MDEDGE.COM/GIHEPNEWS

VOL. 12 NO. 10 OCTOBER 2018

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

CATHERINE B. HACKETT/MDEDGE NEWS

Dr. Erin A. Bohula presented the study data on lorcaserin at the annual congress of the European Society of Cardiology.

Lorcaserin shows cardiovascular safety in CAMELLIA-TIMI 61

BY CATHERINE HACKETT
MDedge News

MUNICH – Lorcaserin is the first weight-loss drug proven to have cardiovascular safety, Erin A. Bohula, MD, DPhil, said in an interview.

Dr. Bohula reported on the results of the CAMELLIA-TIMI 61 trial, which was designed to evaluate the cardiovascular safety of the weight-loss drug lorcaserin in more than 10,000 patients. She presented the data at the annual congress of the European Society of Cardiology.

In CAMELLIA-TIMI 61, the primary safety endpoint, a composite of cardiovascular death, MI, or stroke, was nearly identical between patients on lorcaserin and those given placebo, 2% and 2.1% per year, at *P* less than .001 for noninferiority. Similarly, the primary efficacy outcome comprising heart failure, hospitalization for unstable angina, and coronary revascularization, was very close between the treated and placebo patients, occurring in 4.1% and 4.2% per year, respectively.

In addition, "there was

See **Lorcaserin** · *page 5*

Infliximab biosimilar only moderately less expensive

18% less costly under Medicare Part D

BY ANDREW D. BOWSER
MDedge News

The infliximab-dyyb biosimilar was only moderately less expensive than the originator infliximab product Remicade in the United States in 2017 under Medicare Part D, an analysis shows.

Infliximab-dyyb (Inflectra) cost 18% less than infliximab, with an annual cost exceeding $14,000 in an analysis published online in JAMA by Jinoos Yazdany, MD, of the division of rheumatology at the University of California, San Francisco, and her coauthors.

However, "without biosimilar gap discounts in 2017, beneficiaries would have paid more than $5,100 for infliximab-dyyb, or nearly $1,700 more in projected out-of-pocket costs than infliximab," Dr. Yazdany and her coauthors wrote.

Biologics represent only 2% of U.S. prescriptions but made up 38% of drug spending in 2015 and accounted for 70% of growth in drug spending from 2010 to 2015, according to Dr. Yazdany and her colleagues.

Biologics for rheumatoid arthritis (RA) and gastroenterology cost more than $14,000 per year, and in 2015, 3 were among the top

See **Expensive** · *page 26*

POEM effective for more than achalasia

BY WILL PASS
MDedge News

Peroral endoscopic myotomy (POEM) is safe and effective for several nonachalasia esophageal motility disorders, according to a retrospective study.

The procedure was clinically successful and relieved chest pain in most patients, reported Mouen A. Khashab, MD, director of therapeutic endoscopy at Johns Hopkins Hospital in Baltimore.

POEM was introduced in 2008 as a less-invasive alternative to laparoscopic Heller myotomy. During the procedure, submucosal tunneling is performed

See **POEM** · *page 30*

INSIDE

GI & HEPATOLOGY NEWS
10255 W Higgins Road,
Suite 280
Rosemont, IL 60018

CHANGE SERVICE REQUESTED

Presorted Standard
U.S. Postage
PAID
Permit No. 384
Lebanon Jct. KY

LETTER FROM THE EDITOR: Does this help the patient?

Twenty minutes after Ronald Reagan finished his inaugural address, the Islamic Republic of Iran announced the release of 52 American hostages that Iran had held for the last year of Jimmy Carter's presidency. The timing led to the "October Surprise conspiracy theory," in which some inferred a deliberate plan to influence an American election. We now refer to any political event timed to an election as an "October Surprise." We are awaiting some type of surprise prior to this November's elections. Events unfolding this fall will have generational effects on American politics, our health care delivery models, our financial security, individual rights and the democratic infrastructure of our country. This is not an election to sit out.


DR. ALLEN

The proposed rule the Centers for Medicare & Medicaid published in the summer has generated a massive public response. The major issues (as discussed in last month's *GI & Hepatology News* issue, including the editorial) include a dramatic change in documentation requirements and payment for evaluation and management (E/M) codes for both new and returning patients. While the reduction in documentation is laudable, the reduction in reimbursement for complex visits is not. At Michigan Medicine (2.2 million outpatient visits per year), reimbursements would go down by $3.5 million annually for our E/M visits. Most responses to the proposed rule requested a year's delay and intensive analysis of work involved prior to reducing payments (see further comments at gastro.org, the AGA website).

This month we cover a new anti-obesity drug that shows cardiovascular safety. This is a welcome potential addition to our therapies since another story updates us on the relentless rise in obesity in this country. We cover the world's alcohol use this month. On a financial note, the anticipated savings from biosimilars may be less than we hoped if data from Medicare Part D can be generalized. We also cover a diagnostic update about eosinophilic esophagitis.

I hope you enjoy this issue of *GI & Hepatology News* and all the AGA publications that provide you with up-to-date science, clinical information, and news about gastroenterology in general. Remember to vote. On the wall across my desk as I sit as a leader in ambulatory care at Michigan Medicine, there is a large sign that grounds me. It reads, "Does this help the patient?"

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

Earnings gap seen among Maryland physicians

BY RICHARD FRANKI
MDedge News

Male physicians in Maryland reported higher earnings than did female physicians, even when they all worked 41 or more hours a week, according to a 2018 survey of physicians in the state.

The average pretax income for all 508 respondents was $299,000 in 2016: Male physicians (66.6% of the sample) had an average of $335,000 and women averaged 33% lower at $224,000, MedChi (the Maryland State Medical Society) and Merritt Hawkins reported. Men did report working a longer week: Their average of 50.5 hours was 11% more than the 45.4-hour average for women.

"The biggest disparities we see in compensation are between male and female physicians in Maryland," Gene Ransom, MedChi's chief executive officer, said in a written statement. "Though such disparities have been noted in other research, it is still surprising to see the extent to which they persist."

Of the respondents who worked an average of 41 or more hours per week – an analysis conducted only for the three largest specialties in the survey – female internists earned 27% less than their male counterparts, female psychiatrists earned 24% less, and female family physicians earned 26% less, the survey results showed.

The survey was commissioned by MedChi and conducted by Merritt Hawkins from Jan. 10 to Feb. 23, 2018. The margin of error was plus or minus 4.4%.

rfranki@mdedge.com

WWW.GIHEPNEWS.COM
GI & HEPATOLOGY NEWS
THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

MDedge™

GI & HEPATOLOGY NEWS is the official newspaper of the American Gastroenterological Association (AGA) Institute and provides the gastroenterologist with timely and relevant news and commentary about clinical developments and about the impact of health care policy. Content for **GI & HEPATOLOGY NEWS** is developed through a partnership of the newspaper's medical board of editors (Editor in Chief and Associate Editors), Frontline Medical Communications Inc. and the AGA Institute Staff. "News from the AGA" is provided exclusively by the AGA, AGA Institute, and AGA Research Foundation. All content is reviewed by the medical board of editors for accuracy, timeliness, and pertinence. To add clarity and context to important developments in the field, select content is reviewed by and commented on by external experts selected by the board of editors.

POSTMASTER Send changes of address (with old mailing label) to GI & Hepatology News, Subscription Service, 10255 W Higgins Road, Suite 280, Rosemont, IL 60018-9914.
RECIPIENT To change your address, contact Subscription Services at 1-800-430-5450. For paid subscriptions, single issue purchases, and missing issue claims, call Customer Service at 1-833-836-2705 or e-mail custsvc.gihep@fulcoinc.com
The AGA Institute headquarters is located at 4930 Del Ray Avenue, Bethesda, MD 20814, ginews@gastro.org.
Editorial Offices 2275 Research Blvd, Suite 400, Rockville, MD 20850, 240-221-2400, fax 240-221-2548
GI & HEPATOLOGY NEWS (ISSN 1934-3450) is published monthly for $230.00 per year by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Phone 973-206-3434, fax 973-206-9378

Scan this QR Code to visit mdedge.com/gihepnews

FRONTLINE MEDICAL COMMUNICATIONS SOCIETY PARTNERS
VP/Group Publisher; Director, FMC Society Partners Mark Branca
Editor in Chief Mary Jo M. Dales
Executive Editors Denise Fulton, Kathy Scarbeck
Editor Lora T. McGlade
Creative Director Louise A. Koenig
Director, Production/Manufacturing Rebecca Slebodnik
National Account Manager Artie Krivopal, 973-290-8218, cell 973-202-5402, akrivopal@mdedge.com
Digital Account Manager Rey Valdivia, 973-206-8094, rvaldivia@mdedge.com
Senior Director of Classified Sales Tim LaPella, 484-921-5001, tlapella@mdedge.com
Advertising Offices 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609 973-206-3434, fax 973-206-9378

FRONTLINE MEDICAL COMMUNICATIONS
Corporate
President/CEO Alan J. Imhoff
CFO Douglas E. Grose
SVP, Finance Steven J. Resnick
VP, Operations Jim Chicca
VP, Sales Mike Guire
VP, Society Partners Mark Branca
VP, Editor in Chief Mary Jo M. Dales
VP, Editorial Director, Clinical Content Karen Clemments
Chief Digital Officer Lee Schweizer
VP, Digital Content & Strategy Amy Pfeiffer
President, Custom Solutions JoAnn Wahl
VP, Custom Solutions Wendy Raupers
VP, Marketing & Customer Advocacy Jim McDonough
VP, Human Resources & Facility Operations Carolyn Caccavelli
Data Management Director Mike Fritz
Circulation Director Jared Sonners
Corporate Director, Research & Comms. Lori Raskin
Director, Custom Programs Patrick Finnegan

AllMedx
President Douglas E. Grose
Executive VP, Sales John Maillard
Editorial Director/COO Carol Nathan

In affiliation with Global Academy for Medical Education, LLC
President David J. Small, MBA

Braintree
A PART OF SEBELA PHARMACEUTICALS®

FOR OVER 35 YEARS

Braintree—committed to expanding the universe of quality bowel prep products

1984

GoLYTELY®

(PEG-3350 and electrolytes for oral solution)[2]

1991

NuLYTELY®

(PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution)[1]

2004

HalfLytely® and Bisacodyl Tablets Bowel Prep Kit

(PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed - release tablets)*

2010

SUPREP® BOWEL PREP KIT

(sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

The #1 most prescribed, branded bowel prep kit with more than 15 million kits dispensed since 2010[3,4]

For additional information, please call 1-800-874-6756 or visit www.suprepkit.com.

References: 1. NuLYTELY [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2013. **2.** GoLYTELY [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2013. **3.** SUPREP Bowel Prep Kit [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2017. **4.** IQVIA. National Prescription Audit Report. August 2018.

*This product has been discontinued.

U.S. obesity continues to advance

BY RICHARD FRANKI
MDedge News

The prevalence of adult obesity was at or above 35% for seven states in 2017, which is up from five states in 2016 and no states in 2012, according to the Centers for Disease Control and Prevention.

Iowa and Oklahoma, the two newest states with prevalences at or exceeding 35%, joined Alabama, Arkansas, Louisiana, Mississippi, and West Virginia, which has the country's highest rate of adult obesity at 38.1%. Colorado's 22.6% rate is the lowest prevalence among all states. The District of Columbia and Hawaii also have prevalences under 25%; previously, Massachusetts also was in this group, but its prevalence went up to 25.9% last year, the CDC reported.

Regional disparities in self-reported adult obesity put the South (32.4%) and the Midwest (32.3%) well ahead of the Northeast (27.7%) and the West (26.1%) in 2017. Racial and ethnic disparities also were seen, with large gaps between blacks, who had a prevalence of 39%, and Hispanics (32.4%) and whites (29.3%). Obesity prevalence was 35% or higher among black adults in 31 states and D.C., while this was true among Hispanics in eight states and among whites in one (West Virginia), although the prevalence was at or above 35% for multiple racial groups in some of these states, the CDC reported based on data from the Behavioral Risk Factor Surveillance System.

"Obesity costs the United States health care system over $147 billion a year [and] research has shown that obesity affects work productivity and military readiness," the CDC said in a written statement. "To protect the health of the next generation, support for healthy behaviors such as healthy eating, better sleep, stress management, and physical activity should start early and expand to reach Americans across the lifespan in the communities where they live, learn, work, and play."

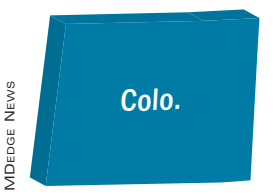
rfranki@mdedge.com

STATES OF OBESITY

Adult obesity prevalence, 2017

38.1%

West Virginia had the highest rate of self-reported obesity. **Colorado** had the lowest.



22.6%

MDedge News

Note: Based on data from the Behavioral Risk Factor Surveillance System.

Source: Centers for Disease Control and Prevention

Safe weight loss drugs needed

Lorcaserin *from page 1*

a sustained weight loss, more than with lifestyle alone or lifestyle plus placebo, which at its peak was about 3 kg. With that there were small, but significant, reductions in heart rate, blood pressure, triglycerides, and hemoglobin A_{1c}, and there was a significant reduction in new-onset diabetes."

"Overall, there's not a lot of use of pharmacologic agents for weight loss in the United States, and a lot of that is based on fear of the historical experience, which is that they were not safe. I suspect that having a drug that is proven safe will now lead people to reach for a pharmacologic agent like lorcaserin," said Dr. Bohula, a cardiologist at of Brigham and Women's Hospital and an investigator at the TIMI study group.

'I suspect that having a drug that is proven safe will now lead people to reach for a pharmacologic agent like lorcaserin.'

Key clinical point: In the study, the primary safety endpoint – a composite of cardiovascular death, MI, or stroke – was nearly identical between patients on lorcaserin and those given placebo.

The AGA Obesity Practice Guide provides physicians with a comprehensive, multidisciplinary process to guide and personalize innovative obesity care for safe and effective weight management. Learn more at https://www.gastro.org/practice-guidance/practice-updates/obesity-practice-guide.

chackett@mdedge.com

DDSEP eight Quick quiz

Digestive Diseases Self-Education Program

Q1. A 60-year-old woman is admitted to the hospital with an upper GI bleed and found to have a gastric ulcer. Biopsies from the ulcer show no malignancy. Gastric biopsies reveal no *Helicobacter pylori* and stool antigen for *H. pylori* is also negative. The patient denies any NSAID use. She is discharged home on twice-daily PPI. Two months later, she returns for a follow-up endoscopy, and the ulcer has healed.

What is your recommendation for this patient?

A. Continue once-daily PPI indefinitely
B. Discontinue PPI
C. Continue once-daily PPI for two more months
D. Discontinue PPI and start sucralfate

Q2. A 59-year-old woman with a history of cirrhosis due to nonalcoholic steatohepatitis presents for endoscopic evaluation of varices. Her past medical history includes obesity, diabetes, hypertension, and mild asthma. She appears well and has no signs of decompensation. Her vitals are: temperature, 98.6 ºF; blood pressure, 90/51 mm Hg; heart rate, 58 beats/minute; O_2 saturation, 98% on room air. Her endoscopy reveals mild portal hypertensive gastropathy, large esophageal varices, and no gastric varices.

Which is the best approach in the management of this patient?

A. Propranolol
B. Endoscopic variceal band ligation
C. Sclerotherapy
D. Transjugular intrahepatic portosytemic shunt (TIPS)
E. Nadolol plus endoscopic variceal band ligation

The answers are on page 19.

AGA CLINICAL PRACTICE UPDATE

Diagnosis of rumination syndrome

BY JEFF CRAVEN
MDedge News

Consider performing a full clinical evaluation for rumination syndrome when patients have symptoms of postprandial regurgitation, vomiting, or gastroesophageal reflux. Additionally, promote diaphragmatic breathing to help manage the condition, advised authors of an expert review of clinical practice updates for rumination syndrome published in Clinical Gastroenterology and Hepatology.

"Patients, not unsurprisingly, typically use the word 'vomiting' to describe rumination events, and many patients are misdiagnosed as having refractory vomiting, gastroesophageal reflux disease, or gastroparesis," Magnus Halland, MD, of the Mayo Clinic in Rochester, Minn., and colleagues wrote in the review. "A long delay in receiving a diagnosis is common and can lead to unnecessary testing, reduced quality of life, and even invasive procedures such as surgery or feeding tubes."

Rumination syndrome differs from vomiting, the authors noted, because the retrograde flow of ingested gastric content does not have an acidic taste and may in fact taste like food or drink recently ingested. Rumination can occur without any preceding events, after a reflux episode or by the swallowing of air that causes gastric straining but typically happens within 1-2 hours after a meal. Patients can experience weight loss, dental erosions and caries, heartburn, nausea, bloating, diarrhea, abdominal pain, abdominal discomfort, and belching, among other symptoms, in the presence of rumination syndrome, the authors said.

Dr. Halland and his colleagues provided seven best practice recommendations for rumination syndrome in their updates, which include:

- Patients who show symptoms of consistent postprandial regurgitation, often misdiagnosed with refractory gastroesophageal reflux or vomiting, should be considered for rumination syndrome.
- Patients who have dysphagia, nausea, nocturnal regurgitation, or gastric symptoms outside of meals are less likely to have rumination syndrome, but those symptoms do not exclude the condition.
- Rome IV criteria are advised to diagnose rumination syndrome after medical work-up, which includes "persistent or recurrent regurgitation of recently ingested food into the mouth with subsequent spitting or remastication and swallowing" not preceded by retching where patients fulfill these symptom criteria for 3 months with a minimum of 6 months of symptoms before diagnosis.
- Patients should receive first-line therapy for rumination syndrome consisting of diaphragmatic breathing with or without biofeedback.
- Patients should be referred to a speech therapist, gastroenterologist, psychologist, or other knowledgeable health practitioners to learn effective diaphragmatic breathing.
- Current limitations in the diagnosis of rumination syndrome include need for expertise and lack of standardized protocols, but "testing for rumination syndrome with postprandial high-resolution esophageal impedance manometry can be used to support the diagnosis."
- Bacloflen (10 mg) taken three times daily is a "reasonable next step" for patients who do not respond to treatment.

The authors acknowledged that many questions, such as the pathophysiology and initiating factors of rumination syndrome, are unknown and noted future studies are needed to address epidemiology, develop validated tools for measuring symptoms, and study diaphragmatic breathing's effect on reducing symptoms of rumination syndrome as well as the condition's impact on quality of life.

"Indeed, the basic question of how subconsciously one can learn to regurgitate still needs to be answered," Dr. Halland and his colleagues wrote.

The authors report no relevant conflicts of interest.

ginews@gastro.org

SOURCE: Halland M et al. Clin Gastroenterol Hepatol. 2018 Jun 11. doi: 10.1016/j.cgh.2018.05.049.

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

FROM THE AGA JOURNALS

Inflammatory diet tied to CRC testing positive for *F. nucleatum*

BY AMY KARON
MDedge News

Diets promoting colonic inflammation were associated with a greater risk of colorectal carcinomas containing *Fusobacterium nucleatum*, according to a report in the October issue of Clinical Gastroenterology and Hepatology.

Proinflammatory diets were not linked to heightened risk for colon cancers without these bacteria, reported Li Liu, MD, PhD, of Dana-Farber Cancer Institute and Harvard Medical School, Boston, and coauthors. "These findings indicate that diet-induced intestinal inflammation alters the gut microbiome to contribute to colorectal carcinogenesis."

Intestinal inflammation is associated with high levels of circulating interleukin 6, C-reactive protein, and tumor necrosis factor–receptor superfamily member 1B. Colonic inflammation impairs the mucosal barrier and alters immune responses, which affects the composition of colonic microbiota. Among these, *F. nucleatum* is known to potentiate colorectal tumors and is associated with proximal tumor location, other tumor features, and cancer progression and chemoresistance.

For the study, the investigators examined self-reported data from more than 124,000 individuals followed for 28 years as part of the Nurses' Health Study and the Health Professionals Follow-Up Study. They calculated average dietary patterns based on the empiric dietary inflammatory pattern (EDIP) score, which sums weighted intake scores for 18 foods (such as red and processed meat, coffee, tea, and leafy green or dark yellow vegetables) that are known to affect plasma levels of interleukin 6, C-reactive protein, tumor necrosis factor–receptor superfamily member 1B, and tumor necrosis factor alpha–receptor 2. A higher EDIP score denotes a more inflammatory diet.

During the 28-year follow-up period, 951 individuals developed colorectal carcinomas that were tested with a polymerase chain reaction assay for *F. nucleatum* DNA. A total of 115 tumors tested positive for *F. nucleatum*. After the researchers controlled for potential confounders, individuals whose EDIP scores were in the highest tertile were significantly more likely to develop *F. nucleatum*–positive CRC than were those who scored in the lowest tertile (adjusted hazard ratio, 1.63; 95% confidence interval, 1.03-2.58; $P = .03$). This differential association "appeared to be stronger in proximal colon cancer than in distal colon and rectal cancer," the researchers said.

More than 90% of individuals in this study were non-Hispanic white, the researchers noted. Tumor tissue was not available from all cases of CRC and a fairly small number of cases tested positive for *F. nucleatum*. Nonetheless, the findings suggest that an inflammatory diet could amplify gut microbiota involved in tumorigenesis. Pending confirmatory studies, they recommended an anti-inflammatory diet with high intake of green leafy vegetables, dark yellow vegetables, coffee, and tea. They also recommended studying whether *F. nucleatum* tumor or stool tests could help personalize dietary interventions.

Funders included the National Institutes of Health, Dana-Farber Harvard Cancer, Project P. Fund for Colorectal Cancer Research, and others. Dr. Liu had no disclosures. One coinvestigator disclosed ties to Genentech/Roche, Lilly, Sanofi, Bayer, and several other companies.

ginews@gastro.org

SOURCE: Liu L et al. Clin Gastroenterol Hepatol. 2018 Apr 24. doi: 10.1016/j.cgh.2018.04.030.

The underlying reasons colorectal cancer (CRC) develops are unknown, but they likely include a complex interaction between genetics and environmental exposures. Recent studies have highlighted important links among diet, the intestinal microbiota, and CRC development and progression.


DR. SHAH

Liu et al. used the Nurses' Health Study and Health Professionals Follow-Up Study cohorts to extend our understanding of these relationships. They utilized validated food frequency questionnaires obtained every 4 years and formalin-fixed paraffin embedded CRC tissue samples collected from 951 individuals. They calculated an EDIP score, which correlates components of the diet with plasma inflammatory markers. After adjusting for confounders, they found high EDIP scores were significantly associated with *Fusobacterium nucleatum*–positive CRC but not with *F. nucleatum*–negative CRC. In addition, they demonstrated this association was stronger for proximal compared with distal CRC. Their findings suggest an inflammatory diet may interact with the intestinal microbiota to promote the development of CRC, and they provide a preliminary recommendation to minimize intake of potentially harmful foods (such as red meat, processed meat, and refined grains). Despite the intriguing results, the authors do recognize limitations including the small number of cases with *F. nucleatum* present (n = 115) and the homogeneous cohort (90% non-Hispanic whites), which may limit generalizability.

As clinicians, we should continue advocating for CRC screening and may consider dietary recommendations to reduce intake of potentially harmful foods. Further research will be needed to confirm these findings.

Rajesh R. Shah, MD, is assistant professor of gastroenterology, department of internal medicine, Baylor College of Medicine, Houston. He has no conflicts of interest.

FROM THE AGA JOURNALS

Cirrhosis study finds no link between screening, liver cancer mortality

BY AMY KARON
MDedge News

In a case-control study of patients with cirrhosis, screening for hepatocellular carcinoma up to 4 years prior to diagnosis was not associated with lower mortality.

Similar proportions of cases and controls underwent screening with abdominal ultrasonography, serum alpha-fetoprotein (AFP) testing, or both, reported Andrew M. Moon, MD, MPH, of the University of North Carolina at Chapel Hill and his associates. "There was also no difference in receipt of these screening tests within 1, 2, or 3 years prior to the index date," they wrote. The report was published in Gastroenterology. The findings "[suggest] that either these screening tests or the currently available treatments [for liver cancer], or both, are suboptimal and need to be improved."

Because cirrhosis significantly increases the risk of hepatocellular carcinoma, the American Association for the Study of Liver Diseases, the European Association for the Study of the Liver, and the Asian Pacific Association for the Study of the Liver recommend screening cirrhotic patients every 6 months with abdominal ultrasonography with or without concomitant serum AFP. But nonliver societies have not endorsed this approach, citing a lack of high-quality data. One problem is that studies have compared patients whose liver cancer was diagnosed by screening with those diagnosed after they became symptomatic, which creates a lead-time bias that inherently favors screening, Dr. Moon and his associates noted.

To help fill the evidence gap, they identified 238 patients from the Veterans Affairs health care system who had died of hepatocellular carcinoma between 2013 and 2015 and who had been diagnosed with cirrhosis at least 4 years beforehand. They compared these cases with an equal number of patients with cirrhosis who had been in VA care for a similar amount of time and had not died of hepatocellular carcinoma. Cases and controls were matched by etiology of cirrhosis, year that cirrhosis was diagnosed, race, age, sex, Model for End-Stage Liver Disease score, and VA medical center. The researchers identified screening tests by reviewing blinded medical charts.

There were no significant differences in the proportions of cases and controls who underwent screening ultrasonography (52.9% versus 54.2%, respectively), screening serum AFP (74.8% versus 73.5%), either test (81.1% versus 79.4%), or both tests (46.6% versus 48.3%) within 4 years of the index date. The result was similar after potential confounders were controlled for and when examining shorter time frames of 1, 2, and 3 years.

It was unlikely that these results reflect delayed diagnosis of liver cancer or a lack of treatment within the VA system, the experts wrote. A total of 51.3% of cases were diagnosed with Milan criteria, which exceeds the proportion in the national Surveillance, Epidemiology, and End Results registry, they noted. None of the fatal cases underwent liver transplantation, but 66.8% received other treatments for liver cancer.

Funders included the National Institutes of Health and the Veterans Affairs Clinical Science Research & Development. The investigators reported having no conflicts of interest.

ginews@gastro.org

SOURCE: Moon AM et al. Gastroenterology. 2018 Jul 5. doi: 10.1053/j.gastro.2018.06.079.

Commentary: Composite risk, not age, is key for timing first colorectal cancer screening

BY AMY KARON
MDedge News

The American Cancer Society's recent recommendation to lower the age of first screening for colorectal cancer (CRC) to 45 years does not reflect clear knowledge of risks versus benefits, experts wrote in a recent commentary.

"In the big picture, [the question of whether to start screening at 45 versus 50 years] seems relatively unimportant compared with using individual patient risk for advanced neoplasia in practical, feasible models" that are geared toward adherence, efficiency, and cost-efficacy, wrote Charles J. Kahi, MD, MSc, AGAF, of Indiana University, Indianapolis, and his associates. The commentary is in the October issue of Clinical Gastroenterology and Hepatology.

Tailoring age of first screening on an individual level, based on other risk factors and patient preferences, might improve uptake and benefit-risk ratios, balance, they argued.

Rates of CRC in persons under age 50 rose by about 22% between 2000 and 2013. However, estimates for the most recent birth cohorts have wide confidence intervals, "indicating imprecision and uncertainty that this trend will continue," the experts wrote. Furthermore, the absolute risk of CRC among individuals younger than 50 years has risen only slightly, from 5.9 cases per 100,000 population to 7.2 cases per 100,000 population. "[This] small increase in incidence may represent a true increase or could be due to increased use of colonoscopy in general and, specifically, for diagnosis or high-risk screening of first-degree relatives of persons with [CRC]," the experts wrote.

Implementing the new recommendation could detect earlier-stage (curable) CRC "in a youthful and productive age group that may be sandwiched between raising children and caring for aging parents," they continued. Earlier detection could reduce mortality and reduce the costs of treating a disease that often exceeds $100,000 per person annually.

However, the recommendation was based on a modeling study that assumed 100% adherence. In reality, uptake among 45- to 49-year-olds might be 15%-20%, and "who actually shows up for screening could make or break this recommendation," the experts said. If younger individuals who underwent screening tended to have few risk factors for CRC, then the new recommendation would lead to many false positives and unnecessary colonoscopies, with the associated fallout of emotional harm and wasted health care resources, they added.

Population-level studies have identified age as the strongest predictor of CRC, but age "does not perform as well" at patient level, the experts said. They emphasized the role of other risk factors, such as male sex, having a first-degree relative with CRC, high body mass index, metabolic syndrome, cigarette smoking, diet, adherence to screening, and use of aspirin, NSAIDS, and hormone therapy. "The goal for providers and health systems is to determine whether and how to change screening practice and policy and how to incorporate this new recommendation into practice, a necessarily complex process that requires knowing patient risk, patient preferences, and the long-term balance of benefits and burdens," they concluded.

Dr. Kahi and coauthor Thomas F. Imperiale, MD, AGAF, had no disclosures. Coauthor Douglas K. Rex, MD, AGAF, disclosed ties to Aries Pharmaceutical, Cosmo Pharmaceuticals, Boston Scientific, Sebela, Medtronic, and others. He also chairs the U.S. Multi-Society Task Force on Colorectal Cancer.

ginews@gastro.org

SOURCE: Imperiale T et al. Clin Gastroenterol Hepatol. 2018 Aug 13. doi: 10.1016/j.cgh.2018.08.023).

FROM THE AGA JOURNALS

Experts update diagnostic guidelines for EoE

BY AMY KARON
MDedge News

The diagnosis of eosinophilic esophagitis (EoE) no longer needs to include a trial of proton pump inhibitor (PPI) therapy, according to an updated international consensus statement published in the October issue of Gastroenterology.

"An initial rationale for the PPI trial was to distinguish eosinophilic esophagitis from gastroesophageal reflux disease, but it is now known that these conditions have a complex relationship and are not necessarily mutually exclusive," wrote Evan S. Dellon, MD, AGAF, of the University of North Carolina at Chapel Hill and his associates. According to current evidence, "PPIs are better classified as a treatment for esophageal eosinophilia that may be due to eosinophilic esophagitis than as a diagnostic criterion," they said.

Diagnostic guidelines for eosinophilic esophagitis were published first in 2007 and were updated in 2011. The guideline authors recommended either pH monitoring or an 8-week trial of high-dose PPI therapy to rule out inflammation from gastroesophageal reflux disease (GERD).

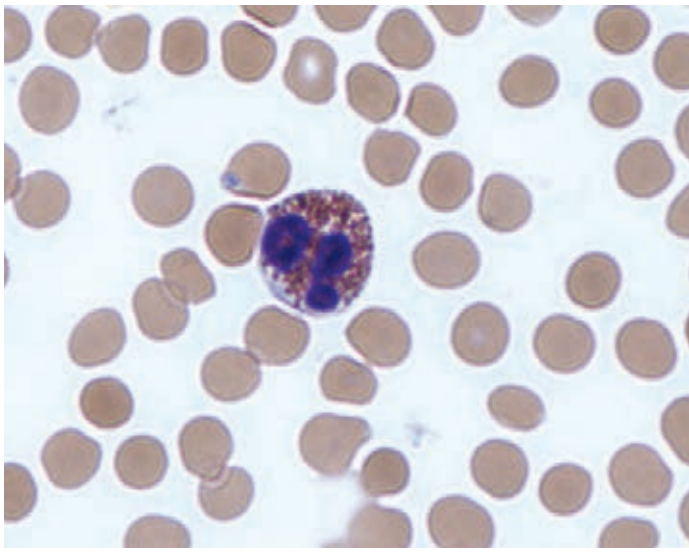
But subsequent publications described patients with symptomatic esophageal eosinophilia who responded to PPIs and lacked classic GERD symptoms. Guidelines called this condition "PPI-responsive esophageal eosinophilia" and considered it a separate entity from GERD.

However, an "evolving body of research" shows that eosinophilic esophagitis can overlap with GERD, Dr. Dellon and his associates wrote. Furthermore, each of these conditions can trigger the other. Eosinophilic esophagitis can decrease esophageal compliance, leading to secondary reflux, while gastroesophageal reflux can erode the esophageal epithelium, triggering antigen exposure and eosinophilia.

Therefore, Dr. Dellon and his associates recommended defining eosinophilic esophagitis as signs and symptoms of esophageal dysfunction and an esophageal biopsy showing at least 15 eosinophils per high-power field, or approximately 60 eosinophils per millimeter, with infiltration limited to the esophagus. They stressed the importance of esophageal biopsy even if endoscopy shows normal mucosa. "As per prior guidelines, multiple biopsies from two or more esophageal levels, targeting areas of apparent inflammation, are recommended to increase the diagnostic yield," they added. "Gastric and duodenal biopsies should be obtained as clinically indicated by symptoms, endoscopic findings in the stomach or duodenum, or high index of suspicion for a mucosal process."

Physicians should increase their suspicion of eosinophilic esophagitis if patients have other types of atopy or endoscopic findings of "rings, furrows, exudates, edema, stricture, narrowing, and crepe-paper mucosa," they added. In addition to GERD, they recommended looking carefully for other conditions that can trigger esophageal eosinophilia, such as pemphigus, drug hypersensitivity reactions, achalasia, and Crohn's disease with esophageal involvement.

To create the guideline, Dr. Dellon and his associates searched PubMed for studies of all designs and sizes published from 1966 through December 2016. Teams of experts on specific topics then reviewed and discussed relevant literature. In May 2017, 43 reviewers met for 8 hours to present and discuss conclusions. There was 100% agreement to remove the PPI trial from the diagnostic criteria, the experts noted.



DR. GRAHAM BEARDS/WIKIMEDIA COMMONS/CC ASA 3.0

Eosinophil

The authors disclosed financial support from the International Gastrointestinal Eosinophilic Diseases Researchers (TIGERS), The David and Denise Bunning Family, and the Rare Disease Clinical Research Network. Dr. Dellon disclosed consulting relationships and receiving research funding from Adare, Celgene/Receptos, Regeneron, and Shire among others. The majority of his coauthors also disclosed relationships with numerous medical companies.

ginews@gastro.org

SOURCE: Dellon ES et al. Gastroenterology. 2018 Jul 12. doi: 10.1053/j.gastro.2018.07.009.

AGREE (A Working Group on Proton Pump Inhibitor Responsive Esophageal Eosinophilia) was an interdisciplinary and international effort that brought together 66 pediatric and adult clinicians and investigators from 14 nations representing the fields of allergy, immunology, gastroenterology, and pathology, as well as patient advocacy groups, to derive consensus on the role of PPI therapy in the management of patients with suspected eosinophilic esophagitis (EoE). The significance of the AGREE recommendation to eliminate the PPI trial from the diagnostic criteria for EoE is best appreciated from a historical perspective. Studies in the 1980s linked the presence of esophageal mucosal eosinophils with increased acid exposure on pH monitoring.

DR. HIRANO

For the next 2 decades, clinicians viewed eosinophils on esophageal biopsies as diagnostic for GERD such that the initial description of EoE by Attwood in 1993 distinguished EoE from GERD by the presence of esophageal eosinophilia in the absence of either reflux esophagitis or abnormal acid exposure on pH testing. Consequently, the initial diagnostic criteria for EoE in 2007 included a lack of response to PPI and/or normal pH testing to establish the diagnosis of EoE. Reflecting growing uncertainty regarding the ability of PPI therapy to differentiate acid-induced from allergic inflammatory mechanisms, an updated consensus in 2011 introduced the terminology "PPI-responsive esophageal eosinophilia (PPIREE)" to describe an increasingly recognized subset of patients with suspected EoE that resolved with PPI. Now, supported by scientific evidence accumulated over the past decade, AGREE has taken a step back by removing the PPI trial from the diagnosis of EoE, thereby abandoning the PPIREE terminology. This step simplifies the diagnosis of EoE and acknowledges that a histologic response to PPI does not "rule in" GERD or "rule out" EoE.

It is important to emphasize that the updated criteria still advocate careful consideration of secondary causes of esophageal eosinophilia prior to the diagnosis of EoE.

Ramifications of the updated diagnostic criteria include the opportunities for clinicians to consider use of topical corticosteroids and diet therapies, rather than mandate an upfront PPI trial, in patients with EoE. On a practical level, based on their effectiveness, safety, and ease of administration, PPIs remain positioned as a favorable initial intervention for EoE. Conceptually, however, the paradigm shift highlights the ability of research to improve our understanding of disease pathogenesis and thereby impact clinical management.

Ikuo Hirano, MD, AGAF, is in the division of gastroenterology, Northwestern University, Chicago. He has received grant support from the NIH Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR, U54 AI117804), which is part of the Rare Disease Clinical Research Network. He has received research funding and consulting fees from Celgene, Regeneron, Shire, and others.

WWW.GIHEPNEWS.COM

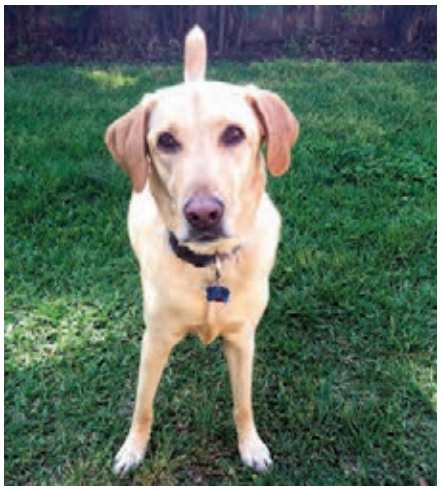
GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

AGA Research Foundation researcher of the month: David L. Boone, PhD

AGA Research Foundation pilot awards are an invaluable tool for investigators – they provide seed funding to explore promising new lines of research and generate preliminary data for larger grants. So, when David L. Boone, PhD, received the 2017 AGA-Pfizer Young Investigator Pilot Research Award in Inflammatory Bowel Disease from the AGA Research Foundation, he was able to double-down on a very targeted project studying innate immunity in IBD. Based on his recent accomplishments – both in and out of the lab – we're excited for you to get to know Dr. Boone, associate professor of microbiology and immunology at Indiana University School of Medicine-South Bend, and our AGA Research Foundation researcher of the month.

Dr. David Boone at Camp Oasis, the Crohn's & Colitis Foundation camp for IBD patients.



Boone lab, so named by a postdoctoral researcher in the lab.

Dr. David Boone, camp counselor at Camp Oasis

Bench to bedside: working toward new treatment options in IBD

The Boone lab AGA-funded project is specifically focused on JAK inhibitors, which are becoming a more popular treatment option for patients with IBD, especially for those patients who don't respond to anti-TNF therapy. Dr. Boone is committed to enhancing our understanding of how these JAK inhibitors work at a cellular level. If we can understand this, Dr. Boone is optimistic it will lead to new approaches for treating inflammation in IBD.

With his AGA Research Foundation grant, Dr. Boone and his lab characterized a new robust mouse model of colitis that is entirely driven by innate immune mechanisms. With this model, his team is investigating the cellular and molecular mechanisms that drive innate immune-mediated inflammation in the intestine, which will provide important insights for future IBD drug development. You can read the specifics of Dr. Boone's research in his recently published work in Mucosal Immunology.

Pilot award provides a stepping stone

Dr. Boone's AGA Research Foundation pilot grant has paved the way for future success. Using the data from his AGA-funded project, as well as the constructive feedback he received from the AGA awards panel, Dr. Boone went on to successfully obtain new funding in the form of a Pfizer ASPIRE research grant. This work is building the foundation for Dr. Boone's next big grant venture: an NIH R01 grant.

Two postdocs, a graduate student, a technician, and a dog named Boone

Dr. Boone shared with us that the best outcome from his AGA grant was that the additional funding made it possible to grow his lab by a postdoctoral researcher and lab technician. One of Dr. Boone's great passions is training the next generation of scientists, both in the lab and through his role as a microbiology and immunology professor for first-year medical students at Indiana University Medical School.

It's clear that Dr. Boone has made a lasting impact on his former mentees and students. One of his former postdoctoral researchers named her labrador retriever "Boone" in his honor (hence Boone lab). In an ironic turn of events, Boone the dog is currently being treated with a JAK inhibitor for an inflammatory condition!

Beyond the lab – a commitment to IBD patients

Dr. Boone wanted to do more to support patients with IBD. He had heard of Camp Oasis – the Crohn's & Colitis Foundation regional camp for patients with IBD – and knew of physicians who provided medical services at the camp. After looking into making a donation to Camp Oasis Michigan, Dr. Boone learned that what the camp really needed was male counselors. So, despite being "older than an average camp counselor," Dr. Boone packed his bags for Michigan. Participating in Camp Oasis the last 2 years has been a great joy for Dr. Boone and provides added inspiration and motivation for his work in the lab.

The AGA Research Foundation is proud to fund researchers who are committed to improving the lives of patients – both in and out of the lab. You can help keep great researchers in GI by making a gift to the AGA Research Foundation, www.gastro.org/foundation.

ginews@gastro.org

A gift to the AGA Research Foundation in your will

A simple, flexible and versatile way to ensure the AGA Research Foundation can continue to help spark the scientific breakthroughs of today so clinicians will have the tools to improve care tomorrow, is through a gift in your will or living trust, known as a charitable bequest.

To make a charitable bequest, you need a current will or living trust. Your gift can be made as a percentage of your estate. Or you can make a specific bequest by giving a certain amount of cash, securities or property. After your lifetime, the Foundation receives your gift.

Including the AGA Research Foundation in your will is a popular gift to give because it is:

- **Affordable.** The actual giving of your gift occurs after your lifetime, so your current income is not affected.
- **Flexible.** Until your will goes into effect, you are free to alter your plans or change your mind.
- **Versatile**. You can give a specific item, a set amount of money or a percentage of your estate. You can also make your gift contingent upon certain events.

We hope you'll consider including a gift to the AGA Research Foundation in your will or living trust. It's simple – just a few sentences in your will or trust are all that is needed. The official bequest language for the AGA Research Foundation is: "I, [name], of [city, state, ZIP], give, devise and bequeath to the AGA Research Foundation [written amount or per-centage of the estate or description of property] for its unrestricted use and purpose."

By including a gift to the AGA Research Foundation in your will, you can help fill the funding gap and protect the next generation of investigators.

For more information, visit http://gastro.planmylegacy.org/ or contact us at foundation@gastro.org.

ginews@gastro.org

Top patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses.

In case you missed it, here are the most popular clinical cases shared in the forum recently:

1. Eosinophilic esophagitis and stricture
A tight stricture in the mid-esophagus of a 25-year-old patient prevented the physician from passing the scope on multiple occasions within 5 weeks.

2. Behcet's disease
A 41-year-old patient with Behcet's disease and celiac disease originally reported joint pain and diarrhea, which subsided after treatment with prednisone and sulfasalazine. Despite a limited diet and therapeutic levels of Humira, her symptoms resurfaced 6 months later with loose stools and urgency.

3. Ectopic varices with portal vein thrombosis
This case involves a 49-year-old male who developed necrotizing pancreatitis due to microlithiasis in 2008, followed by pyrexia with three pyogenic liver abscesses this past May. The attending physician solicited advice from the GI community on management of this patient's portal hypertension.

4. Firefighters at higher CRC risk?
Join this informative discussion about a reported "1.21 times greater risk" for colorectal cancer in firefighters, and increased screening for this demographic.

More clinical cases and discussions are at https://community.gastro.org/discussions.

ginews@gastro.org

Rising microbiome investigator: Ting-Chin David Shen, MD, PhD

We spoke with Dr. Shen, instructor of medicine at the University of Pennsylvania and the recipient of the AGA Research Foundation's 2016 Microbiome Junior Investigator Award, to learn about his passion for gut microbiome research.


DR. SHEN

How would you sum up your research in one sentence?

My research examines the metabolic interactions between the gut microbiota and the mammalian host, with a particular emphasis on amino acid metabolism and nitrogen flux via the bacterial enzyme urease.

What impact do you hope your research will have on patients?

My hope is that by better understanding the biological mechanisms by which the gut microbiota impacts host metabolism, we can modulate its effects to treat a variety of conditions and diseases including hepatic encephalopathy, inborn errors of metabolism, obesity, malnutrition, etc.

What inspired you to focus your research career on the gut microbiome?

My clinical experience as a gastroenterologist inspired my interest in metabolic and nutritional research. When I learned of the impact that the gut microbiota has on host metabolism, it created an entirely different perspective for me in terms of thinking about how to treat metabolic and nutritional disorders. There are tremendous opportunities in modifying our gut microbiota in concert with dietary interventions in order to modulate our metabolism.

What recent publication from your lab best represents your work, if anyone wants to learn more?

The following work examined how the use of a defined bacterial consortium without urease activity can reduce colonic ammonia level upon inoculation into the gut and ameliorate morbidity and mortality in a murine model of liver disease: Shen T.D., Albenberg L.A., Bittinger K., et al, Engineering the gut microbiota to treat hyperammonemia. J Clin Invest. 2015 Jul 1;125(7):2841-50. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4563680/.

ginews@gastro.org

AGA Center for Gut Microbiome Research and Education scientific advisory board welcomes new members

Four leading experts in microbiome research have recently been appointed to the scientific advisory board of the AGA Center for Gut Microbiome Research and Education.

Robert A. Britton, PhD
Baylor College of Medicine, Houston, Texas

Dr. Britton studies the role of microbes in health and diseases, with a focus on identifying microbes with therapeutic properties for a variety of disorders.

Suzanne Devkota, PhD
Cedars-Sinai Medical Center, Los Angeles, California

Dr. Devkota investigates the role of diet in shaping the community of bacteria that live in our intestines (the "gut microbiome").

Lita M. Proctor, PhD
National Human Genome Research Institute, Rockville, Maryland

Dr. Proctor is responsible for coordination of the Human Microbiome Project (HMP), an eight-year NIH Common Fund initiative to create a toolbox of resources for the emerging field of microbiome research.

Liping Zhao, PhD
Rutgers University, New Brunswick, New Jersey

Dr. Zhao studies the interactions between diet and gut microbiota in the onset and progression of chronic diseases such as obesity and diabetes.

AGA recognizes the outgoing members of the scientific advisory board who have made valuable contributions to the center's work over their terms: Lee M. Kaplan, MD, PhD, AGAF; Zain Kassam, MD, MPH; and Ece Mutlu, MD, MBA, AGAF.

ginews@gastro.org

Mayo Clinic announces new president and CEO: Gianrico Farrugia, MD


MAYO CLINIC
Dr. Gianrico Farrugia

The Mayo Clinic Board of Trustees has announced that Gianrico Farrugia, MD, vice president and CEO of Mayo Clinic Florida, will take over as president and CEO of Mayo Clinic at the end of the year. AGA congratulates Dr. Farrugia.

Here's three reasons why AGA is excited by this news:

1. Dr. Farrugia is an accomplished GI investigator. Dr. Farrugia runs an NIH-funded translational laboratory focused on disorders of GI motility. The aim of Dr. Farrugia's work is to understand at a cellular, subcellular and molecular level how the normal functions of the GI tract determine the defects that result in diseases such as diabetic gastroparesis, slow transit constipation, and irritable bowel syndrome

Continued on following page

AGA comments on HHS' drug affordability blueprint

AGA's new drug affordability principles were put into action in July when AGA Chair Sheila Crowe, MD, AGAF, provided comments on the Department of Health & Human Services (HHS) recent policy statement and Request for Information, "HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs" (Blueprint). Comments were limited to four areas of the Blueprint.

Medicare Part B to Part D drug transition

Over the past decade there has been interest in consolidating Part B and Part D drug coverage and payment. AGA urges physician-administered drugs and biologics to remain under Part B due to the complexities surrounding them.

Since Part D does not allow for supplemental coverage and has higher coinsurance, this action would achieve savings by shifting costs to Medicare beneficiaries. Moving them to Part D would also increase the risk of waste leading to unnecessary Medicare spending. AGA urges the administration to avoid policy solutions that achieve Medicare program savings at the expense of Medicare beneficiaries.

Indication-based payments

The Blueprint seems to imply that off-label uses of prescription drugs are inherently less valuable than on-label uses. If the administration moves towards value-based pricing, off-label indications should not automatically be valued less, or priced lower, than on-label indications. Specifically, AGA urges the administration to ensure all medically accepted indications are appropriately valued for a drug or biologic.

Medicare Part B Competitive Acquisition Program (CAP)

AGA does not oppose the idea of a new, voluntary CAP program as it would allow interested physicians and practices to provide Part B drug administration without the burden of high acquisition costs.

AGA strongly opposes a future Part B CAP that includes vendors or Medicare carriers conducting medical reviews or utilization management. Utilization management undermines shared decision-making between physicians and patients, increases physician burden, and often puts patients at risk by delaying access to necessary care.

Reduce patient out-of-pocket spending

As out-of-pocket costs continue to rise, AGA supports the administration's plans to increase cost transparency in the Medicare program as it increases the efficiency of the shared decision-making process between patient and physician. Drug and biologic manufacturers, health plans, and pharmacy managers should work together to lower out-of-pocket expenses for Medicare beneficiaries and for all people with digestive diseases.

Although AGA shares the Blueprint's goal of lowering the cost of prescription drugs, lowering out-of-pocket costs for patients, increasing competition and fostering innovation, we are concerned that the recent proposal by the Trump administration to allow Medicare Advantage (MA) plans to utilize step therapy would threaten the aforementioned goals. Step therapy is a utilization management tool used by insurers that requires patients to fail one or more medications before covering the original therapy that is prescribed by the physician. AGA is concerned that the recent announcement by the Trump administration would not provide patients with the necessary protections, would increase the regulatory burden that physicians already face with step therapy and prior authorization, and could hinder innovation by preferring the lowest cost medication which may not necessarily be the most effective. AGA will continue to push for necessary patient protections to ensure that patients have the ability to appeal step therapy protocols when appropriate and are able to receive the medication that their physician thinks is the most effective to manage their condition.

ginews@gastro.org

Continued from previous page

(IBS), which will ultimately lead to new strategies to treat these diseases by developing targeted disease-modifying agents.

2. Dr. Farrugia is an alumnus of the AGA Research Foundation Research Scholar Award program. Dr. Farrugia received his Research Scholar Award in 1994 for his project titled "Jejunal Smooth Muscle Ion Channel Regulation in Health and Disease."

3. Dr. Farrugia has given back to AGA both with his time – serving on the AGA Nominating Committee, AGA Institute Council, and Cellular and Molecular Gastroenterology and Hepatology editorial board – and by contributing, with his wife Geraldine Farrugia, to the AGA Research Foundation at the highest level as an AGA Legacy Society member.

Join AGA members in congratulating Dr. Farrugia in the AGA Community, community.gastro.org.

ginews@gastro.org

DDSEP eight
Digestive Diseases Self-Education Program

Quick quiz answers

Q1. Correct Answer: A

Rationale

This patient has an idiopathic, nonNSAID, non-*H. pylori*-associated ulcer and should be on daily PPI indefinitely. These patients have a high rate of recurrent bleeding (42%) and mortality when followed prospectively without being on antisecretory therapy. Although no randomized trials have assessed the benefit of medical cotherapy in this population, antiulcer therapy seems to reduce recurrent idiopathic ulcers.

References

1. Wong G.L.H., Wong V.W.S., Chan Y., et al. High incidence of mortality and recurrent bleeding in patients with *Helicobacter pylori*-negative idiopathic bleeding ulcers. Gastroenterology. 2009;137:525-31.
2. Laine L., Jensen D.M. Management of patients with ulcer bleeding. Am J Gastroenterol. 2012;107(3):345-60.

Q2. Correct Answer: B

Rationale

This patient has large varices, which should be treated. In patients with cirrhosis and medium/large varices that have never bled, nonselective beta-blockers reduce the risk of first variceal hemorrhage by 50%. In high-quality randomized-controlled trials, endoscopic variceal ligation (EVL) is as effective as nonselective beta-blockers in preventing first variceal hemorrhage. Therefore, either of these therapies should be used for the prevention of first variceal bleeding. In this case, propranolol is not the best choice in the setting of diabetes, asthma as well as a blood pressure and pulse that are low already. Endoscopic variceal band ligation would be preferred in this patient. It is also more effective than sclerotherapy and is associated with fewer side effects. TIPS would be effective, but more invasive and not first-line for treatment of nonbleeding varices and comes with increased risk of hepatic encephalopathy and potentially mortality. The combination of nadolol and endoscopic variceal band ligation may have more side effects without a further reduction in the risk of first variceal hemorrhage beyond either therapy alone.

References

1. Gluud L.L., Klingenberg S., Nikolova D., Gluud C. Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. Am J Gastroenterol. 2007;102(12):2842-8.
2. Gluud L.L., Krag A. Banding ligation versus betablockers for primary prevention in oesophageal varices in adults. Cochrane Database Syst Rev. 2012;8:CD004544. doi: 10.1002/14651858.CD004544.
3. Villanueva C., Piqueras M., Aracil C., et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. J Hepatol. 2006;45(4):560-7.

ginews@gastro.org

Eosinophils could be a marker for nonceliac gluten or wheat sensitivity

BY NICOLA GARRETT
MDedge News

The presence of duodenal and rectal eosinophils, in the absence of endoscopic findings, could be a marker of nonceliac gluten or wheat sensitivity (NCGWS), new research suggests.

NCGWS could be considered an inflammatory condition of the entire intestinal tract and the eosinophil infiltration "may represent a key candidate player" in its pathogenesis, wrote the authors, led by Antonio Carroccio, MD, of Giovanni Paolo II Hospital, Sciacca, and DiBiMIS University of Palermo, Italy. The report is in Clinical Gastroenterology and Hepatology.

The research team noted that duodenal histology, a lack of villous atrophy, and evaluation of intraepithelial infiltration of the duodenal mucosa were the usual steps involved in the diagnostic work-up of NCGWS.

Many people with NCGWS had symptoms that overlapped with irritable bowel syndrome but no studies had evaluated histologic features of duodenal and rectal biopsies from these patients.

"Alterations of the mucosal immune system are believed to play a role in IBS and some patients may indeed have inflammation of the colonic mucosa. Consequently, it would be logical to study the colon of NCGWS patients for possible inflammation in this site," they wrote.

The current study involved 78 consecutive adult patients attending two tertiary referral centers in Italy. The average age of the patients was 36.4 years and they were diagnosed with NCGWS through a double-blind wheat challenge. A non-NCGWS control group of 55 patients had either celiac disease (n = 16) or self-reported NCGWS but with negative results from the wheat challenge (n = 39).

Both duodenal and rectal biopsies were performed in both groups of patients after they had consumed a wheat-containing diet (a minimum of 100 g) for at least 4 weeks.

The researchers then analyzed intraepithelial CD3+T cells, lamina propria CD45+ cells, CD4+ and CD8+ T cells, mast cells, and eosinophils as well as the presence and size of lymphoid nodules.

Histologic evaluation of the duodenal mucosa showed that none of the NCGWS patients or non-NCGWS controls had a villus/crypt ratio less than 3, whereas all the controls with celiac disease (CD) had villous atrophy.

Mucosal inflammation both in the duodenum and the rectal mucosa was common in patients with NCGWS. For example, intraepithelial CD3+ lymphocytes progressively increased from the non-NCGWS controls (14.3 ± 4.2) to NCGWS patients (19.6 ± 10.7; *P* less than .03) and CD controls (47.7 ± 23.3; *P* less than .001 vs. NCGWS patients).

Lamina propria CD45+ cells, which the authors said represented the "total immunocyte" infiltration were significantly higher in NCGWS patients than in the non-NCGWS controls at both sites.

In patients with NCGWS, the mean eosinophil infiltration was more than 2.5-fold the upper normal limit in the rectum and nearly twice the upper normal limit in the duodenum (*P* less than .0001).

Key clinical point:
Mucosal inflammation in the rectal mucosa was common in patients with NCGWS. In these patients the mean eosinophil infiltration was more than 2.5-fold the upper normal limit in the rectum.

Eosinophil numbers in the duodenal mucosa were also higher in the NCGWS patients with dyspepsia than in the NCGWS patients without upper digestive tract symptoms.

For example, in 33 patients who reported upper digestive tract symptoms, the number of lamina propria eosinophils was significantly higher than in the remaining NCGWS patients who did not report symptoms (8.6 ± 2.6 vs. 6.8 ± 3.6; *P* less than .01).

"Functional dyspepsia is frequently associated with IBS [irritable bowel syndrome], suggesting that these two diseases have a shared pathogenesis," the researchers speculated.

The researchers suggested that in the absence of endoscopic findings, eosinophil infiltration of the rectal mucosa could be a marker of NCGWS, noting that it could not be considered a specific marker as eosinophils were found in the colon and rectal mucosa in several clinical conditions, such as inflammatory bowel diseases and celiac disease.

"However, these clinical conditions have clinical, endoscopic, serologic, and histologic aspects markedly different from NCGWS. ... We would suggest that in clinical practice, subjects showing an IBS clinical presentation and mucosa eosinophil infiltration should be recommended to commence an elimination diet with a subsequent wheat challenge," they said.

The authors said another noteworthy finding from their study was that about 95% of patients had lymphoid follicles that were significantly larger than those of the control group. Although this can be considered a "normal" finding in rectal mucosa, they said in their experience the presence of large follicles was associated with non-IgE mediated food allergy.

"It can be hypothesized that not only eosinophils could play a pathogenetic role in NCGWS, and that a complex immunologic response involving both innate and acquired immunity may be responsible for this disease," they said.

A study limitation was selection bias stemming from the fact that the cohort included patients referred to tertiary centers, they noted. "Our results must not be extended to all self-treated or diagnosed NCGWS patients," they cautioned.

The Italian Foundation for Celiac Disease funded the study. The authors declared no conflicts of interest.

ginews@gastro.org

CHAMELEONSEYE/THINKSTOCK

SOURCE: Carroccio A et al. Clin Gastroenterol Hepatol. 2018 Aug 20. doi: 10.1016/j.cgh.2018.08.043.

INCREASE PATIENT SATISFACTION.
INCREASE PRACTICE REVENUE.

The CRH O'Regan System® is a non-surgical hemorrhoid solution that has been performed over one million times by more than 2,800 physicians across the country.

Half of your patients will experience symptomatic hemorrhoids by age 50. Provide a continuum of care that is simple, proven and effective. And with reimbursement rates on par with colonoscopy on a per hour basis, the CRH O'Regan System® introduces a considerable revenue stream to your practice. Put smiles on your patients' faces and increase your bottom line.

Call us today
1.888.599.7949

Visit us at ACG. Booth 523
Product Theater Oct 8 @ 12:45pm
Lunch provided. Enter to win an iPadPro.

CRH Medical CORPORATION

CRH O'Regan System®
Non-Surgical Hemorrhoid Treatment
Fast. Painless. Proven.

crhmedicalproducts.com | info@crhmedcorp.com | 1.888.599.7949

Will biosimilars help with cost?

Expensive *from page 1*

15 drugs in terms of Medicare expenditures, they added.

While biosimilars are supposed to increase competition and lower prices, it's an open question whether they actually reduce out-of-pocket expenditures for the 43 million individuals with drug benefits under Medicare Part D.

That uncertainty is due in part to the complex cost-sharing design of Part D, which includes an initial deductible, a coverage phase, a coverage gap, and catastrophic coverage.

In 2017, the plan included an initial $400 deductible, followed by the coverage phase, in which the patient paid 25% of drug costs. In the coverage gap, which started at $3,700 in total drug costs, the patient's share of drug costs increased to 40% for biologics, and 51% for biosimilars. In the catastrophic coverage phase, triggered when out-of-pocket costs exceeded $4,950, the patient was responsible for 5% of drug costs.

"Currently, beneficiaries receive a 50% manufacturer discount during the gap for brand-name drugs and biologics, but not for biosimilars," Dr. Yazdany and her coauthors noted.

ISTOCK/THINKSTOCK

To evaluate cost-sharing for infliximab-dyyb, the authors analyzed data for all Part D plans in the June 2017 Medicare Prescription Drug Plan Formulary, Pharmacy Network, and Pricing Information Files.

Out of 2,547 plans, only 10% covered the biosimilar, while 96% covered infliximab, the authors found.

The mean total cost of infliximab-dyyb was "modestly lower," they reported. Eight-week prescription costs were $2,185 for infliximab-dyyb versus $2,667 for infliximab, while annual costs were $14,202 for the biosimilar and $17,335 for infliximab.

However, all plans required coinsurance cost-sharing for the biosimilar, they said. The mean coinsurance rate was 26.6% of the total drug cost for the biosimilar and 28.4% for infliximab.

For beneficiaries, projected annual out-of-pocket costs without the gap discount were $5,118 for infliximab-dyyb and $3,432 for infliximab, the researchers said.

Biosimilar gap discounts are set to start in 2019, according to the authors. However, they said those discounts may not substantially reduce out-of-pocket costs for Part D beneficiaries because of the high price of infliximab-dyyb and a coinsurance cost-sharing rate similar to that of infliximab. Because the RA starting dose is typically 3 mg/kg, compared with the 5-mg/kg starting dose for patients with inflammatory bowel disease, cost issues may be worse for GI patients.

"Further policies are needed to address affordability and access to specialty drugs," Dr. Yazdany and her coauthors concluded.

Key clinical point:
Infliximab-dyyb was 18% less costly than infliximab, with an annual cost exceeding $14,000 under Medicare Part D.

The study was funded in part by grants from the Agency for Healthcare Research and Quality, the Robert L. Kroc Endowed Chair in Rheumatic and Connective Tissue Diseases, and other sources. Dr. Yazdany reported receiving an independent investigator award from Pfizer. Her coauthors reported no conflicts of interest.

ginews@gastro.org

SOURCE: Yazdany J et al. JAMA. 2018;320(9):931-3.

Transfers between hospitals contribute to CDI burden

BY SHARON WORCESTER
MDedge News

ATLANTA – Patient sharing among hospital facilities contributed substantially to the overall *Clostridium difficile* infection rate, an analysis of interhospital contamination effects showed.

In fact, 7.6% of all *Clostridium difficile* infection (CDI) cases at the nearly 400 California hospitals included in the study were directly attributable to the patient-sharing network, Daniel Sewell, PhD, reported at the International Conference on Emerging Infectious Diseases.

"The methods that we employed allowed us to estimate the expected increase in CDI cases due to transfers as a function of the CDI rate at the hospital from which those patients were brought. These transfer patients were responsible for about 3.06 times the number of CDI cases as a normal patient," said Dr. Sewell, a biostatistician at the University of Iowa, Iowa City.

The findings, which underscored the importance of regional (rather than local) efforts to minimize the spread of health care–associated infections, are based on an analysis of 27,200,873 hospital admissions and 532,320 same-day patient transfers identified from the Healthcare Cost and Utilization Project California State Inpatient Database for 2005-2011.

Transfer networks based on the monthly average number of patients discharged from one hospital and admitted to another on the same day were constructed, and the monthly average number of CDI cases per hospital were considered, along with hospital-level characteristics such as patient length of stay, age, and number of diagnoses. Network autocorrelation models that help eliminate bias were then used to assess the contamination effects between hospitals, he explained.

This led to development of an equation that can be used to determine the expected number of CDI cases in a hospital as a function of the number of transfers coming in and the contamination level of the source hospitals. The ability to calculate the expected number of CDI cases in this fashion is an important factor for the success of regional versus local intervention efforts, which are increasingly thought to be important for reducing health care–associated infections.

"If we want to design a coordinated or regional approach, we've got to have a much better understanding of the role that patient transfers have in these diseases," Dr. Sewell said.

As most hospitals included in the study had a low CDI rate and a low transfer rate, the CDIs attributable to transfers represent a minority of cases, but they are a substantial minority, he said, noting that the main concern is with the "perfect storm" of high CDI rate plus high transfer rate.

The methodological approach used in this study to estimate CDI rates can be used for any health care–associated infection of interest, he added.

Dr. Sewell reported that he had no disclosures.

sworcester@mdedge.com

AGA Resource
The AGA Fecal Microbiota Transplantation (FMT) National Registry will assess short- and long-term patient outcomes associated with FMT. Learn more at http://ow.ly/WdQE30lBuSu.

Acute biliary pancreatitis linked to poor outcomes in elderly patients

BY ANDREW D. BOWSER
MDedge News

Compared with younger patients, elderly patients admitted for acute biliary pancreatitis have increased rates of severe acute pancreatitis and mortality, according to an analysis of a nationally representative database.

Mortality was almost three times as high in elderly patients (65 years of age or older) after stringent matching for confounding variables, wrote researcher Kishan Patel, MD, of the Ohio State University, Columbus, and coauthors.

These findings represent a 'current health care concern,' since the elderly population in the United States is expected to double within the next several decades and the prevalence of acute pancreatitis is on the rise.

These findings represent a "current health care concern," since the elderly population in the United States is expected to double within the next several decades and the prevalence of acute pancreatitis is on the rise, Dr. Patel and colleagues wrote in a report on the analysis in the Journal of Clinical Gastroenterology.

The analysis is the first, to the investigators' knowledge, that addresses national-level outcomes associated with acute biliary pancreatitis in elderly patients.

To evaluate clinical outcomes of elderly patients with acute biliary pancreatitis, Dr. Patel and colleagues queried the Nationwide Readmissions Database, which is the largest inpatient readmission database in the United States.

The investigators looked at outcomes associated with index hospitalizations, defined as a patient's first hospitalization in a calendar year, and found 184,763 adult patients who received a diagnosis of acute biliary pancreatitis between 2011 and 2014. Of those, 41% were elderly.

The mortality rate associated with the index admission was 1.96% (n = 356) for the elderly patients, compared with just 0.32% (n = 1,473) for nonelderly patients (less than 65 years of age, *P* less than .001), according to the report.

Mortality was increased in the elderly versus nonelderly patients, with an odds ratio of 2.8 (95% confidence interval, 2.2-3.5), according to results of a propensity score matched analysis. Likewise, severe acute pancreatitis was increased in the elderly, with an OR of 1.2 (95% CI, 1.1-1.3) in that analysis.

By contrast, patient age did not impact 30-day readmission rates, according to results of a multivariate analysis that adjusted for confounding factors.

Key clinical point:
Elderly patients had increased mortality (odds ratio, 2.8; 95% confidence interval, 2.2-3.5) and severe acute pancreatitis (OR, 1.2; 95% CI, 1.1-1.3).

Mortality and severe acute pancreatitis both increased with age within the elderly cohort, further multivariate analysis showed. For example, the ORs for mortality were 1.39 for patients aged 75-84 years and 2.21 for patients aged 85 years and older, the results show.

The elderly population in the United States is expected to almost double by 2050, rising from 48 to 88 million, Dr. Patel and colleagues said. The number of those aged 85 years or older is expected to increase from 5.9 to 18 million by 2050, at which time they will make up nearly 5% of the total U.S. population.

"This specific demographic is more susceptible to common medical ailments; more troubling is acute pancreatitis is one of the most frequent causes of hospitalization in gastroenterology," Dr. Patel and colleagues wrote.

Dr. Patel and coauthors reported no financial conflicts of interest related to the analysis.

ginews@gastro.org

SOURCE: Patel K et al. J Clin Gastroenterol. 2018 Aug 28. doi: 10.1097/MCG.0000000000001108.

CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Yao-Wen Cheng, Mark A. Gromski, and Monika Fischer (Gastroenterology 2016;151[6]:1075-6).

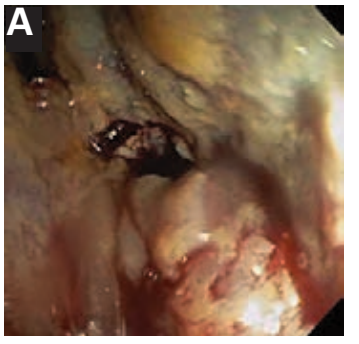
A 25-year-old obese, African man with no significant past medical history except for recent weight loss of 70 pounds presented for evaluation of bloody diarrhea and abdominal pain. The patient described sharp, left lower quadrant pain that progressively worsened over a 6-month period, along with loose bowel movements containing blood and mucous that occurred 20-40 times daily.

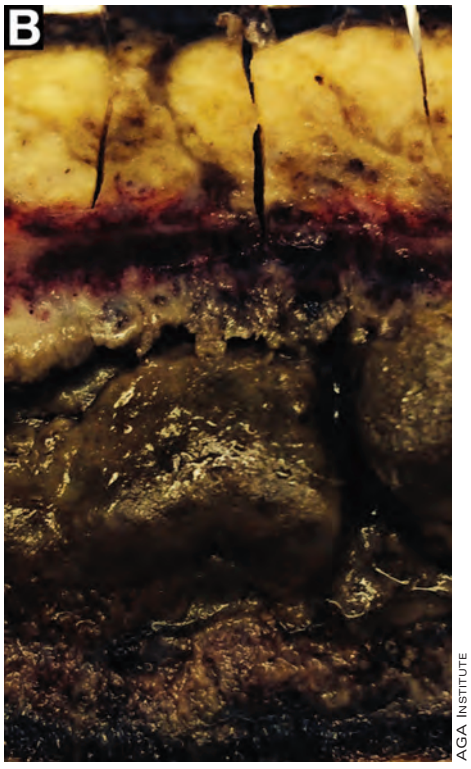
A CT scan of the abdomen revealed colonic wall thickening from the descending colon to the rectum. A flexible sigmoidoscopy demonstrated an area of congested, friable, dusky mucosa with overlying whitish exudate in the rectosigmoid colon (Figure A). Endoscopic biopsies were most consistent with ischemic colitis. A comprehensive work up for infectious colitis (including *Clostridium difficile*, stool culture, ova and parasites, cytomegalovirus, syphilis, herpes simplex virus, gonorrhea, and chlamydia), hypercoagulability, vasculitis, and illicit drugs was negative.

A CT angiogram of the abdomen/pelvis showed widely patent mesenteric vasculature and diffuse mucosal thickening of the sigmoid colon with inflammatory stranding surrounding the mesentery of the sigmoid colon and rectum. There was no portal venous gas or pneumatosis coli.

Owing to ongoing abdominal pain and profuse bloody diarrhea despite optimal resuscitative measures, the patient underwent a laparoscopic-assisted sigmoid resection with end colostomy and a Hartmann procedure, leaving a short rectal stump (Figure B), which completely abolished his symptoms.

The diagnosis is on page 36.





For first-line constipation therapy, stick with the leader

The AGA recommends PEG laxatives (like MiraLAX) as a first-line constipation treatment[1]

- ✔ 96% patient satisfaction rate*
- ✔ #1 GI-recommended laxative for over 10 years

Start with MiraLAX for proven relief of occasional constipation.

MiraLAX®
Polyethylene Glycol 3350, Powder for Solution, Osmotic Laxative

Doctor recommended, patient approved

*Survey of 300 consumers, 2017.

Use as directed on product labeling or as directed by your doctor.

Reference: 1. Clinical decision support tools. American Gastroenterological Association website. http://campaigns.gastro.org/algorithms/constipation/index.html. Accessed May 12, 2017.

May be an 'ideal treatment'

POEM *from page 1*

through the lower esophageal sphincter to the gastric cardia, thereby weakening the lower esophageal sphincter to allow passage of food.

POEM is clinically successful in 80%-90% of patients with achalasia. Although the procedure is regarded as safe and effective for achalasia, it has not been thoroughly researched for treatment of other esophageal motility disorders, including junction outflow obstruction (EGJOO), jackhammer esophagus (JE), or esophagogastric distal esophageal spasm (DES). EGJOO is similar to achalasia but with peristalsis and a mean integrated relaxation pressure (IRP) greater than 15 mm Hg. Both JE and DES are spastic esophageal disorders. Patients with JE exhibit extreme esophageal hypercontractility, whereas patients with DES have a normal mean IRP and at least 20% premature contractions.

"The role POEM plays in management of these disorders is not clear, mainly due to scarcity of studies on this topic," the authors wrote in Endoscopy International Open. "A previous multicenter study investigated the role of POEM in 73 patients with spastic esophageal disorders. However, the vast majority of patients (n = 54) in that study had type III (spastic) achalasia." Since therapies such as botulinum toxin injections and calcium channel blockers are ineffective for many patients with nonachalasia esophageal motility disorders, "POEM is potentially an ideal treatment."

The international, multicenter study involved 11 treatment centers and 50 patients. Patients with JE (n = 18), EGJOO (n = 15), and DES (n = 17) were included, each diagnosed according to the Chicago classification of esophageal motility disorders. Patients with type III achalasia were excluded.

Outcomes included technical success (completion of myotomy) and clinical success (Eckardt score at least 3 and symptom improvement). Prior to the procedure, the mean Eckardt score was 6.9 and chest pain was reported by almost three-quarters of the patients (72%).

Technical success was achieved in all patients. Myotomy thickness varied between cases; approximately half had a selective inner circular myotomy (48%), slightly less had a full-thickness myotomy (44%), and several were undefined (8%). Mean esophageal myotomy length was 12.5 cm and mean gastric myotomy length was 2.5 cm. Mean procedure time was approximately 90 minutes. Median duration of hospital stay was 2 days.

In all subgroups, postprocedural mean Eckardt scores decreased to less than 2. 'Remarkably, chest pain improved in more than 85% of patients,' the authors wrote. 'Chest pain is frequently the major presenting symptom in these disorders and is difficult to treat.'

Nine adverse events (AEs) occurred in eight patients, including submucosal hematoma, aspiration pneumonia, inadvertent mucosotomy, postprocedure pain, esophageal leak, bleed, and symptomatic capnothorax/peritoneum.

"Although AEs occurred in 18% of patients," the authors noted, "55.6% were rated as mild and 44.4% as moderate with no severe events. Most AEs can be managed intraprocedurally."

Median follow-up time was approximately 8 months, during which 42 patients (87.5%) achieved clinical success, with many dramatically improved; over half of the patients (52%) had Eckardt scores of 0 or 1. From the group of patients who had chest pain prior to the procedure, 87% had resolution of chest pain. Although reflux developed in almost a quarter of the patients (22.2%), this was successfully managed with proton pump inhibitors in all instances. Most patients (82.9%) who underwent postoperative manometry had resolution of preoperative abnormalities.

Subgroup analysis also was performed. Clinical success was achieved in 94.1% of patients with DES, 93.3% of patients with EGJOO, and 75.0% with JE. Collectively, the spastic disorders (DES/JE) had a lower numerical response than EGJOO. However, the authors noted that "the difference was not statistically significant (P = .41), likely a type II error due to the relatively small number of included patients." In all subgroups, postprocedural mean Eckardt scores decreased to less than 2. Patients with EGJOO were most likely to achieve Eckardt scores of 0 or 1. AEs were similar between subgroups.

"Remarkably, chest pain improved in more than 85% of patients," the authors wrote. "Chest pain is frequently the major presenting symptom in these disorders and is difficult to treat."

"It is important to mention that a long esophageal myotomy is essential to ensure that proximal esophageal spasms are effectively covered and treated," the authors wrote. "Mean length of esophageal myotomy in patients with DES and JE in the current study was about 14 cm, which is more than twice the length of a typical endoscopic or surgical myotomy performed in achalasia patients."

Even with the need for an extended myotomy, "results from the current study along with published data suggest POEM as an effective technique" for nonachalasia esophageal motility disorders, the authors concluded.

Since retrospective studies are inherently limited by design, the authors encouraged randomized trials to clarify the primary role of POEM in the management of nonachalasia esophageal motility disorders.

The authors reported compensation from Olympus, Boston Scientific, and Cook Medical.

ginews@gastro.org

SOURCE: Khashab MA et al. Endosc Int Open. 2018 Aug 10. doi: 10.1055/a-0625-6288.

Patients who fail PPIs often have functional heartburn

BY HEIDI SPLETE
MDedge News

Key clinical point:
Most (75%) of the patients who failed PPI treatment had functional heartburn or reflux hypersensitivity with GERD.

Abnormal pH results were similar in patients with gastroesophageal reflux disease (GERD) who improved or failed to improve on a once-daily dose of a proton pump inhibitor (PPI), but 75% of patients who failed treatment demonstrated either functional heartburn or reflux hypersensitivity, based on data from 29 adults.

Previous research on PPI failure in GERD patients has focused on twice-daily doses; "the purpose of the study was to compare impedance-pH parameters between patients who failed versus those who responded to PPIs once daily," wrote Jason Abdallah, MD, of Case Western Reserve University in Cleveland and colleagues.

In a study published in Clinical Gastroenterology and Hepatology, the investigators reviewed data from adults diagnosed with GERD who were treated with PPI therapy. The 16 who reported heartburn and/or regurgitation at least twice a week for 3 months while on a standard, once-daily PPI dose were classified as the failure group. The 13 patients who reported complete symptom resolution for at least 4 weeks while on the same standard dose were classified as the success group.

Most of the patients in the PPI-failure group (75%) were found to have either functional heartburn or reflux hypersensitivity with GERD. Impedance and pH parameters did not differ significantly between the PPI-failure and -success group, the researchers noted. Abnormal pH test results were similar between the groups, occurring in four of the patients who were successfully treated with PPI (31%) and four of the patients who failed PPI treatment (25%).

All patients completed the Short-Form 36 (SF-36) and GERD Health-Related Quality of Life (GERD-HRQL) questionnaires, and all underwent upper endoscopy and combined 24-hour esophageal impedance and pH monitoring within 2-4 weeks of study enrollment and while following PPI treatment. There were no significant differences in demographic characteristics between the success and failure groups.

The patients in the success group

Continued on page 32

PLENVU is now available in pharmacies!

When prepping for a colonoscopy

All it takes is Little PEG

PLENVU delivered a powerful bowel cleanse comparable to Suprep® and MoviPrep®, with 33% less total fluid[1-5]

- 92% of PLENVU patients achieved a successful cleanse*,† in the overall colon[1-3]
- 80% of PLENVU patients achieved a high-quality cleanse* in the ascending colon vs 74% of Suprep patients (*P*=.079)[6]
- Superior, high-quality cleansing of the ascending colon vs MoviPrep (*P*<.001)[3]

PLENVU provided a more positive bowel prep experience vs Suprep[2,3]

- 2x as many patients rated the taste of PLENVU "very acceptable" vs patients who took Suprep[2,3]
- 78% of patients were willing to take PLENVU again[3]

Prescribe **PLENVU**—the first and only 1-L PEG. For more information and resources, visit **PLENVUhcp.com**

*Using the Harefield Cleansing Scale, a successful cleanse was defined as a grade A or B. A high-quality cleanse was defined as "excellent," empty and clean, or "good," containing only clear liquid.[3]

†In the per protocol analysis, 93% of patients in the noninferiority comparator arm (Suprep) achieved a successful cleanse. In the modified intent-to-treat analysis, 85% of patients who took either PLENVU or Suprep achieved a successful cleanse.

INDICATION

PLENVU® (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution) is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.

IMPORTANT SAFETY INFORMATION

- PLENVU is contraindicated in patients with gastrointestinal (GI) obstruction, bowel perforation, gastric retention, ileus, toxic megacolon, and hypersensitivity to any of its ingredients.
- Advise patients to hydrate adequately before, during, and after the use of PLENVU. It is encouraged that patients drink additional clear liquids to help avoid cases of fluid and electrolyte abnormalities. Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias, seizures, and renal impairment.
- There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. These occur predominantly in patients with underlying cardiac risk factors and electrolyte disturbances. Consider obtaining ECGs in patients at an increased risk of serious cardiac arrhythmias.
- Use PLENVU with caution in patients with a history of seizures and those at an increased risk of seizures, including patients taking medications that lower the seizure threshold, patients withdrawing from alcohol or benzodiazepines, or patients with hyponatremia.
- Use PLENVU with caution in patients with renal impairment or those taking concomitant medications that affect renal function. Advise these patients to adequately hydrate before, during, and after the use of PLENVU and consider performing laboratory tests in these patients.
- Do not administer PLENVU to patients with GI obstruction or perforation. If GI obstruction or perforation is suspected, perform appropriate diagnostic studies prior to administering PLENVU.
- Use caution in patients with severe ulcerative colitis.
- Patients with impaired gag reflex or those prone to regurgitation or aspiration should be observed during the administration of PLENVU.
- Use PLENVU with caution in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.
- Phenylalanine can be harmful to patients with phenylketonuria (PKU). PLENVU contains phenylalanine, a component of aspartame. Each PLENVU treatment contains 491 mg of phenylalanine.
- PLENVU contains polyethylene glycol and may cause serious hypersensitivity reactions including anaphylaxis, angioedema, rash, urticaria, and pruritus. Inform patients of the signs and symptoms of anaphylaxis and instruct them to seek immediate medical care should signs and symptoms occur.
- In clinical trials, the most common adverse reactions (>2% of patients taking PLENVU) were nausea, vomiting, dehydration, and abdominal pain/discomfort. Adverse reactions were similar between the two dosing regimens.

To report SUSPECTED ADVERSE REACTIONS, contact Salix Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information on adjacent page.

References: 1. Plenvu [package insert]. Hengoed, UK: Norgine Ltd; 2018. **2.** DeMicco MP, Clayton LB, Pilot J, Epstein MS; NOCT Study Group. Novel 1 L polyethylene glycol-based bowel preparation NER1006 for overall and right-sided colon cleansing: a randomized controlled phase 3 trial versus trisulfate. *Gastrointest Endosc*. 2018;87(3):677-687. **3.** Data on file. Salix Pharmaceuticals. **4.** Suprep [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2017. **5.** MoviPrep [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; 2016. **6.** Epstein M, Shing RN, Bekal P. Bowel preparation quality of NER1006 versus oral trisulfate solution as assessed by colonoscopists at site: a post hoc analysis from a randomized controlled trial [ACG 2017 abstract 175]. *Am J Gastroenterol*. 2017;112(suppl 1):S45-S104.

PLV.0043.USA.18 August 2018

Continued from page 30

averaged higher scores on the SF-36 than did the failure group, but the difference was not significant. On the GERD-HRQL, treatment-failure patients reported that overall heartburn and heartburn or bloating while lying down were the symptoms they found most annoying on a daily basis.

Among the treatment-failure patients, 10 (62%) had normal acid exposure and negative symptom-reflux association, 2 patients (13%) had normal acid exposure

The results provide some insight into refractory GERD and suggest that patients who fail to respond to once-daily PPI might benefit from a neuromodulator, as well as psychological interventions.

and positive symptom-reflux association, and 4 patients (25%) had abnormal esophageal acid exposure.

Endoscopy findings were normal in most of the patients in both groups; 81% of the treatment-failure and 69% of the treatment-success patients had normal upper endoscopy findings.

"Our results support the hypothesis that PPI failure is primarily driven by esophageal hypersensitivity," the researchers noted. The similarity in impedance and reflux "implies that the shift to nonacidic reflux is a general PPI phenomenon, as opposed to being unique to PPI-failure patients," they said.

The study was limited by the small patient population, but the results provide some insight into refractory GERD and suggest that patients who fail to respond to once-daily PPI might benefit from a neuromodulator, as well as psychological interventions including cognitive-behavioral therapy, relaxation techniques, and biofeedback, the researchers concluded.

Dr. Abdallah had no conflicts to disclose; a coauthor disclosed relationships with companies including Ironwood Pharmaceuticals, Mederi Therapeutics, and Ethicon Pharmaceuticals.

ginews@gastro.org

SOURCE: Abdallah J et al. Clin Gastroenterol Hepatol. 2018; doi: 10.1016/j.cgh.2018.06.018.

Women, older patients at risk of more aggressive PBC

BY BIANCA NOGRADY
MDedge News

A large, real-world study of primary biliary cholangitis (PBC) has revealed that patients who are female, older, or have other autoimmune diseases are likely to have a more progressed and aggressive disease profile.

In the Journal of Clinical Gastroenterology, researchers reported the findings of a medical records database study involving 15,875 patients with PBC – previously known as primary biliary cirrhosis – a chronic, autoimmune form of liver disease.

Overall, more than one-third of patients (38.3%) had high levels of alkaline phosphatase – a marker for treatment nonresponse, defined as at least 1.5 times the upper limit of the normal range, which is also an indicator of adverse outcomes and of progression to high-risk liver disease.

Key clinical point:
More than one-third of patients with PBC have high levels of alkaline phosphatase.

These patients were more likely to be female, and more likely to have been diagnosed more than 1 year prior than patients whose alkaline phosphatase levels were not high. They were also more likely to be older, from the Midwest or Southern regions of the United States, have cirrhosis, or have other autoimmune diseases such as Sjögren's syndrome and rheumatoid arthritis.

Patients with high alkaline phosphatase also showed higher aminotransferase and bilirubin levels, more cirrhosis, pruritus, and jaundice, and lower albumin levels.

Conversely, male patients had a higher incidence of cirrhosis, the study found. Other factors independently associated with cirrhosis included older age, having Medicaid insurance, having high alkaline phosphatase, and certain autoimmune conditions such as type 1 diabetes, autoimmune hepatitis, and ulcerative colitis.

Zobair M. Younossi, MD, from the Center for Liver Diseases at Inova Fairfax Hospital, Falls Church, Va., and his coauthors said the results suggest many patients with PBC have progressed further in their condition than previously thought.

"This implies that a heightened focus on these patients with a goal toward treating more optimally should be considered to reduce their probability of disease progression," they wrote. "Once cirrhosis develops, adverse patient outcomes such as increased mortality and adverse health care system outcomes such as excessive resource utilization increases substantially."

The authors noted that most patients were female and white – consistent with previous reports of PBC – but the mean age of 60 years was older than expected.

"Our data suggest that PBC patients may be getting older and this

Continued on following page

Outpatient costs soar for Medicare patients with CH-B

BY WILL PASS
MDedge News

The average cost of outpatient care for Medicare recipients with chronic hepatitis B (CH-B) rose by 400% from 2005 to 2014, according to investigators.

"The Centers for Disease Control [and Prevention] estimates that Asians, who comprise 5% of the U.S. population, account for 50% of all chronic CH-B infections," Min Kim, MD, of the Inova Fairfax Hospital Center for Liver Diseases in Falls Church, Va., and her colleagues wrote in the Journal of Clinical Gastroenterology. However, the clinical and economic impacts of an aging immigrant population are unknown. The investigators therefore assessed patient characteristics associated with increased 1-year mortality and the impact of demographic changes on Medicare costs.

The retrospective study began with a random sample of Medicare beneficiaries from 2005 to 2014. From this group, 18,603 patients with CH-B were identified by ICD-9 codes V02.61, 070.2, 070.3, 070.42, and 070.52. Records containing insufficient information were excluded. Patients were analyzed collectively and as inpatients (n = 6,550) or outpatients (n = 13,648).

Cost of care (per patient, per year) and 1-year mortality were evaluated. Patient characteristics included age, sex, race/ethnicity, geographic region, type of Medicare eligibility, length of stay, Charlson comorbidity index, presence of decompensated cirrhosis, and/or hepatocellular carcinoma (HCC).

Most dramatically, outpatient charges rose more than 400% during the study period, from $9,257 in 2005 to $47,864 in 2014 (*P* less than .001). Inpatient charges increased by almost 50%, from $66,610 to $94,221 (*P* less than .001). (All values converted to 2016 dollars.)

The authors noted that costs held steady before spiking dramatically, reaching a peak of $58,450 in 2013 then settling down to $47,864 the following year. This spike may be caused by changes in screening measures and policies. In 2009, the American Association for the Study of Liver Diseases expanded screening guidelines to include previously ineligible patients with CH-B, and in 2010, the Centers for Medicare & Medicaid Services expanded ICD-9 and ICD-10 codes for CH-B from 9 to 25.

The authors reported that 1-year mortality was independently associated most strongly with decompensated cirrhosis (odds ratio, 3.02) and HCC (OR, 2.64). In comparison with white patients, Asians were less likely to die (OR, 0.47).

The authors wrote. "A majority of Asian Medicare recipients with CH-B likely acquired it perinatally and did not develop significant liver disease. ... Whites with CH-B generally acquired it in adulthood, increasing the chance of developing liver disease."

Over the 10-year study period, Medicare beneficiaries with CH-B were more frequently Asian and less frequently male. While the number of outpatient visits and average Charlson comorbidity index increased, decreases were reported for length of stay, rates of 1-year mortality, hospitalization, and HCC – the latter of which is most closely associated with higher costs of care.

The investigators suggested that the decreased incidence of HCC was caused by "better screening programs for HCC and/or more widespread use of antiviral treatment for CH-B."

Study funding was provided by Seattle Genetics. One coauthor reported compensation from Gilead Sciences, AbbVie, Bristol-Myers Squibb, and others.

ginews@gastro.org

SOURCE: Kim M et al. J Clin Gastro. 2018 Aug 13. doi: 10.1097/MCG.0000000000001110.

Continued from previous page

could have major implications for Medicare," they wrote. The study also examined how patients used health care resources, and found those with alkaline phosphatase levels more than 1.5 times the upper range of normal had significantly higher use. For example, they had significantly more all-cause and disease-related visits to the doctor and more use of outpatient resources for all causes.

They also had significantly more cumulative days of treatment with ursodeoxycholic acid – the standard treatment for PBC – at 528.4 days, compared with 41.6 days in individuals without high alkaline phosphatase levels. However they were no more likely to undergo imaging procedures.

Patients with cirrhosis were also more likely to have higher levels of health care utilization, compared with patients without cirrhosis, particularly use of outpatient services, inpatient stays, and ED visits.

Given that more advanced disease and presence of cirrhosis were both major drivers of increased health care use, the authors called for better identification and treatment of these patients. "This should not only potentially improve patients' long-term outcomes but also aid in the reduction or delay of conceivably costly health resource utilization," they wrote.

Two authors declared research funding or consulting fees from the pharmaceutical industry, and one author was an employee of Intercept Pharmaceuticals. No other conflicts of interest were declared.

ginews@gastro.org

SOURCE: Younossi ZM et al. J Clin Gastroenterol. 2018 Aug 24. doi: 10.1097/MCG.0000000000001120.

Study examines the world's alcohol use

BY RICHARD FRANKI
MDedge News

Approximately one-third of the earth's population – that's 2.4 billion people – drinks alcohol, and 2.8 million deaths a year are caused by alcohol-related problems, according to a massive study estimating alcohol use and health effects in 195 countries.

In 2016, males overall consumed more than twice as many drinks per day as females: 1.70 versus 0.73. Alcohol consumption in those aged 15-95 years was highest in the top quintile of countries according to sociodemographic development for both males (2.9 drinks per day) and females (1.9) and lowest in the bottom quintile of countries for males (1.4) and the second-lowest quintile for females (0.3), Max G. Griswold, MA, of the University of Washington, Seattle, and his associates said in the Lancet.

Denmark had the highest prevalence of current drinkers of any country for both males (97%) and females (95%) in 2016; Pakistan was lowest for males (0.8%) and Bangladesh was lowest for females (0.3%). The United States had a prevalence of 72% for males and 60% for females, along with consumption rates of 3.2 drinks per day for males and 1.9 for females. Alcohol-related diseases caused 6.7% of male deaths and 2.3% of female deaths in the United States, both close to the global numbers of 6.8% for males and 2.2% for females, the investigators said.

The analysis, conducted within the framework of the Global Burden of Diseases, Injuries, and Risk Factors Study, showed that even a single alcoholic drink a day increases the risk of developing 1 of the 23 alcohol-related health problems by 0.5% a year for people aged 15-95 years, which translates into a rate of 918 per 100,000 population, compared with 914 per 100,000 for nondrinkers. Consuming two drinks a day raises the risk to 7%, which would be an incidence of 977 per 100,000, and those who have five drinks a day increase their risk by 37%, which works out to 1,252 people per 100,000 who would develop an alcohol-related disease.

In an editorial comment, Robyn Burton, PhD, of King's College London and Nick Sheron, MD, of the University of Southampton (England), wrote that "the conclusions of the study are clear and unambiguous: Alcohol is a colossal global health issue and small reductions in health-related harms at low levels of alcohol intake are outweighed by the increased risk of other health-related harms, including cancer. ... These diseases of unhealthy behaviors, facilitated by unhealthy environments and fueled by commercial interests putting shareholder value ahead of the tragic human consequences, are the dominant health issue of the 21st century. The solutions are straightforward: Increasing taxation creates income for hard-pressed health ministries."

The study was funded by the Bill and Melinda Gates Foundation. Mr. Griswold did not disclose any conflicts, but six of his several hundred coauthors did make such disclosures.

rfranki@mdedge.com

SOURCE: Griswold MG et al. Lancet. 2018 Aug 23. doi: 10.1016/S0140-6736(18)31310-2.

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Prealbumin level predicts outcomes for HCC resection

BY ANDREW D. BOWSER
MDedge News

Preoperative prealbumin levels independently predicted survival after curative liver resection for hepatocellular carcinoma (HCC) in a recent multicenter, retrospective study.

By contrast, preoperative albumin levels did not predict long-term overall or relapse-free survival in the analysis, which was reported by Tian Yang, MD, and Feng Shen, MD, along with their coinvestigators, in the journal HPB.

Those findings suggest that serum prealbumin is superior to the widely used serum albumin level as a marker of nutritional status and liver function in this setting, according to Dr. Yang and Dr. Shen, who are with the department of hepatobiliary surgery at Eastern Hepatobiliary Surgery Hospital, Shanghai, China.

"The importance of preoperative prealbumin level in predicting long-term prognosis after liver resection for HCC should be given adequate attention by hepatic surgeons," they wrote in their report.

The retrospective analysis included a total of 1,483 patients with HCC newly diagnosed at one of six medical institutions in China during 2001-2014. Of those patients, 1,046 (71%) had normal prealbumin levels (above 170 mg/L) measured within a week before surgery, while the remaining 437 (29%) had low prealbumin levels.

Overall survival was a mean of 72 months for the low prealbumin group versus 99 months for the normal prealbumin group (*P* less than .001), with a corresponding 5-year overall survival of 31% versus 43%, respectively, investigators reported

Likewise, relapse-free survival was a mean of 56 months for the low prealbumin group versus 77 months for the normal prealbumin groups (*P* less than .001), with 5-year relapse-free survival rates of 20% and 28%, respectively.

In multivariable Cox-regression analyses, the hazard ratios of low preoperative prealbumin level for risk of decreased overall survival and for risk of decreased relapse-free survival were 1.45 (95% confidence interval, 1.24-1.70) and 1.28 (95% CI, 1.10-1.48), respectively.

By contrast, preoperative albumin level was not an independent predictor of either overall or relapse-free survival in multivariate analyses, according to investigators.

Despite these findings, it remains controversial as to which marker is more accurate as a measure of nutritional status, investigators wrote in their report.

While albumin is more commonly used in clinical practice, they explained, multiple studies have shown prealbumin is more specific and sensitive in evaluating protein malnutrition and liver function.

The present study, although retrospective, is multicenter, has a large sample size, and includes adequately long follow-up. Nevertheless, further studies will be required to determine whether prealbumin could replace albumin for assessments of nutritional status and liver function after curative liver resection for HCC, investigators concluded.

The research was supported in part by the National Natural Science Foundation of China and the Shanghai Pujiang Program. Dr. Yang, Dr. Shen, and their coauthors had no conflicts of interest to disclose.

ginews@gastro.org

SOURCE: Li J-D et al. HPB (Oxford). 2018 Aug 3. doi: 10.1016/j.hpb.2018.06.1803.

FDA approves lenvatinib for HCC

BY LAURA NIKOLAIDES
MDedge News

The Food and Drug Administration approved lenvatinib (Lenvima) for first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).

Approval was based on a noninferiority trial of 954 patients with previously untreated, metastatic or unresectable HCC, comparing treatment with lenvatinib to sorafenib, according to an FDA statement.

Lenvatinib was found noninferior but not statistically superior to sorafenib for overall survival (hazard ratio, 0.92; 95% confidence interval, 0.79-1.06). Median overall survival was 13.6 months for patients in the lenvatinib arm, compared with 12.3 months for patients in the sorafenib arm.

The most common adverse reactions with lenvatinib were hypertension, fatigue, diarrhea, decreased appetite, arthralgia/myalgia, decreased weight, abdominal pain, palmar-plantar erythrodysesthesia syndrome, proteinuria, dysphonia, hemorrhagic events, hypothyroidism, and nausea.

The recommended lenvatinib dosages are 12 mg orally once daily in patients weighing 60 kg or greater actual body weight or 8 mg orally once daily in patients weighing less than 60 kg actual body weight, the FDA said.

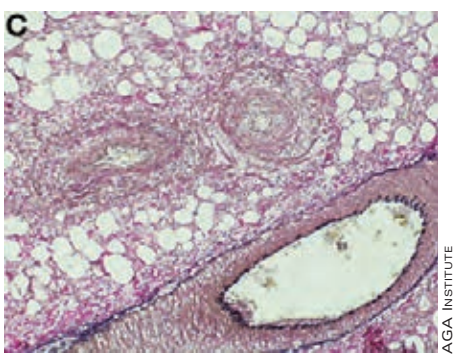
lnikolaides@mdedge.com

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What is your diagnosis?" on page 28: Idiopathic myointimal hyperplasia of the mesenteric veins

Gross examination of the rectosigmoid colon resected from this patient demonstrated transmural fibrosis. The mucosa was necrotic and hemorrhagic with a granular and cobblestone pattern (Figure B). Histopathologic examination of the mucosa revealed veins with myointimal hyperplasia with sparing of arterial vasculature (Figure C; stain: elastin; original magnification, ×10). The combined findings via endoscopy and histopathology confirmed the diagnosis of idiopathic myointimal hyperplasia of the mesenteric veins (IMHMV).



AGA Institute

IMHMV is a rare cause of proctosigmoiditis first described in a case series of four patients in 1991 by Genta and Haggitt.[1] Owing to its clinical presentation of lower quadrant abdominal pain, diarrhea, hematochezia, and mucous in the stools, the diagnosis is often mistaken for inflammatory bowel disease. However, the endoscopic and pathologic findings of IHMVH resemble ischemic colitis. IMHMV is refractory to medical treatment and its definitive diagnosis and curative management involves surgical resection of the involved segment (often the rectosigmoid colon). The precise pathophysiology of IMHMV is unclear. Histopathologic analysis of veins in the involved segment of colon can demonstrate changes similar to those of failed saphenous grafts from coronary artery bypass.[2] Myointimal hyperplasia of the mesenteric veins occurs (best identified with elastin stain on histopathology) with near total occlusion of the venous lumen and without any associated inflammatory infiltrate or arterial involvement.[3]

After colectomy, our patient's abdominal symptoms resolved and follow-up colonoscopy at 6 months did not reveal recurrence of IMHMV, at which time, the patient underwent take-down of his colostomy. In the year after colostomy take-down, the patient showed no clinical or endoscopic signs of colitis while off of all medical therapies. Here, we present the first case of a successful take-down of a curative colostomy for an IMHMV patient, a treatment course not described previously in the literature. Prompt diagnosis and timely surgical intervention may allow for avoidance of permanent colostomy in patients with IMHMV.

References

1. Genta R.M., Haggitt, R.C. Idiopathic myointimal hyperplasia of mesenteric veins. Gastroenterology. 1991;101:533-9.

2. Abu-Alfa A.K., Ayer U., West A.B. Mucosal biopsy findings and venous abnormalities in idiopathic myointimal hyperplasia of the mesenteric veins. Am J Surg Pathol. 1996;20:1271-8.

3. Chiang C.K., Lee C.L., Huang C.S., et al. A rare cause of ischemic proctosigmoiditis: Idiopathic myointimal hyperplasia of mesenteric veins. Endoscopy. 2012;44:54-5.

ginews@gastro.org

1 important option
for every liver patient:
Living Donation

UPMC | CARE CONNECT

UPMC has performed more liver transplants than any other transplant center in the country. And this expertise means that we give more patients hope by accepting some of the most difficult and complex cases. For someone in need of a liver transplant, every moment spent on the waiting list is critical. Living-donor liver transplants can be a life-saving option for patients with end-stage liver disease.

Through our innovative UPMC Complex Care Connect™ program, UPMC extends our expertise to hospitals across the country that want to offer patients the option of living-donor liver transplant. Through a collaborative approach, we work with partner hospitals to coordinate transplant surgery at UPMC and to provide pre- and post-surgery care at the partner hospital.

To learn more about our living-donor program, visit **UPMC.com/GiveLife**.

For information about UPMC Complex Care Connect™, visit **careconnect.upmc.com**.

Doctors decry inaction on physician-focused APMs

BY GREGORY TWACHTMAN
MDedge News

Doctors have expressed their displeasure at the lack of response by the Centers for Medicare & Medicaid Services to launch physician-focused advanced alternative payment models (APMs).

As part of the MACRA law, Congress created a process by which physicians could seek to implement specialty-specific APMs that they had developed and tested. The purpose was to provide more avenues for specialist participation in the Quality Payment Program's APM track.

The process goes like this: Doctors create and implement an APM that focuses on providing value-based care in their particular specialty arena. They submit the program and early outcomes to the Physician-Focused Payment Model Technical Advisory Committee or PTAC. PTAC reviews the APM and, if it has merit, recommends it to the Secretary of Health and Human Services. The secretary may approve the APM, implement it for limited-scale testing, or reject it.

COURTESY HEALTH SUBCOMMITTEE

Dr. David Barbe, immediate past president of the AMA, testifies before the House Energy & Commerce Health Subcommittee.

So far, PTAC has sent at least 10 APMs to CMS. To date, not a single one has been approved or even been tested on a limited scale.

"Physicians want to be engaged and involved in this process," David Barbe, MD, immediate past president of the American Medical Association, told members of the House Energy and Commerce Health subcommittee during a July 26 hearing. "PTAC was created for that very reason. They have received dozens of proposals that come from the ground level. Physicians that are practicing know what will work in their practices and perhaps in their specialty. And yet, none of these have been adopted by CMS or really, we think, given serious consideration."

Frank Opelka, MD, medical director for quality and health policy at the American College of Surgeons, noted that a proposal they had submitted to PTAC appears to be the one that has gotten farthest along in the process.

The model was "accepted in a letter by the secretary for consideration by the [CMS Innovation Center]," Dr. Opelka testified at the hearing. "The innovation center had a few conference calls with us

Continued on following page

Tuition-free med school touches off debate

BY JULIE ROVNER, KAISER HEALTH NEWS

New York University is learning that no good deed goes unpunished.

Its highly ranked medical school announced with much fanfare Aug. 16 that it is raising $600 million from private donors to eliminate tuition for all its students – even providing refunds to those currently enrolled. Before the announcement, annual tuition was $55,018.

NYU leaders said the move would help address the increasing problem of student debt among young doctors, which many educators argue pushes students to enter higher-paying specialties instead of primary care or deters them from becoming doctors in the first place.

"A population as diverse as ours is best served by doctors from all walks of life, we believe, and aspiring physicians and surgeons should not be prevented from pursuing a career in medicine because of the prospect of overwhelming financial debt," Robert Grossman, MD, the dean of the medical school and CEO of NYU Langone Health, said in a statement. NYU declined a request to elaborate further on its plans.

The announcement generated headlines and cheers from students. But not everyone thinks that making medical school tuition-free for all students, including those who can afford it, is the best way to approach the complicated issue of student debt.

"As I start rank ordering the various charities I want to give to, the people who can pay for medical school in cash aren't at the top of my list," said Craig Garthwaite, a health economist at Northwestern University's Kellogg School of Management.

Still, medical education debt is a big issue in health care. According to the Association of American Medical Colleges, which represents U.S. medical schools and academic health centers, 75% of graduating physicians had student loan debt as they launched their careers, with a median tally of $192,000 in 2017. Nearly half owed more than $200,000.

But it is less clear how much of an impact that debt has on students' choice of medical specialty. The AAMC's data suggests debt does not play as big a role in specialty selection as some analysts claim.

If debt were a huge factor, one would expect that doctors who owed the most would choose the highest-paying specialties. But that's not the case.

"Debt doesn't vary much across the specialties," said Julie Fresne, AAMC's director of student financial services and debt management.

Mr. Garthwaite agrees. He said surveys in which young doctors claim debt as a reason for choosing a more lucrative specialty should be viewed with suspicion. "No one [who chooses a higher-paying job] says they did it because they want two Teslas," he said. "They say they have all this debt."

Aaron Carroll, MD, MS , questioned how much difference even $200,000 in student debt makes to people who, at the lowest end of the medical spectrum, still stand to make six figures a year. "Doctors in general do just fine," he said. "The idea we should pity physicians or worry about them strikes me as odd."

Choice of specialty is also influenced by more than money. Some specialties may bring less demanding lifestyles than primary care or more prestige. Dr. Carroll said his surgeon father was not impressed when he opted for pediatrics, calling it a "garbageman" specialty.

There is also an array of government programs that help students afford medical school or forgive their loans, although usually in exchange for agreeing to serve for several years either in the military or in a medically underserved location. The federal National Health Service Corps, for example, provides scholarships and loan repayments to medical professionals who agree to work in mostly rural or inner-city areas with a shortage of medical professionals. And the Department of Education oversees the Public Service Loan Forgiveness program, which cancels outstanding loan balances after 10 years for those who work for nonprofit employers.

Medical schools themselves are addressing the student debt problem. Many – including NYU – have created programs that let students finish medical school in three years rather than four, which reduces the cost by 25%. And the Cleveland Clinic, together with Case Western Reserve University, has a tuition-free medical school aimed at training future medical researchers that takes 5 years but grants graduates both a doctor of medicine title and a special research credential or master's degree.

This latest move by NYU, however, is part of a continuing race among top-tier medical schools to attract the best students – and possibly improve their national rankings.

In 2014, University of California, Los Angeles announced it would provide merit-based scholarships covering the entire cost of medical education (including not just tuition, like NYU, but also living expenses) to 20% of its students. Columbia University announced a similar plan earlier this year, although unlike NYU and UCLA, Columbia's program is based on students' financial need.

The programs are funded, in whole or in part, by large donors whose names brand each medical school – entertainment mogul David Geffen at UCLA, former Merck CEO P. Roy Vagelos at Columbia, and Home Depot co-founder Kenneth Langone at NYU.

Mr. Garthwaite said it is all well and good if top medical schools want to compete for top students by offering discounts. But if their goal is to encourage more students to enter primary care or to steer more people from lower-income families into medicine, giving free tuition to all "is not the most target-efficient way to reach that goal."

Kaiser Health News is a nonprofit national health policy news service. It is an editorially independent program of the Henry J. Kaiser Family Foundation that is not affiliated with Kaiser Permanente.

Continued from previous page

and one 2-hour in-person meeting on a product that we'd developed that took almost 5 years in the making. There are no resources and no capability in the innovation center to complete a design and then to create an implementation and have a sandbox or pilot area in which to test. The PTAC has done a fantastic job. The secretary vetted us. I think [ours was] the only one that went from the secretary and was recommended to the innovation center, and it died in there because [the Center] is just not wired to really innovate and we really need to turn that on."

The CMS issued a letter essentially rejecting eight of the models that PTAC recommended. The AMA asked the agency to reconsider at least four of the proposals.

AMA leadership does not think that CMS gave serious consideration to any of the PTAC recommendations, Dr. Barbe said. "These span from very focused proposals in GI medicine to reduce rehospitalization in Crohn's patients all the way up to the end-stage renal disease that could have very broad effect on improving care and reducing cost for dialysis patients. We think there is great opportunity there if CMS will listen to us."

The AMA is "especially concerned because the statute to reform Medicare physician payment provided only 6 years of bonus payments to facilitate physicians' migration to APMs," according to the group's letter to CMS. "We are approaching the 3-year mark for the initial implementation and there is still not a robust APM pathway for physicians."

CMS "seems to be interested in coming up with ideas on their own, and I think that's not only reinventing the wheel potentially but it is not taking advantage of some very creative and innovative proposals that have come forward," Dr. Barbe said.

The AMA recognizes "that the APMs recommended by PTAC needed some refinement. ... PTAC has indicated in its recommendations to HHS that it felt the issues it had identified could be resolved with assistance from CMS. Moreover, PTAC concluded that the positive attributes of the APM proposals outweigh the concerns they had identified, but the department does not seem to agree."

gtwachtman@mdedge.com

INDEX OF ADVERTISERS

Physician groups call for CMS to drop E/M proposal

BY GREGORY TWACHTMAN
MDedge News

More than 170 physician groups are calling on the Centers for Medicare & Medicaid Services to withdraw a provision in the proposed 2019 physician fee schedule that would flatten evaluation and management payments.

The controversial proposal would set the payment rate for a level 1 evaluation and management (E/M) office visit for a new patient at $44, down from the $45 using the current methodology. Payment for levels 2-5 would be $135. Currently, payments for level 2 new-patient visits are set at $76, level 3 at $110, level 4 at $167, and level 5 at $211. For E/M office visits with established patients, the proposed rate would be $24 for level 1, up from the current payment of $22. Payment for levels 2-5 would be $93. Under the current methodology, payments for established patient level 2 visits are set at $45, level 3 at $74, level 4 at $109, and level 5 at $148.

In an Aug. 28 letter to the CMS, led by the American College of Rheumatology, physician groups applauded CMS recognition of the problems with the current E/M documentation guidelines and codes but urged them to reconsider plans to "cut and consolidate evaluation and management services." Doing so would "severely reduce Medicare patients' access to care by cutting payments for complex office visits, adversely affecting the care and treatment of patients with complex conditions, and potentially exacerbate physician workforce shortages."


DR. MARGOLIS

A separate letter, led by the American Medical Association, made similar assertions that the current proposal has the potential to "hurt physicians and other health care professionals in specialties that treat the sickest patients, ultimately jeopardizing patients' access to care."

The American Gastroenterological Association (AGA) signed on to both letters.

AGA, along with the American College of Gastroenterology and the American Society for Gastrointestinal Endoscopy, sent out a member alert, asking their members to tell CMS not to move forward with the proposed change because all three societies believe that such a payment system undervalues care provided to their sickest and most vulnerable seniors and other Medicare beneficiaries.

Another concern related to the implementation of this proposal is the financial impact on physicians.

Implementation of the CMS proposal, as currently written, "would be amazingly expensive for private practice [doctors] and really for anyone else because we would have to change our EMRs," Barbara Levy, MD, cochair of the CPT/RUC Work Group at the AMA.

"CMS has clearly heard from physicians about the need to reduce administrative burdens for physicians, and AGA appreciates that they're listening," said Peter S. Margolis, MD, AGAF, AGA Practice Councillor, University Gastroenterology, Providence, RI. "However, CMS's proposal drastically undervalues the care gastroenterologists and hepatologists provide to complex patients, including but not limited to those with inflammatory bowel disease, motility disorders, and chronic liver disease. Additionally, our experience shows that utilization management methods, such as prior authorization and step therapy appeals, are far more burdensome to physicians and physician practices than current E/M documentation requirements."

Another element of the proposal that is raising concerns among physician groups is a proposed payment reduction when a visit involves more than one service. For example, when a single office visit includes both an E/M code and a procedure code, the proposal calls for the E/M code to be cut in half.

Our experience shows that utilization management methods, such as prior authorization and step therapy appeals, are far more burdensome to physicians and physician practices than current E/M documentation requirements.

"From the patients' perspective, the potential threat is that doctors could be incentivized to spend less time with patients or potentially bring patients back for subsequent visits to handle multiple problems," Angus Worthing, MD, chair of the American College of Rheumatology's Committee on Government Affairs, said in an interview.

gtwachtman@mdedge.com

Red flag raised on CMS indication-based formulary policy

BY GREGORY TWACHTMAN
MDedge News

Physician groups are expressing concerns regarding a new policy that will allow indication-based formulary design in the Medicare Part D prescription drug benefit.

The Centers for Medicare & Medicaid Services announced the new policy in an Aug. 29 memo to Part D plan sponsors.

According to a fact sheet issued by CMS on the same day, indication-based formulary design "is a formulary management tool that allows health plans to tailor on-formulary coverage of drugs predicated on specific indications."

Current Part D policy requires plan sponsors to cover all Food and Drug Administration–approved indications for each drug that is on a plan formulary. Sponsors can begin to implement the new indication-based formulary design policy for plans issued in 2020.

The memo notes that, if a Part D plan sponsor chooses to opt into this policy, "it must ensure that there is another therapeutically similar drug on formulary for the nonformulary indication. For example, if a tumor necrosis factor (TNF) blocker is FDA-approved for both Crohn's disease and plaque psoriasis, but the Part D plan will include it on formulary for plaque psoriasis only, the plan must ensure that there is another TNF blocker on formulary that will be covered for Crohn's disease."

Beneficiaries can use the exceptions process to get coverage for a drug that has an indication not on the formulary.

"By allowing Medicare's prescription drug plans to cover the best drug for each patient condition, plans will have more negotiating power with drug companies, which will result in lower prices for Medicare beneficiaries," CMS Administrator Seema Verma said in a statement.

However, physician groups should be concerned about the definition of "best drug." Is this definition based upon efficacy, results of clinical trials, clinical effectiveness research, or just cost? Will there be transparenecy surrounding rebates?

The "proposed changes will exacerbate many of the access issues patients currently face with plan usage of existing utilization management practices, such as step therapy," the American College of Rheumatology said in a statement. "Unlike step therapy, which often delays effective treatments, this proposal would go even further and allow plans to remove therapies from the formulary altogether, leaving patients completely unable to access treatments that doctors and patients choose together. ... We also have concerns on what this would mean for work being done on compendia inclusion to secure off-label drug coverage if plans don't have to cover all FDA-approved indications."

A similar situation exists in patients with inflammatory bowel disease in which step therapy has largely been replaced by risk assessments. The AGA Crohn's and UC Care Pathways are based on this principle.

"Under the plan, Medicare patients will face increased challenges as they navigate health plans to make sure that their needed drug is on their selected formulary, which can change based on what health conditions they have," AMA President Barbara McAneny, MD, said in a statement. Dr. McAneny added that it will be even more difficult for physicians who are working with patients to get them on the best medicines covered by the patient's formulary.

"Physicians already lack ready access to accurate formulary information – preferred/tier status, on/off formulary, PA [prior authorization] and step therapy requirements – at the point of care in their EHRs," she said. "These transparency problems will expand by an order of magnitude by the complications this change introduces."

gtwachtman@mdedge.com

CLASSIFIEDS

Also available at MedJobNetwork.com

PROFESSIONAL OPPORTUNITIES

Posted Date: 6/7/2018
Position Number: PSN 37047, 53295, & 53296
Salary: To be Determined
Location: LSU Health Science Center Shreveport
Closing Date: Open until filled

Assistant Professor, Medicine—Gastroenterology & Hepatology

LSU Health SHREVEPORT

Job Requirements:
MD/DO or foreign equivalent with Louisiana state medical license or ability to obtain licensure. Graduate from an accredited residency program. Candidates should be board-certified or board-eligible in Gastroenterology.

Job Summary:
The Department of Medicine, Division of Gastroenterology and Hepatology at the LSU Health Shreveport is seeking to fill faculty positions for full-time Gastroenterologist. Candidates who require J1 & H1 Waivers are welcome. The appointment would include a community staffing position along with a team of experienced gastroenterology, and hepatology physicians in a supportive, and friendly environment.

Clinical duties would require weekly teaching responsibilities in GI outpatient clinics, endoscopic procedures, and inpatient consult services. Academic rank and salary will be commensurate with qualification and experience. The ideal candidate will have a broad knowledge of gastroenterological diseases, commitment to scholarly activity, and clinical care. Currently, the gastroenterology section has nine fellows and five full-time faculty members.

Shreveport is an attractive, comfortable, small Southern city with excellent schools, restaurants, and multiple cultural opportunities.

To Apply:
Applicants should submit a CV and three letters of reference to the Faculty Staffing Office at LSUHSC-Shreveport via email to **ShvFacultyRecruitment@lsuhsc.edu** and Dr. Paul A. Jordan - **pjorda1@lsuhsc.edu** or by mail to the address below.

LSU Health Sciences Center-Shreveport, Department of Human Resource Management
Attn: Faculty Recruitment
1501 Kings Highway; P.O. Box 33932
Shreveport, LA 71130-3932

Job Benefits:
The LSU Systems Office has provided LSUHSC-Shreveport employees with excellent benefit options designed with you and your dependents in mind. Our Benefits Section is available between 8:00 a.m. and 4:30 p.m., Monday through Friday, to help answer any questions you might have about these benefits.

LSUHSC—Shreveport is an equal opportunity employer and all qualified applicants will receive consideration for employment without regard to race, color, religion, sex, national origin, disability status, protected veteran status, or any other characteristic protected by law.

PRACTICE MANAGEMENT TOOLBOX: Employing irritable bowel syndrome patient-reported outcomes in the clinical trenches

BY CHRISTOPHER V. ALMARIO, MD, MSHPM, AND BRENNAN M.R. SPIEGEL, MD, MSHS, AGAF

Patients often seek care because they experience symptoms that negatively affect their health-related quality of life (HRQOL). Health care providers must then elicit, measure, and interpret patient symptoms as part of their clinical evaluation. To assist with this goal and to help bridge the gap between patients and providers, investigators have developed and validated a wide range of patient-reported outcomes (PROs) across the breadth and depth of the human health and illness experience. These PROs, which measure any aspect of a patient's biopsychosocial health and come directly from the patient, may help direct care and improve outcomes. When PROs are collected systematically, efficiently, and in the right place at the right time, they may enhance the patient–provider relationship by improving communication and facilitating shared decision making.[1-3]

Within gastroenterology and hepatology, PROs have been developed for a number of conditions, including irritable bowel syndrome (IBS), chronic idiopathic constipation, cirrhosis, eosinophilic esophagitis, inflammatory bowel disease, and gastroesophageal reflux disease, among many other chronic diseases. IBS in particular is well suited for PRO measurement because it is symptom based and significantly impacts patients' HRQOL and emotional health.

DR. ALMARIO

DR. SPIEGEL

Moreover, it is the most commonly diagnosed gastrointestinal condition and imparts a significant economic burden. In this article, we review the rationale for measuring IBS PROs in routine clinical practice and detail available measurement instruments.

Importance of IBS PROs in clinical practice

IBS is a functional GI disorder that is characterized by recurrent abdominal pain and altered bowel habits (i.e., diarrhea, constipation, or a mix of both). It has an estimated worldwide prevalence of 11%, and total costs are estimated at $30 billion annually in the United States alone.[4] Because of the chronic relapsing nature of IBS, along with its impact on physical, mental, and social distress, it becomes important to accurately capture a patient's illness experience with PROs. This is especially relevant to patients with IBS because we currently lack objective measurable biomarkers to assess their GI symptom burden. Instead, clinicians often are relegated to informal assessments of the severity of a patient's symptoms, which ultimately guide their treatment recommendations: How many bowel movements have you had in the past week? Were your bowel movements hard or soft? How bad is your abdominal pain on a scale of 1 -10? However, these traditional outcomes measured by health care providers often fail to capture other aspects of their health. For example, simply asking patients about the frequency and character of their stools will not provide any insight into how their symptoms impact their HRQOL and psychosocial health. An individual may report only two loose stools per day, but this may lead to substantial anxiety and negatively affect his or her performance at work. Similarly, the significance of the symptoms will vary from person to person; a patient with IBS who has five loose daily bowel movements may not be bothered by it, whereas another indi-

vidual with three loose stools per day may feel that it severely hampers his or her daily activities. This is where PROs provide value because they provide a key component to understanding the true burden of IBS and account for the HRQOL and psychosocial decrement engendered by the disease.

Although past literature has reported inconsistent benefits of using PROs in clinical practice,[5] including that from our own work,[6] there is a growing number of studies that have noted improved clinical outcomes through employing PROs.[7-9] A compelling example is provided by Basch et al.,[7] who randomized patients receiving chemotherapy for metastatic cancer to either weekly symptom reporting using electronically delivered PRO instruments vs. usual care, which consisted of symptom reporting at the discretion of clinicians. Here, they found that the intervention group had higher HRQOL, were less likely to visit the emergency department, and remained on chemotherapy for a longer period of time. Interestingly, the benefits from PROs were greater among participants who lacked prior computer experience vs. those who were computer savvy. Basch et al.[9] also noted that the use of PROs extended survival by 5 months when compared with the control group (31.2 vs. 26.0 months; $P = .03$). Longitudinal symptom reporting among IBS patients using PROs, when implemented well, may similarly lead to improved patient satisfaction, HRQOL, and clinical outcomes.

Measuring PROs in the clinical trenches

PROs generally are measured with patient questionnaires that collect data across several areas, including physical, social, and psychological functioning. Although PROs may enhance the patient-provider relationship and improve communication and shared decision making, we acknowledge that there are important barriers to their use in routine clinical practice.[10] First, many providers (and their patients) may find use of PRO instruments burdensome, and it can be time consuming to collect PROs from patients and securely transmit the data into the EHR. This can make it untenable for use in busy practices. Second, many gastroenterologists have not received formal training in performing complete biopsychosocial evaluations with PROs, and it can be difficult to understand and act upon PRO scores. Third, there are many PROs to choose from and there is a lack of measurement standards across questionnaires. These challenges limit widespread use of PROs in clinical practice, and it is understandable why most providers instead opt for informal measurement of symptoms and function. Later, we detail strategies for overcoming the earlier-described challenges in employing PROs in everyday practice along with relevant IBS PRO instruments.

IBS–specific PRO instruments

There have been several IBS-specific PRO instruments described in the literature, all of which vary in length, content, and amount of data supporting their validity (Table 1). Examples of IBS symptoms scales include the Adequate Relief measure, Irritable Bowel Syndrome Severity Scoring System, Gastrointestinal Symptom Rating Scale in IBS, Functional Bowel Disorder Severity Index, IBS Symptom Questionnaire, and Birmingham IBS Symptom Questionnaire.[15,24] There are also IBS-specific HRQOL instruments, such as the Irritable Bowel Syndrome Quality of Life measurement, Digestive Health Status Instrument, Functional Digestive Disorder Quality of Life questionnaire, Irritable Bowel Syndrome Health Related Quality of Life questionnaire, and IBS-36.[21,24]

Bijkerk et al.[24] evaluated and compared the validity and appropriateness of both the symptom and QOL scales. Among the examined IBS symptom instruments, they found that the Adequate Relief question (Did you have adequate relief of IBS-related abdominal pain or discomfort?) is the best choice for assessing global symptomatology, and the Irritable Bowel Syndrome Severity Scoring System is optimal for obtaining information on more specific symptoms.[24] As for the QOL scales, the Irritable Bowel Syndrome Quality of Life measurement, which comprises 34 items, is the preferred instrument for assessing changes in HRQOL because it is the most extensively validated.[24] Bijkerk et al.[24] also concluded that although the studied instruments showed reasonable psychometric and methodologic qualities, the use of these instruments in daily clinical practice is debatable because the measures (save for the Adequate Relief question) are lengthy and/or cumbersome to use. Because these instruments may not be practical for use during everyday care, this leads to a discussion of the National Institutes of Health Patient Reported Outcomes Measurement Information System (PROMIS), a novel approach to measuring PROs in the clinical trenches.

NIH PROMIS

Although there have been many efforts to implement PROs in routine clinical care, a recent confluence of scientific, regulatory, and political factors, coupled with technological advancements in PRO measurement techniques, have justified reevaluation of the use of PROs in everyday practice. In response to the practical and technical challenges to employing PROs in the clinical trenches as described earlier, the NIH PROMIS (www.healthmeasures.net) was created in 2004 with the goal of developing and validating a toolbox of PROs that cover the breadth and depth of the human health and illness experience. The PROMIS initiative also was borne from the realization that patients are the ultimate consumers of health care and are the final judge on whether their health care needs are being addressed adequately.

By using modern psychometric techniques, such as item response theory and computerized adaptive testing, PROMIS offers state-of-the-art psychometrics, establishes common-language benchmarks for symptoms across conditions, and identifies clinical thresholds for action and meaningful clinical improvement or decline. PROMIS questionnaires, in light of accelerated EHR adoption in recent years, also are designed to be administered electronically and efficiently, which allows implementation in busy clinical settings. As of December 2017, these instruments can be administered and scored through EHRs such as Epic (Epic Systems, Verona, Wisc.) and Cerner (Cerner Corporation, North Kansas City, Mo.), the PROMIS iPad (Apple Inc, Cupertino, Calif.) App, and online data collection tools such as the Assessment Center (www.assessmentcenter.net) and REDCap (Research Electronic Data Capture; Vanderbilt University, Nashville, Tenn.).[25] An increasing number of health systems are making PROMIS measures available through their EHRs. For example, the University of Rochester (N.Y.) Medical Center collects PROMIS scores for physical function, pain interference, and depression from more than 80% of their patients with in-clinic testing, and individual departments are able to further tailor their administered questionnaires.[26]

Gastrointestinal PROs measurement information system scales

Because of the extraordinary burden of illness from digestive diseases, the PROMIS consortium added a GI item bank, which our research group developed.[23] By using the NIH PROMIS framework, we constructed and

Continued on following page

Table 1. Patient-reported outcome instruments for IBS

Name of instrument	Number of items
IBS-specific symptom severity instruments	
Adequate Relief measure[11]	1
Irritable Bowel Syndrome Severity Scoring System[12]	5
Gastrointestinal Symptom Rating Scale in IBS[13]	13
Functional Bowel Disorder Severity Index[14]	3
Birmingham IBS Symptom Questionnaire[15]	14
IBS-specific health-related quality-of-life instruments	
Irritable Bowel Syndrome Quality of Life measurement[16]	34
Irritable Bowel Syndrome Quality of Life questionnaire[17]	30
Digestive Health Status Instrument[18]	34
Functional Digestive Disorder Quality of Life questionnaire[19]	43
Irritable Bowel Syndrome Health Related Quality of Life questionnaire[20]	26
IBS-36[21]	36
Irritable Bowel Syndrome-Specific Health-Related Quality of Life Instrument[22]	16
National Institutes of Health gastrointestinal PROMIS instruments[23]	
Abdominal pain PROMIS scale	6
Constipation PROMIS scale	9
Diarrhea PROMIS scale	6

PROMIS = Patient Reported Outcomes Measurement Information System.

MDEDGE NEWS

Content from this column was originally published in the "Practice Management: The Road Ahead" section of *Clinical Gastroenterology and Hepatology (2018;16:462-6)*.

Continued from previous page

validated eight GI PROMIS symptom scales: abdominal pain, bloating/gas, constipation, diarrhea, bowel incontinence, dysphagia, heartburn/reflux, and nausea/vomiting.[23] GI PROMIS was designed from the outset to not be a disease-targeted item bank (e.g., IBS-, cirrhosis-, or inflammatory bowel disease specific), but rather symptom targeted, measuring the physical symptoms of the GI tract, because it is more useful across the population as a whole. In Supplementary Figure 1 (at https://doi.org/10.1016/j.cgh.2017.12.026), we include the abdominal pain, constipation, and diarrhea PROMIS scales because they form the cardinal symptoms of IBS.

GI PROMIS scales are readily accessible via the Assessment Center,[25] and we also have made them freely available via MyGiHealth – an iOS (Apple) and online app (go.mygihealth.io) endorsed by the American Gastroenterological Association. The patient's responses to the questionnaires are converted to percentile scores and compared with the general U.S. population and then displayed in a symptom heat map. The app also allows users to track GI PROMIS scores longitudinally, empowering IBS patients (and any patient with GI symptoms for that matter) and their providers to see whether they are objectively responding to prescribed therapies and potentially improving satisfaction and patient–provider communication.

Take-away points:

1. Irritable bowel syndrome (IBS) is well suited for patient-reported outcome (PRO) measurement because it is symptom based and significantly impacts patients' health-related quality of life.
2. There are several IBS-specific PRO questionnaires, but many are beset by lengthy completion times and are impractical for use in everyday care.
3. NIH Gastrointestinal (GI) PROMIS scales, on the other hand, are symptom targeted (e.g., belly pain, diarrhea, constipation, etc.) rather than disease specific.
4. GI PROMIS is a versatile and efficient instrument for collecting PRO data from IBS patients as well as others who seek care in our GI clinics.

Conclusions

IBS is a common, chronic, relapsing disease that often leads to physical, mental, and social distress. Without objective measurable biomarkers to assess IBS patients' GI symptom burden, along with health care's increased emphasis on patient-centered care, it becomes important to accurately capture a patient's illness experience with PROs. A number of IBS symptom and QOL PRO instruments have been described in the literature, but most are beset by lengthy completion times and are impractical for use in everyday care. GI PROMIS, on the other hand, is a versatile and efficient instrument for collecting PRO data from not only IBS patients but also all those who seek care in our GI clinics. Improvements in PRO and implementation science combined with technological advances have lessened the barriers to employing PROs in routine clinical care, and an increasing number of institutions are beginning to take up this challenge. In doing so and by seamlessly incorporating PROs in clinical practice, it facilitates placement of our patients' voices at the forefront of their health care, changes how we monitor and manage patients, and ultimately, may improve patient satisfaction and clinical outcomes.

References

1. Detmar S.B., Muller M.J., Schornagel J.H., et al. Role of health-related quality of life in palliative chemotherapy treatment decisions. J Clin Oncol. 2002;20:1056-62.
2. Detmar S.B., Muller M.J., Schornagel J.H., et al. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. JAMA. 2002;288:3027-34.
3. Neumann M., Edelhauser F., Kreps G.L., et al. Can patient-provider interaction increase the effectiveness of medical treatment or even substitute it? An exploration on why and how to study the specific effect of the provider. Patient Educ Couns. 2010;80:307-14.
4. Lembo A.J. The clinical and economic burden of irritable bowel syndrome. Pract Gastroenterol. 2007;31:3-9.
5. Valderas J.M., Kotzeva A., Espallargues M., et al. The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Qual Life Res. 2008;17:179-93.
6. Almario C.V., Chey W.D., Khanna D., et al. Impact of National Institutes of Health gastrointestinal PROMIS measures in clinical practice: results of a multicenter controlled trial. Am J Gastroenterol. 2016;111:1546-56.
7. Basch E., Deal A.M., Kris M.G., et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. J Clin Oncol. 2016;34:557-65.
8. Kotronoulas G., Kearney N., Maguire R., et al. What is the value of the routine use of

patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol. 2014;32:1480-501.

9. Basch E., Deal A.M., Dueck A.C., et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. JAMA. 2017;318:197-8.

10. Spiegel B.M. Patient-reported outcomes in gastroenterology: clinical and research applications. J Neurogastroenterol Motil. 2013;19:137-48.

11. Mangel A.W., Hahn B.A., Heath A.T., et al. Adequate relief as an endpoint in clinical trials in irritable bowel syndrome. J Int Med Res. 1998;26:76-81.

12. Francis C.Y., Morris J., Whorwell P.J. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther. 1997;11:395-402.

13. Wiklund I.K., Fullerton S., Hawkey C.J., et al. An irritable bowel syndrome-specific symptom questionnaire: development and validation. Scand J Gastroenterol. 2003;38:947-54.

14. Drossman D.A., Li Z., Toner B.B., et al. Functional bowel disorders. A multicenter comparison of health status and development of illness severity index. Dig Dis Sci. 1995;40:986-95.

15. Roalfe A.K., Roberts L.M., Wilson S. Evaluation of the Birmingham IBS symptom questionnaire. BMC Gastroenterol. 2008;8:30.

16. Patrick D.L., Drossman D.A., Frederick I.O., et al. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Dig Dis Sci. 1998;43:400-11.

17. Hahn B.A., Kirchdoerfer L.J., Fullerton S., et al. Evaluation of a new quality of life questionnaire for patients with irritable bowel syndrome. Aliment Pharmacol Ther. 1997;11:547-52.

18. Shaw M., Talley N.J., Adlis S., et al. Development of a digestive health status instrument: tests of scaling assumptions, structure and reliability in a primary care population. Aliment Pharmacol Ther. 1998;12:1067-78.

19. Chassany O., Marquis P., Scherrer B., et al. Validation of a specific quality of life questionnaire for functional digestive disorders. Gut. 1999;44:527-33.

20. Wong E., Guyatt G.H., Cook D.J., et al. Development of a questionnaire to measure quality of life in patients with irritable bowel syndrome. Eur J Surg Suppl. 1998;583:50-6.

21. Groll D., Vanner S.J., Depew W.T., et al. The IBS-36: a new quality of life measure for irritable bowel syndrome. Am J Gastroenterol. 2002;97:962-71.

22. Lee E.H., Kwon O., Hahm K.B., et al. Irritable bowel syndrome-specific health-related quality of life instrument: development and psychometric evaluation. Health Qual Life Outcomes. 2016;14:22.

23. Spiegel B.M., Hays R.D., Bolus R., et al. Development of the NIH Patient-Reported Outcomes Measurement Information System (PROMIS) gastrointestinal symptom scales. Am J Gastroenterol. 2014;109:1804-14.

24. Bijkerk C.J., de Wit N.J., Muris J.W., et al. Outcome measures in irritable bowel syndrome: comparison of psychometric and methodological characteristics. Am J Gastroenterol. 2003;98:122-7.

25. HealthMeasures. Data collection tools. 2017. Available from http://www.healthmeasures.net/resource-center/data-collection-tools. Accessed August 20, 2017.

26. Baumhauer J.F. Patient-reported outcomes – are they living up to their potential?. N Engl J Med. 2017;377:6-9.

Dr. Almario is assistant professor-in-residence of medicine and public health, division of digestive and liver diseases, Dr. Spiegel professor-in-residence of medicine and public health, division of digestive and liver diseases, Cedars-Sinai Medical Center; Cedars-Sinai Center for Outcomes Research and Education, Los Angeles. Dr. Spiegel is a principal at My Total Health, which operates and maintains MyGiHealth; Dr. Almario has a stock option grant in My Total Health.

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE