators wrote in *Techniques and Innovations in Gastrointestinal Endoscopy* (2024 Mar. doi: 10.1016/j.tige.2024.03.007). "Manual extraction methods such as self-assessment forms and chart reviews are both time intensive and error prone, and current automated extraction methods, such as natural language processing, can require substantial resources to implement and undesirably complicate the endoscopy work flow."

To overcome these challenges, Dr. Singh and colleagues designed an analytics tool that automatically collects ERCP quality indicators from endoscopy reports with "minimal input" from the endoscopist, and is compatible with "any electronic reporting system."

Development relied upon endoscopy records from 2146 ERCPs performed by 12 endoscopists at four facilities. The most common reason for ERCP was choledocholithiasis, followed by malignant and benign biliary stricture. Most common procedures were stent placement and sphincterotomy.

Data were aggregated in a Health Level–7 (HL-7) interface, an international standard system that enables compatibility between different types of EHRs. Some inputs were entered by the performing endoscopist via drop-down menus. Next, data were shifted into an analytics suite, which evaluated quality indicators, including cannulation difficulty and success rate, and administration of post-ERCP pancreatitis prophylaxis.

Manual review showed that this approach yielded an accuracy of 96.5%-100%.

Beyond this high level of accuracy, Dr. Singh and colleagues described several reasons why their tool may be superior to previous attempts at an automated ERCP report card.

"Our HL-7–based tool offers several advantages, including versatility via compatibility with multiple types of commercial reporting software and flexibility in customizing the type and aesthetic of the data displayed," they wrote. "These features improve the user interface, keep costs down, and allow for integration into smaller or nonacademic practice settings."

They also highlighted how the tool measures quality in relation to procedure indication and difficulty at the provider level.

"Unlike in colonoscopy, where metrics such as adenoma detection rate can be ubiquitously applied to all screening procedures, the difficulty and risk profile of ERCP is inextricably dependent on patient and procedural factors such as indication of the procedure, history of interventions, or history of altered anatomy," Dr. Singh and colleagues wrote. "Prior studies have shown that both the cost-effectiveness and complication rates of procedures are influenced by procedural indication and complexity. As such, benchmarking an individual provider's performance necessarily requires the correct procedural context."

With further optimization, this tool can be integrated into various types of existing endoscopy reporting software at a reasonable cost, and with minimal impact on routine work flow, the investigators concluded.

The investigators disclosed relationships with AbbVie, Boston Scientific, Organon, and others. ■

Dog Ownership Linked With Reduced Crohn's Risk

BY WILL PASS
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

People who live with at least two other people in their first year of life and have a dog during childhood may be at reduced risk of developing Crohn's disease (CD), according to investigators.

Those who live with a pet bird may be more likely to develop CD, although few participants in the study lived with birds, requiring a cautious interpretation of this latter finding, lead author Mingyue Xue, PhD, of Mount Sinai Hospital, Toronto, Ontario, Canada, and colleagues reported.

"Environmental factors, such as smoking, large families, urban environments, and exposure to pets, have been shown to be associated with the risk of CD development," the investigators wrote in *Clinical Gastroenterology and Hepatology* (2024 May. doi: 10.1016/j.cgh.2024.03.049). "However, most of these studies were based on a retrospective study design, which makes it challenging to understand when and how environmental factors trigger the biological changes that lead to disease."

The present study prospectively followed 4289 asymptomatic first-degree relatives (FDRs) of patients with CD. Environmental factors were identified via regression models that also considered biological factors, including gut inflammation via fecal calprotectin (FCP) levels, altered intestinal permeability measured by urinary fractional excretion of lactulose to mannitol ratio (LMR), and fecal microbiome composition through 16S rRNA sequencing.

After a median follow-up period of 5.62 years, 86 FDRs (1.9%) developed CD.

Living in a household of at least three people in the first year of life was associated with a 57% reduced risk of CD development (hazard ratio [HR], 0.43; $P = .019$). Similarly, living with a pet dog between the ages of 5 and 15 also demonstrated a protective effect, dropping risk of CD by 39% (HR, 0.61; $P = .025$).

"Our analysis revealed a protective trend of living with dogs that transcends the age of exposure, suggesting that dog ownership could confer health benefits in reducing the risk of CD," the investigators wrote. "Our study also found that living in a large family during the first year of life is significantly associated with the future onset of CD, aligning with prior research that indicates that a larger family size in the first year of life can reduce the risk of developing IBD."

'Our analysis revealed a protective trend of living with dogs that transcends the age of exposure, suggesting that dog ownership could confer health benefits in reducing the risk of CD.'

In contrast, the study identified bird ownership at time of recruitment as a risk factor for CD, increasing risk almost threefold (HR, 2.84; $P = .005$). The investigators urged a careful interpretation of this latter finding, however, as relatively few FDRs lived with birds.

"[A]lthough our sample size can be considered large, some environmental variables were uncommon, such as the participants having birds as pets, and would greatly benefit from replication of our findings in other cohorts," Dr. Xue and colleagues noted.

They suggested several possible ways in which the above environmental factors may impact CD risk, including effects on subclinical inflammation, microbiome composition, and gut permeability.

"Understanding the relationship between CD-related environmental factors and these predisease biomarkers may shed light on the underlying mechanisms by which environmental factors impact host health and ultimately lead to CD onset," the investigators concluded.

The study was supported by Crohn's and Colitis Canada, Canadian Institutes of Health Research, the Helmsley Charitable Trust, and others. The investigators disclosed no conflicts of interest. ■

Stool-Based Methylation Test May Improve CRC Screening

BY WILL PASS
MDedge News

FROM GASTROENTEROLOGY

A new stool-based syndecan-2 methylation (mSDC2) test may improve the detection of colorectal cancer (CRC) and advanced colorectal neoplasia (ACN), based on a prospective, real-world study.

These findings suggest that the mSDC2 assay could improve the efficacy and resource utilization of existing screening programs, reported co–lead authors Shengbing Zhao, MD, and Zixuan He, MD, of Naval Medical University, Shanghai, China, and colleagues.

"Conventional risk-stratification strategies, such as fecal immunochemical test (FIT) and life risk factors, are still criticized for being inferior at identifying early-stage CRC and ACN, and their real-world performance is probably further weakened by the low annual participation rate and compliance of subsequent colonoscopy," the investigators wrote in *Gastroenterology* (2024 Aug. doi: 10.1053/j.gastro.2024.04.019).

Recent case studies have reported "high diagnostic performance" using stool-based testing for mSDC2, which is "the most accurate single-targeted gene" for colorectal neoplasia, according to the investigators; however, real-world outcomes have yet to be demonstrated, prompting the present study.

The prospective, multicenter, community-based trial compared the diagnostic performance of the mSDC2 test against FIT and Asia-Pacific Colorectal Screening (APCS) scores.

The primary outcome was detection of ACN. Secondary outcomes included detection of CRC, early-stage CRC, colorectal neoplasia (CN), and clinically relevant serrated polyp (CRSP). Screening strategies were also compared in terms of cost-effectiveness and impact on colonoscopy workload.

The final dataset included 10,360 participants aged 45-75 years who underwent screening between 2020 and 2022.

After determining APCS scores, stool samples were analyzed for mSDC2 and FIT markers. Based on risk stratification results, participants were invited to undergo colonoscopy. A total of 3381 participants completed colonoscopy, with 1914 from the increased-risk population and 1467 from the average-risk population.

Participants who tested positive for mSDC2 had significantly higher detection rates for all measured outcomes than those who tested negative (all, $P < .05$). For example, the detection rate for ACN was 26.6% in mSDC2-positive participants, compared with 9.3% in mSDC2-negative participants, with a relative risk of 2.87 (95% CI, 2.39-3.44). For CRC, the detection rate was 4.2% in mSDC2-positive participants vs 0.1% in mSDC2-negative participants, yielding a relative risk of 29.73 (95% CI, 10.29-85.91). Performance held steady across subgroups.

The mSDC2 test demonstrated cost-effectiveness by significantly reducing the number of colonoscopies needed to detect one case of ACN or CRC. Specifically, the number of colonoscopies needed to screen for ACN and CRC was reduced by 56.2% and 81.5%, respectively. Parallel combinations of mSDC2 with APCS or FIT enhanced both diagnostic performance and cost-effectiveness.

"This study further illustrates that the mSDC2 test consistently improves predictive abilities for CN, CRSP, ACN, and CRC, which is not influenced by subgroups of lesion location or risk factors, even under the risk stratification by FIT or APCS," the investigators wrote. "The excellent diagnostic ability of mSDC2 in premalignant lesions, early-stage CRC, and early-onset CRC indicates a promising value in early detection and prevention of CRC. ... The mSDC2 test or a parallel combination of multiple screening methods might be promising to improve real-world CRC screening performance and reduce colonoscopy workload in community practice."

The study was supported by the National Key Research and Development Program of China, Deep Blue Project of Naval Medical University, the Creative Biosciences, and others. The investigators reported no conflicts of interest. ■

Risk Stratification May Work Well for FIT-Based CRC Screening in Elderly

BY CAROLYN CRIST
MDedge News

FROM DDW 2024

WASHINGTON — A risk-stratified upper age limit may be beneficial for colorectal cancer (CRC) screening among patients who are ages 75 and older, according to a study presented at the annual Digestive Disease Week® (DDW).

In particular, interval CRC risk can vary substantially based on the fecal hemoglobin (f-Hb) concentration in the patient's last fecal immunochemical test (FIT), as well as the number of prior screening rounds.

"Less is known about what happens after the upper age limit has been reached and individuals are not invited to participate in more screening rounds. This is important as life expectancy is increasing, and it is increasingly important to consider the most efficient way of screening the elderly," said lead author Brenda van Stigt, a PhD candidate focused on cancer screening at Erasmus University Medical Center in Rotterdam, the Netherlands.

In the Netherlands, adults between ages 55 and 75 are invited to participate in stool-based CRC screening every 2 years. Based on a FIT threshold of 47 µg Hb/g, those who test positive are referred to colonoscopy, and those who test negative are invited to participate again after a 2-year period.

FIT can play a major role in risk stratification, Ms. van Stigt noted, along with other factors that influence CRC risk, such as age, sex, and CRC screening history. Although this is documented for ages 55-75, she and colleagues wanted to know more about what happens after age 75.

Ms. Van Stigt and colleagues conducted a population-based study by analyzing Dutch national cancer registry data and FIT results around the final screening at age 75, looking at those who were diagnosed with CRC within 24 months of their last negative FIT. The researchers assessed interval CRC risk and cancer stage, accounting for sex, last f-Hb concentration, and the number of screening rounds.

Among 305,761 people with a complete 24-month follow-up after a negative FIT, 661 patients were diagnosed with interval CRC, indicating an overall interval CRC risk of 21.6 per 10,000 individuals with a negative FIT. There were no significant differences by sex.

However, there were differences by screening rounds, with those who had participated in three or four screening rounds having a lower risk than those who participated only once (hazard ratio [HR], 0.49).

In addition, those with detectable f-Hb (> 0 µg Hb/g) in their last screening round had a much higher interval CRC risk (HR, 4.87), at 65.8 per 10,000 negative FITs, compared with 13.8 per 10,000 among those without detectable f-Hb. Interval CRC risk also increased over time for those with detectable f-Hb.

About 15% of the total population had detectable f-Hb, whereas 46% of those with interval CRC had detectable f-Hb, Ms. van Stigt said, meaning that nearly half of patients who were diagnosed with interval CRC already had detectable f-Hb in their prior FIT.

In a survival analysis, there was no association between interval CRC risk and sex. However, those who participated in three or four screening rounds were half as likely to be diagnosed than those who participated once or twice, and those with detectable f-Hb were five times as likely to be diagnosed.

For late-stage CRC, there was no association with sex or the number of screening rounds. Detectable f-Hb was associated with not only a higher risk of interval CRC but also a late-stage diagnosis.

"These findings indicate that one uniform age to stop screening is suboptimal," Ms. van Stigt said. "Personalized screening strategies should, therefore, also ideally incorporate a risk-stratified age to stop screening."

The US Preventive Services Task Force recommends that clinicians personalize screening for ages 76-85, accounting for overall health, prior screening history, and patient preferences.

"But we have no clear guidance on how to quantify or weigh these factors. This interesting study highlights how one of these factors (prior screening history) and fecal hemoglobin level (an emerging factor) are powerful stratifiers of subsequent colorectal cancer risk," said Sameer D. Saini, MD, AGAF, director and research investigator at the VA Ann Arbor Healthcare System's Center for Clinical Management Research. Dr. Saini wasn't involved with the study.

At the clinical level, Dr. Saini said, sophisticated modeling is needed to understand the interaction with competing risks and identify the optimal screening strategies for patients at varying levels of cancer risk and life expectancy. Models could also help to quantify the population benefits and cost-effectiveness of personalized screening.

"Finally, it is important to note that, in many health systems, access to quantitative FIT may be limited," he said. "These data may be less informative if colonoscopy is the primary mode of screening."

Ms. van Stigt and Dr. Saini reported no relevant disclosures. ■

PPI Prophylaxis Prevents GI Bleed in Ventilated Patients

BY MARILYNN LARKIN

Proton-pump inhibitor (PPI) prophylaxis in patients undergoing mechanical ventilation can prevent upper gastrointestinal (GI) bleeding and appears to have no effect on mortality, according to a randomized trial and a systematic review led by researchers at McMaster University, Hamilton, Ontario, Canada.

Patients in the intensive care unit (ICU) who need mechanical ventilation typically are given a PPI, such as pantoprazole, to prevent upper GI bleeding caused by stress-induced stomach ulcers, but some evidence suggested that their use might increase the risk for pneumonia and death in the most severely ill patients.

As a result, recent guidelines have issued only weak recommendations for stress ulcer prophylaxis, especially with PPIs, in critically ill patients at a high risk for bleeding, Deborah Cook, MD, professor of medicine at McMaster University, and colleagues noted.

To address clinical questions, they investigated the efficacy and safety of PPIs to prevent upper GI bleeding in critically ill patients.

Both the randomized trial in *The New England Journal of Medicine* (2024 Jun 14. doi: 10.1056/NEJMoa2404245) and the systematic review in *NEJM Evidence* (2024 Jun 14. doi: 10.1056/EVIDoa2400134) were published online in June.

Significantly Lower Bleeding Risk

The REVISE trial, conducted in eight countries, compared pantoprazole 40 mg daily with placebo in critically ill adults on mechanical ventilation.

The primary efficacy outcome was clinically important upper GI bleeding in the intensive care unit (ICU) at 90 days, and the primary safety outcome was death from any cause at 90 days.

A total of 4821 patients in 68 ICUs were randomly assigned to the pantoprazole group or placebo group.

Clinically important upper GI bleeding occurred in 25 patients (1%) receiving pantoprazole and in 84 patients (3.5%) receiving placebo. At 90 days, 696 patients (29.1%) in the pantoprazole group died, as did 734 (30.9%) in the placebo group.

No significant differences were found on key secondary outcomes, including ventilator-associated pneumonia and *Clostridioides difficile* infection in the hospital.

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The authors concluded that pantoprazole resulted in a significantly lower risk for clinically important upper GI bleeding than placebo, and it had no significant effect on mortality.

Disease Severity as a Possible Factor

The systematic review included 12 randomized controlled trials comparing PPIs with placebo or no prophylaxis for stress ulcers in a total of 9533 critically ill adults. The researchers performed meta-analyses and assessed the certainty of the evidence. They also conducted a subgroup analysis combining within-trial subgroup data from the two largest trials.

They found that PPIs were associated with a reduced incidence of clinically important upper GI bleeding (relative risk [RR], 0.51, with high certainty evidence) and may have little or no effect on mortality (RR, 0.99, with low-certainty evidence).

However, the within-trial subgroup analysis with intermediate credibility suggested that the effect of PPIs on mortality may differ based on disease severity. The results also raised the possibility that PPI use may decrease 90-day mortality in less severely ill patients (RR, 0.89) and increase mortality in more severely ill patients (RR, 1.08). The mechanisms behind this possible signal are likely multifactorial, the authors noted.

In addition, the review found that PPIs may have no effect on pneumonia, duration of ICU stay, or duration of hospital stay, and little or no effect on *C difficile* infection or duration of mechanical ventilation (low-certainty evidence).

"Physicians, nurses, and pharmacists working in the ICU setting will use this information in practice right away, and the trial results and the updated meta-analysis will be incorporated into international practice guidelines," Dr. Cook said.

Both studies had limitations. The REVISE trial did not include patient-reported disability outcomes, and the results may not be generalizable to patients with unassisted breathing. The systematic review included studies with diverse definitions of bleeding and pneumonia, and with mortality reported at different milestones, without considering competing risk analyses. Patient-important GI bleeding was available in only one trial. Other potential side effects of PPIs, such as infection with multidrug-resistant organisms, were not reported.

In an editorial accompanying both studies (N Engl J Med. 2024 June. doi: 10.1056/NEJMe2405782), Samuel M. Brown, MD, a pulmonologist and vice president of research at Intermountain Health, Salt Lake City, Utah, said that the REVISE trial was "well designed and executed, with generalizable eligibility criteria and excellent experimental separation." He said the researchers had shown that PPIs "slightly but significantly" decrease the risk of important GI bleeding and have a "decent chance" of slightly decreasing mortality in less severely ill patients during mechanical ventilation. At the same time, he noted, PPIs "do not decrease — and may slightly increase — mortality" in severely ill patients.

Dr. Brown wrote that, in his own practice, he intends to prescribe prophylactic PPIs to patients during mechanical ventilation "if they have an APACHE II score of less than 25" or a reasonable equivalent. The APACHE II scoring system is a point-based system that estimates a patient's risk of death while in an ICU.

"For sicker patients, I would probably reserve the use of proton-pump inhibitors for those who are being treated with antiplatelet agents, especially in the presence of therapeutic anticoagulants," he added.

REVISE was supported by numerous grants from organizations in several countries. No funding was specified for the systematic review. Author disclosures and other supplementary materials are available with the full text of the article. ■

Environment Linked to Age of IBD Diagnosis

BY DIANA SWIFT

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Early-life and environmental exposures are more strongly linked to age at diagnosis of inflammatory bowel disease (IBD) than genetic factors, a large study of IBD patients reported.

Published in *Clinical Gastroenterology and Hepatology* (2024 Jan. doi: 10.1016/j.cgh.2024.01.020), the study found that environment influences the onset of both ulcerative colitis (UC) and Crohn's disease (CD), and exposures typical in Western society lower the age of diagnosis. These factors include birth in a developed nation, delivery by C-section, and more bathrooms in the home, according to Oriana M. Damas, MD, MSCTI, an associate professor of clinical medicine at the University of Miami Miller School of Medicine in Florida and colleagues.

Environmental factors explained 21% of the variance in age of CD diagnosis and 39% of the variance in age of UC diagnosis. In models incorporating both genetic and environmental risk scores, the environment was the only significant factor associated with younger age of IBD diagnosis in all groups.

Several epidemiologic studies have examined environmental culprits in IBD, and others have examined genetic risk factors, Dr. Damas said in an interview. "But we had not seen any studies that examined the influence of both [of] these on age of IBD development." Her group's working hypothesis that environment would have a greater effect than genetics was borne out.

"Additionally, very few studies have examined the contribution of genetics or environmental factors in Hispanic individuals, and our study examined the contribution of these factors in this understudied population," she added.

According to Dr. Damas, the findings' most immediate clinical relevance is for counseling people with a family history of IBD. "I think it's important for concerned patients to know that IBD is not solely genetic and that several environmental factors can shape disease risk to a greater extent than genetic predisposition," she said

Westernization is increasingly considered a contributor to the global increase in IBD, which has been diagnosed in an estimated 2.39 million Americans (Gastroenterology. 2023 July. doi: 10.1053/j.gastro.2023.07.003). In genetically predisposed individuals, environmental culprits in developed countries are thought to negatively shape the intestinal microbiome's composition into a less tolerant and more proinflammatory state, the authors noted.

Dr. Damas

'It was interesting to find an association between reported plastic water bottle use and younger age of IBD diagnosis. Because this is a self-reported intake, we need more studies to confirm this. However, this finding falls in line with other recent studies showing a potential association between microplastics and disease states, including IBD.'

According to the "hygiene hypothesis" (Inflamm Bowel Dis. 2016 Sept. doi: 10.1097/MIB.0000000000000852), the oversanitization of life in the developed world is partly to blame. "A cleaner environment at home, part of the hygiene hypothesis, has been postulated as a theory to help explain the rise of autoimmune diseases in the 21st century and may play an important part in explaining our study findings," the authors wrote.

Population-based studies have also pointed to antibiotics, nonsteroidal anti-inflammatory drugs, smoking, cesarean delivery, lack of breastfeeding, and nonexposure to farm animals as other risk factors for IBD.

Study Details

To compare the effect of environmental vs genetic risk factors, the questionnaire-based study surveyed 2952 IBD patients from a tertiary care referral center — 58.9% with CD, 45.83% of Hispanic background, and 53.18% of non-Hispanic White (NHW) ethnicity. There were too few available Black and Asian patients to be included in the cohort. Data were collected from 2017 to 2022.

The mean age of patients was 39.71 years, and 34.14% were defined as born outside of the US mainland. Foreign-born patients were further characterized as from developed nations vs developing nations; 81.3% in this subgroup came from the latter. A detailed questionnaire probed 13 potential environmental factors from type of birth to domestic living conditions, medications, and smoking across several different age groups. Blood was drawn to genotype participants and to create a genetic risk score.

Early plastic water bottle use — which has been linked to inflammatory microplastics in the intestines — and residing in homes with more than one bathroom (and presumably less exposure to infections) were also associated with younger age at diagnosis. Susceptibility to environmental exposures was similar in Hispanic and NHW patients.

"It was interesting to find an association between reported plastic water bottle use and younger age of IBD diagnosis," said Dr. Damas. "Because this is a self-reported intake, we need more studies to confirm this. However, this finding falls in line with other recent studies showing a potential association between microplastics and disease states, including IBD. The next step is to measure for traces of environmental contaminants in human samples of patients with IBD."

Dr. Ananthakrishnan

Unlike previous studies, this analysis did not find parasitic infections, pets, and antibiotics to be associated with age of IBD diagnosis.

"This is an interesting and important study," commented Ashwin Ananthakrishnan, MBBS, MPH, AGAF, director of the Crohn's and Colitis Center at Massachusetts General Hospital in Boston, who was not involved in the study. "There are few environmental risk factor studies looking at non-White populations and to that end, this is a very large and well-done analysis looking at environmental factors among Hispanic patients with IBD."

He added that, while most studies have just compared factors between cases and controls, "this is an interesting examination of the impact of such factors on age of onset."

Dr. Ananthakrishnan stressed, however, that further work is needed to expand on these findings." The addition of a control group would help determine how these factors actually modify disease risk. It is also intriguing that environmental factors more strongly predict age of onset than genetic risk. That only highlights the fact that IBD is in large part an environmentally influenced disease, suggesting there is exciting opportunity for environmental modification to address disease onset."

Offering another outsider's perspective, Manasi Agrawal, MD, MS, an assistant professor of medicine at Icahn School of Medicine at Mount Sinai in New York City and not a participant in the study, agreed that the findings highlight the contribution of early life and childhood environmental factors to IBD risk relative to genetic variants.

"The relative importance of the environment compared to genetic risk toward IBD, timing of exposure, and impact on age at IBD diagnosis is a novel and important finding. These data will help contextualize how we communicate disease risk and potential prevention approaches."

Dr. Agrawal

She added that future research should measure various exposures, such as pollutants in preclinical biological samples. "Mechanistic data on their downstream effects are needed to understand IBD pathogenesis and develop prevention efforts."

According to the authors, theirs is the first study of its kind to examine the contribution of cumulative environmental factors, age-dependent exposures, and genetic predisposition to age of IBD diagnosis in a diverse IBD cohort.

The authors listed no specific funding for this study and had no conflicts of interest to declare. Dr. Ananthakrishnan and Dr. Agrawal had no relevant competing interests. ■

FMT Could Prevent Recurrence of Hepatic Encephalopathy in Patients With Cirrhosis

BY BECKY MCCALL

FROM EASL 2024

MILAN — Fecal microbiota transplantation (FMT), also known as intestinal microbiota transplantation, significantly reduced recurrence of hepatic encephalopathy, compared with placebo, in patients with cirrhosis on standard-of-care treatment, results of a phase 2 randomized controlled trial show.

"Not only was FMT more beneficial, but also it didn't matter which route of administration was used — oral or enema — which is good because people don't really like enemas," said Jasmohan S. Bajaj, MD, AGAF, professor, School of Medicine, Virginia Commonwealth University, Richmond, and hepatologist at Richmond VA Medical Center.

Donor background (including vegan or omnivore) and dose range also did not affect the efficacy of FMT, Dr. Bajaj said.

Dr. Bajaj presented the findings (Abstract GS-001) at the opening session of the annual European Association for the Study of the Liver (EASL) Congress 2024.

Hepatic encephalopathy is a complication of advanced liver disease that causes a dementia-like state. Standard treatment with lactulose and rifaximin often results in a lack of patient response, meaning the patient is constantly being readmitted to the hospital, Dr. Bajaj said.

"This is a burden for the family as well as the patients," and is very difficult to manage from a clinical and psychosocial perspective, he said in an interview.

With FMT, "we are transferring an ecosystem of good microbes," which modifies the gut microbiome in patients with advanced liver disease and reduces associated brain toxicity, Dr. Bajaj explained.

Resetting the Gut

The double-blind, randomized, placebo-controlled trial enrolled a total of 60 patients with cirrhosis who had experienced hepatic encephalopathy. Aged 61-65 years, participants had Model for End-Stage Liver Disease (MELD) scores of 12-13, all were taking lactulose and rifaximin, and all had experienced their last hepatic encephalopathy episode 8-13 months prior.

Participants had similar baseline cognition, Sickness Impact Profile (SIP), and cirrhosis severity. Those with recent infections, taking other antibiotics, with a MELD score > 22, had received a transplant, or were immunosuppressed were excluded.

Study participants were divided into four dose administration groups (n = 15 each): oral and enema active FMT therapy (group 1), oral active FMT and enema placebo (group 2), oral placebo and enema active FMT (group 3), and oral and enema placebo (group 4).

Dr. Bajaj

'I think many patients in Western countries are underserved because apart from lactulose and rifaximin, there is little else to give them. The assumption is because rifaximin kills everything, we shouldn't give FMT. But here, we administered it to a harsh and hostile wasteland of microbiota, and it still got a toehold.'

The range of FMT dose frequency was zero (all placebo), or one, two, or three FMT administrations, each given 1 month apart.

Two thirds of those receiving active FMT were given omnivore-donor FMT, and one third were given vegan-donor FMT, in addition to receiving standard of care.

"Colony-forming units were standard and the same whether given via oral capsule or enema," Dr. Bajaj said. This is "similar to what we used in our phase 1 study."

Intent-to-treat (ITT) analysis was performed with 6-month data. The primary outcomes were safety and hepatic encephalopathy recurrence defined as ≥ grade 2 on West-Haven criteria. Secondary outcomes included other adverse events, changes in infections, severity of cirrhosis and cognition, and patient-reported outcomes. A statistical regression for hepatic encephalopathy recurrence was also performed. Patients were followed for 6 months or until death.

One Dose of FMT Better Than None

Hepatic encephalopathy recurrence was highest (40%) in group 4 patients, compared with those in group 1 (13%), group 2 (13%), and group 3 (0%), as were liver-related hospitalizations (47% vs 7%-20%).

SIP total/physical and psych scores improved with FMT (P = .003).

When all patients were included in the analysis, the hepatic encephalopathy recurrence was related to dose number (odds radio [OR], 0.27; 95% CI, 0.10-0.79; P = .02), male sex (OR, 0.16; 95% CI, 0.03-0.89; P = .04), and physical SIP (OR, 1.05; 95% CI, 1.01-1.10, P = .05). However, when analyzing results from FMT recipients only, FMT dose, route of administration, and donor source were not found to affect recurrence.

Of those on placebo alone, six patients (40%) had a recurrence, compared with four on FMT (8.8%) in the combined FMT groups.

"As long as a patient received at least one FMT dose, they had a better response than a patient who had none," Dr. Bajaj said.

Six patients dropped out; two in group 1 died after hepatic encephalopathy and falls, and one in group 2 died after a seizure. Three others did not return for follow-up visits. Four patients developed infections, including spontaneous bacterial peritonitis, cholecystitis, and cellulitis, all unrelated to FMT.

"I think many patients in Western countries are underserved because apart from lactulose and rifaximin, there is little else to give them," Dr. Bajaj said. "The assumption is because rifaximin kills everything, we shouldn't give FMT. But here, we administered it to a harsh and hostile wasteland of microbiota, and it still got a toehold and generated a reduction in hepatic encephalopathy."

He pointed out that in smaller prior studies, the effects lasted up to 1 year.

That the administration route doesn't matter is also an important finding as oral administration is much more feasible than enema, said Dr. [Colleen] Kelly, who went on to point out the importance of finding an alternative to rifaximin and lactulose, which are often poorly tolerated.

Dr. Kelly

Setting the Stage for Phase 3 Trials

Dr. Bajaj noted that this phase 2 study sets the stage for larger phase 3 trials in patients not responding to first-line therapy.

"Given how well-tolerated and effective FMT appears to be in these patients, if the larger phase 3 trial shows similar results, I can imagine FMT becoming a standard therapy," said Colleen R. Kelly, MD, AGAF, gastroenterologist at Brigham and Women's Hospital and Harvard Medical School, Boston, who was not involved in the study.

This study was built on Dr. Bajaj's prior work that established the safety of FMT by enema, she added, stressing that this new research was incredibly important in these immunocompromised patients who are at higher risk for infection transmission.

That the administration route doesn't matter is also an important finding as oral administration is much more feasible than enema, said Dr. Kelly, who went on to point out the importance of finding an alternative to rifaximin and lactulose, which are often poorly tolerated.

The study highlights the central role played by the gut microbiota in dysbiosis in the pathophysiology of hepatic encephalopathy, Dr. Kelly said. "It is another exciting example of how gut microbiota can be manipulated to treat disease."

Dr. Bajaj and Dr. Kelly report no relevant financial relationships to this study. ■

Alternative Paths to Recertification

Dear colleagues,

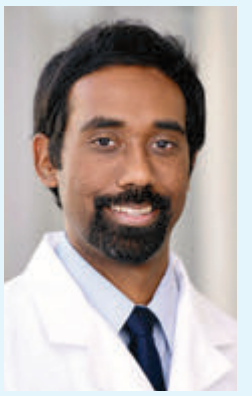
When the American Board of Internal Medicine (ABIM) made changes to its recertification process, introducing its continuous Maintenance of Certification (MOC), there was significant controversy across subspecialties. In response, the ABIM accreditation process has evolved. Currently, there remains the traditional 10-year MOC exam, and a newly introduced Longitudinal Knowledge Assessment (LKA) where questions are answered every quarter. But which is the better one for you?

In this issue of Perspectives, Dr. Petr Protiva and Dr. Maggie Ham discuss their experiences with these differing assessment methods. Dr. Ham touches on the flexibility and convenience of the LKA, while Dr. Protiva writes about the benefits of the focused preparation and clear endpoint that the 10-year exam offers.

We hope their experiences will help you decide on your approach to recertification. Good luck!

We look forward to hearing your thoughts on board recertification on X @AGA_GIHN.

Gyanprakash A. Ketwaroo, MD, MSc, is associate professor of medicine, Yale University, New Haven, Conn., and chief of endoscopy at West Haven (Conn.) VA Medical Center. He is an associate editor for GI & Hepatology News.



Dr. Ketwaroo

Traditional 10-Year ABIM Exam: A Personal Perspective

BY PETR PROTIVA, MD, MPH, AGAF

The American Board of Internal Medicine (ABIM) offers board certification in gastroenterology, a mark of professional excellence. Physicians can maintain their certification through the traditional 10-year examination or the newer Longitudinal Knowledge Assessment (LKA).

Dr. Protiva

I completed my initial certification exam in 2003 and currently practice gastroenterology full time at the West Haven VA, where I am associate chief of gastroenterology, and the Yale School of Medicine. I am a clinician educator, running clinical trials and performing general and some advanced endoscopy.

As an academic gastroenterologist, I recertified in November 2023 using the traditional 10-year examination. An informal survey among my colleagues revealed that most opted for the LKA route. The traditional exam offers consistency, a clear endpoint, and a comprehensive review but comes with high stakes, significant preparation requirements, and potential for outdated information. In contrast, the LKA promotes continuous learning, flexibility, and immediate feedback, though it requires ongoing commitment. The LKA is generally perceived as the preferable option for maintaining and enhancing a current knowledge base.

In a highly academic environment with ample opportunities for learning and staying current with clinical science, the traditional exam's drawbacks can be mitigated. My decision to opt for the 10-year exam was based on prior experience and the ease of accessing and maintaining knowledge in an academic setting. I considered the LKA as well, but there's no clear answer as to which exam is "better." The choice ultimately depends on individual physician preferences, learning styles, and professional circumstances. This piece recounts my experience with the 10-year recertification exam in 2023.

Preparing for the 10-Year Exam

In the year my recertification was due, I logged into my ABIM account to verify requirements and deadlines. After signing up for the recertification exam on the ABIM website, I was directed to the Pearson Vue website to select my testing center and date. The process was straightforward and glitch-free.

For the Maintenance of Certification (MOC) point requirements, it is necessary to systematically accumulate points through accredited Continuing Medical Education (CME) activities. The ABIM web portal indicates how many MOC

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The Longitudinal Knowledge Assessment: Flexible and Convenient

BY MAGGIE HAM, MD, AGAF

I completed my initial certification exam in 2013 when I concluded gastroenterology fellowship training at the Beth Israel Deaconess Medical Center in Boston. I am currently in clinical practice at Southern California Permanente Medical Group in Ventura, where I see patients and perform endoscopy daily.

Dr. Ham

I practice general gastroenterology and hepatology with an emphasis on inflammatory bowel disease, colon cancer prevention, and women's health. I am also the medical director of the gastroenterology lab at Community Memorial Hospital in Ventura, physician in charge of a building at Kaiser, and assistant chief of gastroenterology. My husband and I are both gastroenterologists and have a child in elementary school.

Two years ago, I decided to embark upon the Longitudinal Knowledge Assessment (LKA) for gastroenterology. This is offered by the American Board of Internal Medicine (ABIM) in lieu of the 10-year recertification examination. As a full-time working mother, I could not fathom the time it would take to study and sit down for the high-stakes 10-year exam.

The LKA consists of 30 questions per quarter, which equates to 600 questions over 5 years. One hundred questions may be skipped over the 5-year period. The questions can be answered from anywhere with an internet-connected device without any camera monitoring. I would often answer questions from the comfort of my own home using my laptop, but could also do so using my phone while waiting in line at the store or on a long plane ride. The 30 questions do not need to be answered in the same sitting, so within the quarter I can save my progress and answer the remaining questions at my convenience. This has worked well for me alongside my personal and professional obligations.

I can download my progress report which informs me of my score, and what the passing score is. I can see what the average score is, how I am performing relative to that, and how I am faring in each category (ie, esophagus, stomach and duodenum, liver, etc). I also receive Maintenance of Certification (MCC) points with each LKA question I answer correctly. With the 10-year ABIM recertification exam, I would still need to complete MOC.

While there is a 4-minute time limit for each question, it really has not been an issue. If needed, I can request to extend the time, to read or to look things up. It is an open book exam, so I have learned and

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FDA OKs Voquezna for Heartburn Relief in Nonerosive Gastroesophageal Reflux Disease

BY MEGAN BROOKS

The US Food and Drug Administration (FDA) approved Voquezna (vonoprazan, Phathom Pharmaceuticals) 10-mg tablets for the relief of heartburn associated with nonerosive gastroesophageal reflux disease (GERD) in adults.

It represents the third indication for the potassium-competitive acid blocker, which is already approved to treat all severities of erosive esophagitis and to eradicate *Helicobacter pylori* infection in combination with antibiotics.

The approval in nonerosive GERD was supported by results of the PHALCON-nonerosive GERD-301 study, a phase 3 randomized, placebo-controlled, double-blind, multicenter study evaluating the safety and efficacy of once-daily Voquezna in more than 700 adults with nonerosive GERD experiencing at least 4 days of heartburn per week.

"Vonoprazan was efficacious in reducing heartburn symptoms in patients with [nonerosive GERD], with the benefit appearing to begin as early as the first day of therapy. This treatment effect persisted after the initial 4-week placebo-controlled period throughout the 20-week extension period," the study team wrote in *Clinical Gastroenterology and Hepatology* (2024 May. doi: 10.1016/j.cgh.2024.05.004).

Voquezna "provides physicians with a novel, first-in-class treatment that can quickly and significantly reduce heartburn for many adult patients" with nonerosive GERD, said Colin W. Howden, MD, AGAF, professor emeritus, University of Tennessee College of Medicine in Memphis.

The most common adverse events reported in patients treated with Voquezna during the 4-week placebo-controlled period were abdominal pain, constipation, diarrhea, nausea, and urinary tract infection. Upper respiratory tract infection and sinusitis were also reported in patients taking Voquezna in the 20-week extension phase of the trial. ■

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points you are missing for the recertification cycle. I converted my UpToDate CME credits into ABIM MOC points, a straightforward process if you follow the necessary steps and keep your accounts updated.

Numerous resources are available for assessing and testing your knowledge prior to the exam. My first assessment included an online GI Board question bank, followed by a virtual Board Review Course. Next, I used the GI society-based Self-Assessment Test, which was well-suited for honing testing skills as well as reviewing the questions and answers in detail. Both the online question bank and GI society tests offered additional MOC points upon successful completion of practice exams. I also found it useful to reread guidelines in areas outside my usual practice and use UpToDate on an ongoing basis, like in everyday clinical practice. Completing the MOC requirements well ahead of my exam date was relatively easy.

Exam Experience

The exam itself is a 10-hour, grueling experience, but I was familiar with the format and expectations. The exam day was divided into several sessions, each containing a maximum of 60 multiple-choice questions, usually totaling 220 questions with an average of 2 minutes per question. The use of UpToDate is permitted during the recertification exam. While UpToDate is an excellent clinical resource, it cannot substitute for comprehensive knowledge. It is useful for verifying specific facts but cannot fill knowledge gaps during the exam.

Pros and Cons of the 10-Year Exam

Pros:

- **Focused Preparation:** Preparing for a single, comprehensive exam leads to an in-depth review of the entire subspecialty, reinforcing foundational knowledge and ensuring breadth in less familiar areas.
- **Clear Endpoint:** The 10-year exam offers a clear endpoint. Once passed, the certification is valid for the next decade, allowing focus on practice or academic endeavors without a need for ongoing assessments.
- **Consistency:** The standardized nature of the exam ensures consistency in the assessment process, with all physicians tested under the same conditions.
- **Benchmarking:** A decade-long interval provides a significant time frame for measuring knowledge and expertise, allowing comparison with other test takers.

Cons:

- **High Stakes:** The exam is high stakes, creating significant stress. Failure can have serious professional consequences, potentially affecting credentials and career.
- **Rigidity:** The fixed schedule offers little flexibility, requiring careful planning and preparation, which may not align with personal or professional circumstances.
- **Comprehensive Nature:** Extensive preparation is challenging for busy physicians. Balancing study time with clinical responsibilities can be difficult.
- **Outdated Information:** Medical knowledge evolves rapidly, and the 10-year interval may not reflect the most current practices, leading to gaps in knowledge.

Conclusion

While I cannot directly compare my experience to the LKA, the traditional 10-year exam has both strengths and weaknesses. It requires extensive preparation and is high stakes, but it offers a clear endpoint and comprehensive review. The choice between the 10-year exam and the LKA depends on individual preferences, learning styles, and professional circumstances. In an academic environment, the traditional exam can be a good option, but continuous medical education remains essential regardless of the recertification method chosen. ■

Dr. Protiva is associate chief of gastroenterology at the West Haven (Conn.) VA Medical Center, and associate professor of medicine (digestive diseases) at Yale School of Medicine, New Haven, Conn. He has no disclosures related to this article.

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kept abreast of GI knowledge. Any references other than another human may be used. I typically use UpToDate and the GI society guidelines, which have been sufficient. Occasionally there are experimental questions sprinkled throughout the exam, so I may never know the answer. Otherwise, the solution to each question will be presented to me immediately upon answering, with an explanation accompanied by references. I appreciate that this keeps me updated with the latest guidelines and recommendations, which was my primary reason for selecting the LKA.

At the end of the 5 years, you may choose to continue the LKA cycle, or take the 10-year exam. If you do not pass the LKA, they do give you a 1-year grace period to pass the exam if you want to continue to participate in MOC.

The quarter does seem to come around fairly quickly, but they do send frequent reminders by email or text as the deadline approaches. And if you forget to answer all the questions in a quarter, the LKA allows for 100 questions that may be skipped over the 5-year period.

Being able to answer questions from anywhere at any time is incredibly flexible and convenient. The immediate feedback is also great and helps me identify my strengths and weaknesses. While I will not know until the end of the 5-year period whether I have passed or not, I can check my progress report which gives me an idea of where I stand. Overall, I would say I am satisfied with the LKA, as it has been easy to maintain certification while effectively contributing to my continuing medical education. ■

Dr. Ham is a gastroenterologist at Southern California Permanente Medical Group in Ventura. She is also medical director of the gastroenterology lab at Southern Community Memorial Hospital in Ventura. She has no disclosures related to this article.

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Gastroenterologists Can Play a Critical Role in Obesity Management

BY CAROLYN CRIST
MDedge News

As the prevalence of obesity grows in the United States and worldwide, more solutions are needed at more levels of care to help patients, according to a series of presentations during the American Gastroenterological Association (AGA) Postgraduate Course held at Digestive Disease Week® (DDW) in May.

Gastroenterologists can step up as part of a multidisciplinary response to provide treatment — with a range of lifestyle interventions, pharmacological options, and bariatric endoscopic possibilities — based on a patient's needs and preferences.

"Obesity is in our clinics. We're usually the first line of obesity, and that's why we need to know it, learn how to manage it, and understand the complications," said Andres Acosta, MD, an associate professor of medicine and gastroenterologist at Mayo Clinic, Rochester, Minnesota, and principal investigator of Mayo's Precision Medicine for Obesity Laboratory.

Obesity tops the charts as the most significant chronic disease in the world, affecting 130 million patients in the United States and 1 billion globally, he said, and those numbers will climb only higher in coming years. By 2030, the United States is projected to have an obesity prevalence of 50% and overweight prevalence of 80%, with every state having a prevalence greater than 35%.


Dr. Acosta

'Choose the organ you like, and obesity is a major contributor to its most important disease. Obesity affects every single disease and every single organ in the gastrointestinal system, so it's essential that we actually manage this.'

The alarming prevalence rates matter not because of aesthetics or personal preference, he noted, but because of the major associations with premature death, cardiovascular disease, stroke, type 2 diabetes, numerous cancers, and 280 other diseases.

"Choose the organ you like, and obesity is a major contributor to its most important disease," Dr. Acosta said. "Obesity affects every single disease and every single organ in the gastrointestinal [GI] system, so it's essential that we actually manage this."

Based on current recommendations focused on body mass index (BMI), diet, exercise, and behavioral therapy are suggested for a BMI of 25 or higher, followed by pharmacotherapy for a BMI greater than 27 with comorbidities, endoscopic procedures for a BMI greater than 30, and surgical options for a BMI greater than 40 or BMI greater than 30 with comorbidities. At each step, clinicians can start shared decision-making conversations with patients about the best options for them.

"We're moving from a pyramid approach where we tell patients to choose one intervention toward multidisciplinary programs where we offer interventions in combination," Dr. Acosta said, recommending AGA's POWER - Practice Guide on Obesity and Weight Management Education and Resources (Clin Gastroenterol Hepatol. 2017 Feb. doi:10.1016/j.cgh.2016.10.023). Other AGA resources for physicians treating patients with obesity include the AGA Clinical Practice Guideline on Pharmacological Interventions for Adults With Obesity (Gastroenterology. 2022 Nov. doi: 10.1053/j.gastro.2022.08.045), and the Obesity Resource Center on the AGA website (www.patient.gastro.org/obesity/).

Progress in Pharmacotherapy

In recent years, developments focused on glucagon-like peptide 1 (GLP-1) receptor agonists, such as semaglutide and tirzepatide, have "changed the conversation about obesity," Dr. Acosta said. For the first time, medications reduce not only weight but also cardiovascular disease risks, which were previously observed only with bariatric surgery.

Additional GLP-1 options are in research pipelines. During the next 3 years, for instance, more medications will focus on how the gut signals to the brain through intestinal hormones, targeting GLP-1, glucose-dependent insulinotropic polypeptide, and other receptors. Leading the pipeline, Eli Lilly's retatrutide shows promise, with weight loss and comorbidity improvement reported similar to or better than tirzepatide. Additional data from phase 3 trials are forthcoming.

In clinical practice, major conversations remain about gastrointestinal side effects, particularly gastroparesis, that may pose a risk for aspiration in upper endoscopy. Gastroenterologists should feel comfortable about managing these types of side effects when starting patients on these medications, Dr. Acosta said, but also continue to ask questions about side effects and the latest research developments.

Of course, major obstacles remain regarding patient access, insurance coverage, cost-effective options, and heterogeneous patient responses. At the Mayo Clinic, Dr. Acosta and colleagues are researching and targeting obesity phenotypes — such as the "hungry gut" or "hungry brain" — to improve weight loss outcomes and patient adherence.

Ultimately, he said, the most

important obstacle is our healthcare system. "We cannot afford to manage obesity with expensive procedures or expensive medications."

Efficacy of Endobariatrics

For patients with a BMI of 30 or higher, minimally invasive bariatric endoscopic procedures can lead to weight loss, improvement in metabolic outcomes, and fewer adverse events compared to bariatric surgery, said Violeta Popov, MD, director of bariatric endoscopy at the New York Veterans Affairs Harbor Healthcare System in New York City.

For example, intragastric balloons — marketed under the names Orbera and Spatz — work by altering the rate of gastric emptying. They're placed temporarily and removed after several months, and Spatz can be adjusted while in place, either by removing or adding volume if needed. Data show that associated weight loss can lead to improvements in insulin resistance, visceral obesity, dyslipidemia, high blood pressure, liver enzymes, metabolic dysfunction–associated steatotic liver disease (MASLD), and metabolic dysfunction–associated steatohepatitis (MASH).

Although the majority of patients undergoing minimally invasive procedures do experience adverse events such as nausea and vomiting, symptoms tend to subside in the first few weeks, Dr. Popov said. At the same time, gastroesophageal reflux disease (GERD) can worsen in patients who have experienced it, so proton-pump inhibitors are recommended for as long as the balloon is inserted.

Endoscopic sleeve gastroplasty has become the most prevalent endobariatric method in Dr. Popov's practice during the past few years. The procedure uses full-thickness sutures placed with an endoscopic suturing device called OverStitch, to decrease the size of the opening into the stomach. In previous trials, patients lost up to 40 pounds, and more than 80% maintained the lost weight up to 5 years. The procedure, which showed no worsening of GERD, works by preserving gastric contractility while delaying gastric emptying.

Dr. Popov noted one of the main challenges is training and credentialing, with many patients not having access to those who can perform these procedures. As a diplomate of the American Board of Obesity Medicine, Dr. Popov highlighted the need for bariatric endoscopy fellowships or training during GI fellowships, post-fellowship hands-on courses, and competency training with simulators.

"It's not just technical competency in performing a procedure — it's also the administrative work of setting up a multidisciplinary program," she said. "It's very important to understand obesity as a disease and learn how to manage it."

Monitoring MASLD

Linked strongly to insulin resistance, MASLD prevalence is increasing worldwide as obesity increases, reaching 30% in the United States and even higher among certain patient populations, said Sonali Paul, MD, an assistant professor of medicine and hepatologist at the Center for Liver Diseases at the University of Chicago Medicine in Illinois.

Dr. Popov

One of the main challenges is training and credentialing, with many patients not having access to those who can perform these procedures. Dr. [Violeta] Popov highlighted the need for bariatric endoscopy fellowships or training during GI fellowships, post-fellowship hands-on courses, and competency training with simulators.

The good news is that the associations between MASLD and obesity also move the other way — if patients lose weight and improve cardiovascular risk factors, MASLD can improve as well. Notably, steatosis can disappear at 3% weight loss, inflammation decreases at 5% weight loss, MASH resolution occurs at 7% weight loss, and fibrosis improves at 10% weight loss.

Dr. Paul

Primarily, Dr. Paul and colleagues have focused on lifestyle interventions, especially diet, by working carefully with dietitians. A modified Mediterranean diet with olive oil and monounsaturated fats can decrease steatosis on MRI, as compared with a high-fat/low-carb diet, and it also appears to decrease mortality, cardiovascular disease, and obesity. As part of the modified diet, carbohydrates are limited to 30 grams per meal per day.

"We really want to tailor the diet to cultural and personal preferences," she said. "I'm South Asian, and when I tell my South Asian patients not to eat rice, they don't love that, so we work with them to meet them where they are."

Dr. Paul recommends physical activity interventions, proper sleep hygiene, treatment of obstructive sleep apnea, pharmacological options, and bariatric solutions to reduce weight, improve insulin resistance, and target MASLD risk factors. For instance, recent phase 2b studies indicate semaglutide can lead to MASH resolution, with phase 3 trial data expected by the end of 2024.

In addition, resmetirom, a liver-directed thyroid hormone receptor beta-selective agonist — the first Food and Drug Administration–approved drug for MASH — achieved both primary endpoints of MASH resolution and fibrosis improvement. American Association for the Study of Liver Diseases guidelines are forthcoming about who should use the drug, Dr. Paul said.

Dr. Singhal

"In terms of the paradigm that I think about with MASLD, we want to target other causes and diagnose advanced fibrosis, treat risk factors, and target MASH through treatment," she said.

Considering the Community Perspective

Community-based clinicians face a unique set of challenges when addressing obesity through a multidisciplinary approach and longitudinal care, but it remains vital as more practices see increased patient loads with obesity-related GI comorbidities, said Pooja Singhal, MD, assistant professor of medicine at the University of Oklahoma Health Sciences Center, Oklahoma City, and founder/president of Oklahoma Gastro Health and Wellness.

Dr. Singhal noted obesity-related associations with earlier presentations of GERD, elevated liver enzymes, MASLD, MASH, irritable bowel syndrome, inflammatory bowel disease, gallbladder disease, colon polyps, and GI cancers.

"Gastroenterologists, as most of us are board-certified internists, are in a unique position to offer both pharmacotherapy and endoscopic treatment," she said. "The GI comorbidities provide an opportunity for early intervention, and we're seeing a lot of side effects of antiobesity medications, so whether we like it or not, we are involved."

The best practices at the community level start with a patient-centric approach, Dr. Singhal said. Although clinicians are already time constrained and focused on addressing GI-related comorbidities, using the 5A's framework can help:

- Asking if the patient is ready to talk
- Assessing for factors contributing to obesity
- Advising them of treatment options
- Agreeing on goals based on shared decision-making
- Assisting or arranging the agreed-on plan.

During the assessment phase, Dr. Singhal suggested not only looking at medical and physical values but also secondary causes of weight gain, including the patient's relationship with food, micronutrient deficiencies, psychosocial concerns, body image disorders, and triggers for eating.

During the advising phase, clinicians should consider multiple targets — such as diet, physical activity, and behavior — with a supervised and structured approach. Dr. Singhal and colleagues include a meal plan, aerobic activity, resistance training, behavior modification of eating habits, sleep hygiene, and patient self-monitoring through smartphone apps and wearables. Pharmacotherapy may be relevant and effective for some patients but less accessible for many, she noted.

Above all, Dr. Singhal recommended training through the American Board of Obesity Medicine, major GI society guidelines and conferences, American Society for Gastrointestinal Endoscopy STAR courses, and connecting with a multidisciplinary team of dietitians, coaches, physical therapists, and other GI specialists when possible.

"Most importantly, we're dealing with decades of stigma and bias around this disease, where 'you are what you eat,' " she said. "This mentality of 'I can lose weight without help' is a real challenge." ■

Snare Tip Soft Coagulation Leaves Clean Margins

BY CAROLYN CRIST
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

After endoscopic mucosal resection (EMR), both snare tip soft coagulation (STSC) and argon plasma coagulation (APC) appear superior to no thermal margin treatment, according to a recent study.

Since STSC was faster to apply than APC and results in lower cost and plastic waste (because of APC requiring an additional catheter), STSC was the preferred option.

"The reduction in recurrence rate with thermal margin treatment is arguably the most important development in endoscopic mucosal resection in the past 2 decades," said lead author Douglas Rex, MD, AGAF, a distinguished professor emeritus at the Indiana University School of Medicine and director of endoscopy at Indiana University Hospitals, both in Indianapolis.

"Margin thermal therapy with STSC should now be standard treatment after piecemeal EMR in the colorectum," he said. "Before applying STSC, the endoscopist must ensure that the entire lesion is resected down to the submucosa. Then STSC should be aggressively applied to 100% of the margin."

The study was published in *Clinical Gastroenterology and Hepatology* (2024 Mar. doi: 10.1016/j.cgh.2023.09.041).

Comparing Treatments

Dr. Rex and colleagues performed a randomized three-arm trial in nine US centers, comparing STSC with APC and no margin treatment in patients undergoing colorectal EMR of nonpedunculated lesions of 15 mm or greater.

Dr. Rex

'Margin thermal therapy with STSC should now be standard treatment after piecemeal EMR in the colorectum. Before applying STSC, the endoscopist must ensure that the entire lesion is resected down to the submucosa. Then STSC should be aggressively applied to 100% of the margin.'

All lesions underwent conventional injection and snare resection EMR using electrocautery, but the endoscopist chose the injection fluid and snare type and size. Areas with residual polyp that weren't removable by snare resection because of flat shape or fibrosis were removed by hot or cold avulsion. After that, patients were randomized to one of the three arms.

Patients were scheduled for a follow-up appointment 6 months after the initial EMR. Any visible recurrence was resected using methods at the discretion of the endoscopist, and if no visible recurrence was present, EMR site biopsies were recommended.

Among 384 patients with 414 lesions, 308 patients with 328 lesions completed at least one follow-up appointment. The median interval to the first follow-up was 6.4 months, ranging from 2 to 37 months. The primary endpoint was the presence of recurrent or residual polyp at first follow-up.

Dr. Wallace

'The single most important message now is that patients shouldn't be getting surgical resections for endoscopically treatable polyps. We see many patients who are told they need to get surgery, but overwhelmingly, the data shows we can remove polyps without surgery.'

The median polyp size was 25 mm, and 65 of the 414 polyps (15.7%) were 15-19 mm in size. Overall, 14.8% of lesions were resected en bloc, with no difference between the study arms.

The proportion of lesions with residual polyp at first follow-up was 4.6% with STSC, 9.3% with APC, and 21.4% among control subjects with no margin treatment.

The odds of having a residual polyp at first follow-up were lower for STSC and APC when compared with control subjects (odds ratio [OR], 0.182 and 0.341; or $P = .001$ and $P = .01$, respectively). There wasn't a significant difference in the odds of recurrence between STSC and APC (OR, 1.874).

In 259 lesions in 248 patients that were 20 mm or greater, the recurrence rates at first follow-up were 5.9% for STSC, 10.1% for APC, and 25.9% for the control group. In these lesions, STSC and APC remained associated with a lower risk of recurrence versus the control (OR, 0.18 and 0.323, respectively). The difference in recurrence rates between STSC and APC wasn't significant.

Also, STSC took less time to apply than APC, with a median time of 3.35 minutes vs 4.08 minutes.

The rates of adverse events were low, with no difference between the three arms. There were no immediate or delayed perforations in any arm, and the overall occurrence of delayed bleeding was low at 3.6%.

"I think STSC won the trial because it was numerically (though not statistically) superior to APC, was faster to apply, and using STSC results in lower cost and less plastic compared to APC," Dr. Rex said.

Additional Considerations

Based on charges at the nine US centers and a survey of two manufacturers, APC catheters typically cost $175-$275 each, the study authors wrote, noting that APC results in increased cost, plastic waste because of the catheter, and carbon emissions associated with its manufacture.

Continued on following page

FDA Approves First Blood Test for Colorectal Cancer

In late July, the US Food and Drug Administration (FDA) approved the first use of a liquid biopsy (blood test) for colorectal cancer (CRC) screening. The test, called Shield, launched commercially the first week of August and is the first blood test to be approved by the FDA as a primary screening option for CRC that meets requirements for Medicare reimbursement.


Dr. Lieberman


Dr. Carethers

While the convenience of a blood test could potentially encourage more people to get screened, expert consensus is that blood tests can't prevent CRC and should not be considered a replacement for a colonoscopy. Modeling studies and expert consensus published earlier this year in *Gastroenterology* (2024 Mar. doi: 10.1053/j.gastro.2024.03.011) and in *Clinical Gastroenterology and Hepatology* (2024 Mar. doi: 10.1016/j.cgh.2024.01.034) shed light on the perils of liquid biopsy.

"Based on their current characteristics, blood tests should not be recommended to replace established colorectal cancer screening tests, since blood tests are neither as effective nor as cost-effective, and would worsen outcomes," said David Lieberman, MD, AGAF, chair, AGA CRC Workshop chair and lead author of an expert commentary on liquid biopsy for CRC screening.

Five Key Takeaways

- A blood test for CRC that meets minimal Centers for Medicare & Medicaid Services criteria for sensitivity and performed every 3 years would likely result in better outcomes than no screening.
- A blood test for CRC offers a simple process that could encourage more people to participate in screening. Patients who may have declined colonoscopy should understand the need for a colonoscopy if findings are abnormal.
- Because blood tests for CRC are predicted to be less effective and more costly than currently established screening programs, they cannot be recommended to replace established methods.
- Although blood tests would improve outcomes in currently unscreened people, substituting blood tests for a currently effective test would worsen patient outcomes and increase cost.
- Potential benchmarks that industry might use to assess an effective blood test for CRC going forward would be sensitivity for stage I-III CRC of > 90%, with sensitivity for advanced adenomas of > 40%-50%.

"Unless we have the expectation of high sensitivity and specificity, blood-based colorectal cancer tests could lead to false-positive and false-negative results, which are both bad for patient outcomes," said John M. Carethers, MD, AGAF, AGA past president and vice chancellor for health sciences at the University of California San Diego. ■

Continued from previous page

"What we're seeing — now over several trials — is STSC appears to be the most effective method of treating the edges, and it's inexpensive because it uses the same device used for snare resection, so there's no incremental cost for the device," said Michael Wallace, MD, professor of medicine and director of the digestive diseases research program at Mayo Clinic, Jacksonville, Florida.

Dr. Wallace, who wasn't involved with this study, has researched thermal ablation after EMR, including both the margins and the base.

"The single most important message now is that patients shouldn't be getting surgical resections for endoscopically treatable polyps," he said. "We see many patients who are told they need to get surgery, but overwhelmingly, the data shows we can remove polyps without surgery."

Dr. Rex and several authors declared fees and grants from numerous companies outside of this study. Dr. Wallace reported no relevant disclosures. ■

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Explore our new, all-in-one toolkit designed to enhance your care for irritable bowel syndrome (IBS) patients. AGA's new irritable bowel syndrome toolkit gathers all our clinical guidance, continuing education materials, patient education resources, and FAQs in one convenient place. Be sure to check it out and bookmark it for easy access!

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The toolkit includes clinical guidance on:

- Pharmacological management of IBS with diarrhea
- Pharmacological management of IBS with constipation

For more resources for ulcerative colitis patients, visit the Patient Center on the AGA website. The AGA Patient Center has a variety of information that can be shared with your patients, including tips on diet, vaccine recommendations, and information on biosimilars. ■

‘We’re really good at reactionary medicine’

Obesity *from page 1*

Dr. Laster is also working with members of Congress to get bills passed for coverage of obesity medication and procedures. In an interview with *GI & Hepatology News*, she spoke more about the intersection between nutrition, medicine and bariatric procedures, and the importance of offering patients multiple solutions.

Q: Why did you choose GI?
It allowed me a little bit of everything. You have clinic, where you can really interact with patients and get to the root of their problem. You have preventative care with routine colonoscopies and upper endoscopies to prevent cancer. But then you also have fun stuff — which my mom told me to stop saying out loud — ‘bleeders’ and acute things that you get to fix immediately. So, you get the adrenaline rush too. I like it because you get the best of all worlds, and it’s really hard to get bored.

Q: How did you become interested in nutrition and bariatric endoscopy?
My parents had a garden and never let us eat processed foods. In residency, I kept seeing the same medical problems over and over again. Everybody had high blood pressure, high cholesterol, and diabetes. Then in GI clinic, everybody had abdominal pain, bloating, constipation, heartburn, and a million GI appointments for these same things. Everyone’s upper endoscopy or colonoscopy was negative. Something else had to be going on.

And that’s sort of where it came from: figuring out the common denominator. It had to be what people were eating. There’s also the prevalence of patients with obesity going up every single year. Correlating all these other medical problems with people’s diets led me down the rabbit hole of, What else can we be doing?

Most people don’t want to undergo surgery. Only 2% of people eligible for surgery actually do it, even though it works. The reasons are because it’s invasive or there’s shame behind it. Bariatric endoscopy is another option that’s out here, that’s less invasive. I’m an endoscopist and gastroenterologist. I should be able to offer all those things and I should know more about nutrition. We don’t talk about it enough.

Q: Do you think more GI doctors should become better educated about nutrition?
100%. Every patient I see has seen a GI doctor before and says, ‘No one has ever told me that if I have carbonated beverages and cheese every day, I’m going to be bloated and constipated.’ And that shouldn’t be the case.

Q: Why do you think that more GI doctors don’t get the education on nutrition during their medical training?
I think it’s our healthcare system. It’s very much focused on secondary treatment rather than preventative care. There’s no emphasis on preventing things from happening.

We’re really good at reactionary medicine. People who have an ulcer, big polyps and colon cancer, esophageal cancer — we do those things really well. But I think because there’s no ICD-10 codes for preventive care via nutrition education, and no good reimbursement, then there’s no incentive for hospital systems to pay for these things. It’s a system based on RVUs [relative value units] and numbers. That’s been our trajectory. We’ve been so focused on reactionary medicine rather than saying, ‘Okay, let’s stop this from happening.’

We just didn’t talk about nutrition in medical school, in residency, or in fellowship. It was looked at as a soft science. When I was in school, people would also say, ‘No one’s going to change. So it’s a waste of your time essentially to talk to people about making dietary changes.’ I feel like if you give people the opportunity, you have to give them the chance. You can’t just write everybody off. Some people won’t change, but that’s okay. They should at least have the opportunity to do so.

Q: How do you determine whether a patient is a good candidate for bariatric surgery?
It’s based on the guidelines: If they meet the BMI [body mass index] requirements, if they have obesity-associated comorbidities, their risk for surgery is low. But it’s also whether they want to do it or not. A patient has to be in the mindset and be ready for it. They need to *want* to have surgery or bariatric endoscopy, or to use medications, or start to make a change. Some people aren’t there yet — that preemptive stage of making a change. They want the solution, but they’re not ready to do that legwork yet.

And all of it is work. I tell patients, ‘Whether it’s medication or bariatric endoscopy or bariatric surgery, you still have work to do. None of it is going to just magically happen where you could just continue to do the same thing you’re doing now and you’re going to lose weight and keep it off.’

Q: What advances in obesity prevention are you excited about?
I’m excited that bariatric endoscopy came about in the first place, because in every other field there are less invasive approaches that have become available. I’m also excited about the emergence of weight loss medication, like GLP-1[glucagon-like peptide 1]s. I think they are a tool that we need.

Q: Do you think the weight loss medications may negate the need for surgery?
I don’t think they necessarily reduce the need for surgery. There’s still a lot we don’t know about why they work in some patients and why they don’t work in others.

Some of our colleagues have come up with phenotypes and blood tests so we can better understand which things will work in different patients. Surgery doesn’t work for some patients. People may need a combination of both after they reach a plateau. I’m excited that people see this as something that we should be researching and putting more effort into — that obesity isn’t a disease of moral failure, that people with excess weight just need to ‘move more’ or ‘eat less’ and it’s their fault. I’m glad people are starting to understand that.

Q: What teacher or mentor had the greatest impact on you?
Probably two. One of them is Andrea E Reid, MD, MPH, a dean of medicine at Harvard. She gives you such motivation to achieve things, no matter how big your idea is or how crazy it may seem. If you have something that you think is important, you go after it. Another person is Christopher C. Thompson, MD, at Brigham and Women’s Hospital, the father of bariatric endoscopy in a sense. He embodies what Dr. Reid talks about: crazy big ideas. And he goes after them and he succeeds. Having him push me and giving me that type of encouragement was invaluable.

Q: Describe how you would spend a free Saturday afternoon.
Every Saturday is yoga or some type of movement. Spending some time outside doing something, whether it’s messing around with plants that I’m not very good at, or going for a walk. ■

Lightning Round

Favorite city in U.S. besides the one you live in?
New York

Favorite breakfast?
Avocado toast

Place you most want to travel to?
Istanbul

Favorite season?
Fall

Favorite ice cream flavor?
Raspberry sorbet

Best place you ever went on vacation?
Greece

Favorite type of music?
Old school R&B

Dream job if you weren’t a gastroenterologist?
Clothing store owner

Number of cups of coffee you drink per day?
One

Favorite movie genre?
Romantic comedy or drama

Cat person or dog person?
Dog

Favorite sport?
Football

Favorite holiday?
Christmas

Optimist or pessimist?
Optimist

‘Convincing results’

MASH *from page 1*

such a strategy in a phase 3 setting, Dr. Loomba said.

MASH Resolution, No Worsening of Fibrosis

The dose-finding, multicenter, double-blind, placebo-controlled trial randomly assigned a total of 190 participants to receive once-weekly subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 52 weeks. Participants had biopsy-confirmed MASH and stage F2 or F3 (moderate or severe) fibrosis.

Overall, approximately 42% of participants had F2 fibrosis and over 57% had F3 fibrosis. The proportion of F3 fibrosis was numerically higher in the placebo (64.6%) and 5-mg tirzepatide (63.8%) groups. The mean age of the study cohort was 54 years; 57% were female, 86% were White, and 36% were Hispanic; the mean body mass index was 36; 58% had type 2 diabetes; and A1c was 6.5. NAFLD activity score (NAS) was 5.3. Baseline noninvasive test results were consistent with the study population of MASH with F2/F3 fibrosis and NAS ≥ 4.

The primary endpoint was resolution of MASH without worsening of fibrosis at 52 weeks, and the key secondary endpoint was an improvement (decrease) of at least one fibrosis stage without worsening of MASH. Other secondary endpoints included a ≥ 2-point decrease in NAS with ≤ 1-point decrease in two or more NAS components.

A total of 157 participants (83%) underwent liver biopsies at week 52, providing results for the current analysis.

Among tirzepatide-treated patients, 43.6% in the 5-mg group, 55.5% in the 10-mg group, and 62.4% in the 15-mg group met the criteria for resolution of MASH without worsening of fibrosis compared with 10% in the placebo group ($P < .001$ for all three comparisons).

Fibrosis improved by at least one stage without worsening of MASH in 54.9% of participants in the 5-mg tirzepatide group, 51.3% in the 10-mg tirzepatide group, and 51.0% in the 15-mg tirzepatide group compared with 29.7% in the placebo group ($P < .001$ for all risk differences with placebo).

Changes in NAS and subscores for the individual components of NAS, including steatosis, lobular inflammation, and hepatocellular ballooning, were also seen in participants on tirzepatide.

The researchers used a composite endpoint of a ≥ 2-point decrease in NAS with a ≥ 1-point decrease in at least two NAS components. Of the tirzepatide-treated groups, 71.7%,78.3%, and 76.6% in the 5-mg, 10-mg, and 15-mg groups, respectively, met this endpoint compared with 36.7% in placebo.

Dr. Loomba

Imaging of liver fat with MRI-based proton density fat fraction (MRI-PDFF) showed reductions from baseline of -45.7, -41.3, -57.0 in participants on 5-mg, 10-mg, and 15-mg tirzepatide, respectively. Differences from placebo were all statistically significant.

Percentage of body weight change from baseline was -10.7%, -13.3%, and -15.6% in the 5-mg, 10-mg, and 15-mg tirzepatide groups, respectively, compared with weight loss of -0.8% in the placebo group.

“Tirzepatide led to significant weight loss in both patients with diabetes and those without diabetes,” reported Dr. Loomba.

There were more adverse events in patients on tirzepatide (92.3%) compared with patients on placebo (83.3%).

“The most common adverse events were gastrointestinal in nature, with 96% of them mild to moderate in severity,” said Dr. Loomba. “Discontinuations occurred in 4.2% of participants, which was similar between patients on tirzepatide and those on placebo.”

He pointed out that the safety profile of tirzepatide in a MASH population “was generally similar to that observed in the phase 3 trials of type 2 diabetes and obesity.”

Incidence of serious adverse events was also similar at 6.3% for participants on tirzepatide vs 6.2% for those on placebo; 2.8% on tirzepatide and 4.2% on placebo progressed to cirrhosis. There was no evidence of drug-induced liver injury.

‘Convincing Results’

Commenting on the study, co-moderator Sven Francque, MD, hepatologist and head of department at the University Hospital of Antwerp, Belgium, said that the study was in a relatively “severe” patient population, which was one of its strengths.

“These are convincing results in terms of MASH resolution, showing a strong response and dose-dependence,” he said.

“In terms of fibrosis, the results look numerically strong but are somewhat more puzzling to interpret, as there was no dose-response relationship and no data on NITs [noninvasive tests] that could support the results,” he added.

Dr. Francque

“Patients with no-end-of-treatment biopsies were handled differently than in previous trials, which makes it difficult to appreciate antifibrotic potency,” he said. But “such a strong effect on MASH should translate into a reduction in fibrosis even in the absence of direct antifibrotic effects.”

Given that “about one third of patients in the active-treatment arms” did not have end-of-treatment biopsy, these “are rather small numbers precluding firm conclusions,” he added.

However, Dr. Francque said that he believes the findings are compelling enough for the drug to go into phase 3 trials.

Dr. Francque has no disclosures of relevance to this study. Dr. Loomba serves as a consultant to Aardvark Therapeutics, Altimmune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympse Bio, Hightide, Inipharma, Intercept, Inventiva, Ionis, Janssen, Madrigal, Metacrine, NGM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Sagimet, Theratechnologies, 89 bio, Terns Pharmaceuticals, and Viking Therapeutics. In addition, his institutions received research grants from Arrowhead Pharmaceuticals, AstraZeneca, Boehringer-Ingelheim, Bristol Myers Squibb, Eli Lilly, Galectin Therapeutics, Galmed Pharmaceuticals, Gilead, Intercept, Hanmi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, NGM Biopharmaceuticals, Novo Nordisk, Merck, Pfizer, Sonic Incytes, and Terns Pharmaceuticals. Dr. Loomba is a co-founder of LipoNexus. ■

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