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Courtesy Stephanie Barnes

Dr. Edward L. Barnes and his associates noted that disparities in care start with later diagnosis of IBD, followed by issues with continuity.

Rising IBD rates in minorities heighten need for awareness

BY AMY KARON
MDedge News

Inflammatory bowel disease (IBD) is rapidly increasing among racial and ethnic minorities, which makes it important to consider for patients with compatible symptoms, experts wrote in Gastroenterology.

Crohn's disease and ulcerative colitis are "chronic diseases with intermittent periods of flare and remission, so access to specialists, appropriate therapies, and frequent follow-up visits are vital to good outcomes," wrote Edward L. Barnes, MD, MPH, of University of North Carolina at Chapel Hill, with his associates. However, Blacks with IBD tend to be diagnosed later than Whites, are less likely to receive recommended biologics and immunomodulators, and are more likely to receive care at an emergency department, to experience delays in colectomy, and to miss regular visits to IBD specialists because of financial and transportation barriers, they added.

These disparities are

See **Minorities** · *page 28*

Start CRC screening at age 45, USPSTF now suggests

BY ROXANNE NELSON, RN, BSN

Screening for colorectal cancer (CRC) should begin at age 45 years instead of 50 years, as recommended in the current guideline, the U.S. Preventive Services Task Force said in a draft recommendation that is open for public comment.

"This is the only change that was made," said task force member Michael Barry, MD, director of the Informed Medical Decisions Program in the Health Decision Sciences Center at Massachusetts General Hospital, Boston.

The recommendation is that all adults aged 45-75 years be screened for CRC.

This is an "A" recommendation for adults aged 50-75 and a "B" recommendation for adults aged 45-49. Dr. Barry explained that the reason for this difference is that the benefit is smaller for the 45- to 49-year age group. "But there's not much difference between A and B from a practical standpoint," he explained.

For adults aged 76-85, the benefits and harms of screening need to be weighed against the individual's overall health and personal circumstances. This is a "C" recommendation.

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Study IDs microbial signature of celiac disease in children

BY AMY KARON
MDedge News

Eleven operational taxonomic units (OTUs) of fecal bacteria were less abundant in children with celiac disease than in healthy children, according to the findings of a study published in Gastroenterology.

This microbial signature correctly identified approximately four out of five cases of celiac disease, regardless of whether children were newly diagnosed or had already modified their diet, reported Konstantina Zafeiropoulou and Ben Nichols, PhD, of the Glasgow Royal Infir-

See **Celiac** · *page 9*

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LETTER FROM THE EDITOR

Scientific firepower will save us

COVID-19 numbers again are increasing dramatically. Community infection rates have nearly doubled, and hospitals and health care workers are stretched beyond their limits. It is difficult not to feel anger about how poorly this pandemic was managed (mismanaged) by so many officials in charge and by a large segment of our population who still refuse protective actions to limit spread. While politics and ideology continue to cost American lives, scientific firepower will emerge as our saving grace.

Dr. Allen

My editorial board and I are entering our final year at the helm of GI & Hepatology News. AGA issued a search for the next Editor in Chief (EIC), who will take over October 2021. I urge anyone interested to apply (https://gastro.org/news/prestigious-aga-publications-seek-new-editors-in-chief/). As EIC, you will choose the next editorial board and forge professional friendships that are gratifying. You will assume responsibility for the content, where you must balance your own views with those of both the AGA and our readership.

As EIC, each month I am given space for 300 words to communicate interesting ideas and opinions. The AGA gives the newspaper great editorial freedom, and I hope we have supported AGA's mission and values when we publish its official newspaper. I always have next month's editorial in mind, and I look for useful phrases, quotes, ideas, and opinions. If you are interested in becoming EIC, please email ginews@gastro.org for more information.

As EIC, you will choose the next editorial board and forge professional friendships that are gratifying. You will assume responsibility for the content, where you must balance your own views with those of both the AGA and our readership.

I would be remiss not to acknowledge the contribution that Lora T. McGlade, MS, has made to *GI & Hepatology News*. She has been my partner, as the Frontline Medical Communications Editor in charge of *GI & Hepatology News*. Next month, she will move on to assume a new role. I cannot thank her enough for helping make this newspaper work. As the months go on, I will highlight the contributions of others from the AGA, our Board, and Frontline.

Please stay safe and do not let your guard down. COVID-19 is merciless and relentless. "If you think research is expensive, try disease." – Mary Lasker.

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

Top AGA Community patient cases

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

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

- **Practice update:** Small intestinal bacteria overgrowth (SIBO) (https://community.gastro.org/posts/22838)
- **Case:** Polypectomy with low neutrophils (https://community.gastro.org/posts/22844)
- **Case:** Esophagus adenocarcinoma after sleeve gastrectomy (https://community.gastro.org/posts/22868)
- **Case:** Restarting infliximab after shingles – when is it safe? (https://community.gastro.org/posts/22890)
- **Case:** Flatulence in Colorado (https://community.gastro.org/posts/22901)
- **Case:** Serrated epithelial change (SEC) in IBD (https://community.gastro.org/posts/22948)
- **Case:** Multiloculated pancreatic cyst (https://community.gastro.org/posts/22935)

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

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Link between gastroparesis symptoms, constipation?

BY AMY KARON
MDedge News

Severe constipation affected 34% of adults with gastroparesis symptoms and showed a significant positive correlation with symptom severity in a multicenter prospective study.

Henry P. Parkman, MD, of Temple University in Philadelphia and his associates used a modified GI symptoms questionnaire, gastric-emptying scintigraphy, and wireless motility capsule studies of 338 participants in the National Institutes of Health Gastroparesis Registry, which enrolls individuals with gastroparesis symptoms (whether or not they have delayed gastric emptying). In the multivariable analysis, severe constipation (a score of 4 or 5 on a 5-point scale) correlated significantly with a higher score on the Gastroparesis Cardinal Symptoms Index (GCSI), with an odds ratio of 1.85 (95% confidence interval, 1.30-2.67). In addition, patients with gastroparesis symptoms were significantly more likely to report pain in the lower abdomen (OR, 1.34; 95% CI, 1.06-1.69) and to use medications to manage constipation (OR, 5.09; 95% CI, 2.75-9.41). The findings were published online in Clinical Gastroenterology and Hepatology.

Constipation was not significantly linked with the use of individual drug classes, including opiates, tricyclic antidepressants, 5HT3 receptor antagonists, or cannabinoids. However, many patients were taking combinations of medications, and it is unclear if these induced constipation or if patients had primary disorders, such as abnormal colonic motility or anorectal dysfunction, said Adil E. Bharucha, MBBS, MD, AGAF, a professor of medicine in the gastroenterology and hepatology division and a medical director in the office of clinical trials at Mayo Clinic, Rochester, Minn., who was not involved in the study. For patients with gastroparesis and constipation, clinicians should consider withdrawing constipating medications, performing anorectal testing, and referring patients for pelvic floor biofeedback

Continued on page 14

Question cause or consequence

Celiac *from page 1*

mary. "It is not clear whether the microbes identified [in this study] contribute to the pathogenesis of celiac disease or are the result of it. Future research should explore the role of the disease-specific species identified here," the researchers wrote in Gastroenterology.

Celiac disease is multifactorial. While up to 40% of people are genetically predisposed, only a small proportion develop it, suggesting that environmental factors are key to pathogenesis. Recent studies have linked celiac disease with alterations in the gut microbiome, but it is unclear whether dysbiosis is pathogenic or a secondary effect of disease processes such as nutrient malabsorption, or whether dysbiosis is present at disease onset or results from a gluten-free diet.

For the study, the researchers performed gas chromatography and 16S ribosomal RNA sequencing of fecal samples from 141 children, including 20 with newly biopsy-confirmed, previously untreated celiac disease; 45 children previously diagnosed and on a gluten-free diet; 19 unaffected siblings; and 57 healthy children who were not on regular medications and had no history of chronic gastrointestinal symptoms. A single fecal sample was tested for all but the previously untreated children, who were tested at baseline and then after 6 and 12 months on a gluten-free diet.

Children with new-onset celiac disease showed no evidence of dysbiosis, while a gluten-free diet explained up to 2.8% of variation in microbiota between patients and controls. Microbial alpha diversity, a measure of species-level diversity, was generally similar among groups, but between 3% and 5% of all taxa differed. Irrespective of treatment, the decreased abundance of the 11 OTUs was diagnostic for celiac disease with an error rate of 21.5% ($P < .001$ vs. random classification). Notably, most of these 11 discrepant OTUs were associated with nutrient or food-group intake and with biomarkers of gluten ingestion, the researchers said. Gas chromatography showed that, after patients started a gluten-free diet, fecal levels of butyrate and ammonia decreased.

"Even though we identified differences in the abundance of a few species between patients with untreated celiac disease and healthy controls, the profound microbial dysbiosis noted in Crohn's disease was not observed, at least using crude diversity indices," the investigators commented. "Although several alterations in the intestinal microbiota of children with established celiac disease appear to be effects of a gluten-free diet, there are specific bacteria that are distinct biomarkers of celiac disease."

Future research might involve performing in vitro tests of "candidate" bacteria, coculturing these bacteria with human immune cells, and studying whether dietary interventions alter the relative abundance of these bacteria in the gut microbiome, the researchers said.

Nutricia Research Foundation, the Biotechnology and Biological Sciences Research Council, and The Catherine McEwan Foundation provided funding. Three coinvestigators disclosed ties to Nutricia, 4D Pharma, AbbVie, Celltrion, Janssen, Takeda, and several other pharmaceutical companies. One coinvestigator reported chairing the working group for ISLI Europe. The remaining investigators reported having no conflicts of interest.

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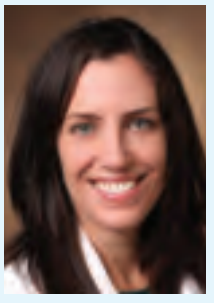
SOURCE: Zafeiropoulou K et al. Gastroenterology. 2020 Aug 10;S0016-5085(20)35023-X. doi: 10.1053/j.gastro.2020.08.007.

It is well known that gluten ingestion in genetically susceptible individuals does not guarantee celiac disease, and research over the past decade has searched for environmental triggers. Gut microbiota play a role in activation of innate immunity, which leads to the adaptive immune response and the small-bowel damage that is characteristic of celiac disease. The authors of this study sought to identify whether there is a distinct microbial pattern among celiac disease patients, both those with treated and untreated disease, in comparison with healthy controls and healthy siblings.



Dr. Adams

The authors identified three groups of bacterial taxa: 1) unique to celiac disease independent of treatment, 2) new-onset disease and treatment responsive, and 3) reflective of diet changes and not unique to disease. Within the first group, 11 distinct operational taxonomic units (OTUs) could highly predict celiac disease regardless of treatment. From these results, we cannot determine if the microbial signature is a result of disease or a contributor to disease development; however, it reinforces that this unique signature is present at diagnosis and identifies taxa for further investigation.

A significantly different microbial profile and metabolites were identified in subjects on gluten-free diets. The consequences of the gluten-free diet are an important consideration when committing a patient to this life-long therapy. The microbiome changes may play a role in persistent symptoms and the increased health conditions we see in treated celiac disease. Those on a gluten-free diet have other micronutrient deficiencies in addition to microbiome changes and the health sequelae of this are not fully understood. A gluten-free diet focused on restoring the normal gut flora through probiotic or gluten-free prebiotic or fiber supplementation in celiac disease patients could prove beneficial.

Dawn Wiese Adams, MD, MS, is assistant professor and medical director, Center for Human Nutrition, department of gastroenterology, hepatology, and nutrition, Vanderbilt University Medical Center, Nashville, Tenn. She has no conflicts of interest.

Continued from page 9

therapy if anorectal tests are positive, he said while acknowledging the need for more data on these approaches. For patients without evidence of anorectal disorders, he recommended "simple laxatives or, if necessary, prescription medications, some of which may also benefit upper gastrointestinal symptoms."

In this study, constipation also did not correlate with gastric emptying, which suggests that "motility disturbances in the foregut are separable from those in the hindgut," said David Levinthal, MD, PhD, director of the neurogastroenterology and motility center at the University of Pittsburgh Medical Center, who also was not involved in the work. Constipation was only marginally linked with colonic transit time (OR, 1.04; 95% CI, 1.00-1.07), and delayed gastric emptying did not predict the severity of dyspepsia, he noted. "These observations highlight that sensory mechanisms are very important factors that are not interrogated by physiological motility tests, but that nonetheless may have an outsized impact on how patients feel."

Despite "fairly good phenotyping of patients [based on] physiological measures, medication use, and detailed symptom questionnaires," the study's method of grouping patients based on continuous variables could mask relevant clinical nuances, Dr. Levinthal said. He emphasized that individual physiological tests do not reliably predict the presence or severity of GI symptoms: "What would you make of a 50-hour colonic transit time [CTT]? Or a 60-hour CTT? One could have either no constipation or severe constipation with those values. In clinical practice, it is less certain how useful it is to know a specific CTT result [when] formulating a treatment plan."

'These observations highlight that sensory mechanisms are very important factors that are not interrogated by physiological motility tests, but that nonetheless may have an outsized impact on how patients feel.'

Therefore, future studies of patients with gastroparesis and constipation should forgo grouping patients based on GI motor patterns and instead validate patient-reported symptom measures by using novel sensory tests with stimuli such as eating, drinking, and balloon distension, Dr. Levinthal said. He also recommended studying cognitive and emotional functioning in this patients, given that conditions such as depression and anxiety are known to affect GI sensation.

The National Institute of Diabetes and Digestive and Kidney Diseases provided funding. The investigators reported having no conflicts of interest. Dr. Bharucha reported having filed patents for anorectal devices jointly with Minnesota Medical Technologies, Medspira, and Medtronic and receiving royalties from Medspira. Dr. Levinthal reported having served on advisory boards for Takeda Pharmaceuticals and Alexza Pharmaceuticals.

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SOURCE: Parkman HP et al. Clin Gastroenterol Hepatol. 2020 Oct 28. doi: 10.1016/j.cgh.2020.10.045.

FIT unfit for inpatient, emergency settings

BY MICHAEL VLESSIDES

Most fecal immunochemical tests (FIT) in the hospital setting or the ED are performed for inappropriate indications, according to new data.

"This is the largest study that focuses exclusively on the use of FIT in the ED, inpatient wards, and in the ICU, and it shows significant misuse," said investigator Umer Bhatti, MD, from Indiana University, Indianapolis.

The only "validated indication" for FIT is to screen for colorectal cancer. However, "99.5% of the FIT tests done in our study were for inappropriate indications," he reported at the annual meeting of the American College of Gastroenterology, where the study was honored with an ACG Presidential Poster Award.

And the inappropriate use of FIT in these settings had no positive effect on clinical decision-making, he added.

For their study, Dr. Bhatti and colleagues looked at all instances of FIT use in their hospital's electronic medical records from November 2017 to October 2019 to assess how often FIT was being used, the indications for which it was being used, and the impact of its use on clinical care.

They identified 550 patients, 48% of whom were women, who underwent at least one FIT test. Mean age of the study cohort was 54 years. Only three of the tests, or 0.5%, were performed to screen for colorectal cancer (95% confidence interval, 0.09%-1.52%).

'Another option – and this has been done in many settings with the fecal occult blood test – is just take FIT off the units or out of the ER, so providers won't be tempted to use it as an assessment of these patients.'

Among the indications documented for FIT were anemia in 242 (44.0%) patients, suspected GI bleeding in 225 (40.9%), abdominal pain in 31 (5.6%), and change in bowel habits in 19 (3.5%).

The tests were performed most often in the ED (45.3%) and on the hospital floor (42.2%), but were also performed in the ICU (10.5%) and burn unit (2.0%).

Overall, 297 of the tests, or 54%, were negative, and 253, or 46%, were positive.

"GI consults were obtained in 46.2% of the FIT-positive group, compared with 13.1% of the FIT-negative patients" (odds ratio, 5.93; 95% CI, 3.88-9.04, $P < .0001$), Dr. Bhatti reported.

Among FIT-positive patients, those with overt bleeding were more likely to receive a GI consultation than those without (OR, 3.3; 95% CI, 1.9-5.5; $P < .0001$).

Of the 117 FIT-positive patients who underwent a GI consultation, upper endoscopy was a more common outcome than colonoscopy (51.3% vs. 23.1%; $P < .0001$). Of the 34 patients who underwent colonoscopy or sigmoidoscopy, one was diagnosed with colorectal cancer and one with advanced adenoma.

Overt GI bleeding was a better predictor of a GI consultation than a positive FIT result. In fact, use of FIT for patients with overt GI bleeding indicates a poor understanding of the test's utility, the investigators reported.

"For patients with overt GI bleeding, having a positive FIT made no difference on how often a bleeding source was identified on endoscopy, suggesting that FIT should not be used to guide decisions about endoscopy or hospitalization," Dr. Bhatti said.

In light of these findings, the team urges their peers to consider measures to reduce FIT tests for unnecessary indications.

"We feel that FIT is unfit for use in the inpatient and emergency settings, and measures should be taken to curb its use," Dr. Bhatti concluded. "We presented our data to our hospital leadership and a decision was made to remove the FIT as an orderable test from the EMR."

These results are "striking," said Jennifer Christie, MD, from Emory University, Atlanta.

"We should be educating our ER providers and inpatient providers about the proper use of FIT," she said in an interview. "Another option – and this has been done in many settings with the fecal occult blood test – is just take FIT off the units or out of the ER, so providers won't be tempted to use it as an assessment of these patients. Because often times, as this study showed, it doesn't really impact outcomes."

In fact, unnecessary FIT could put patients at risk for unnecessary procedures. "We also know that calling for an inpatient or ER consult from a gastroenterologist may increase both length of stay and costs," she added.

Dr. Bhatti and Dr. Christie disclosed no relevant financial relationships.

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

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GI & HEPATOLOGY NEWS

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Task force: Best practices for malignant CR polyps

BY AMY KARON
MDedge News

For patients with malignant colorectal polyps, endoscopists should look for features of deep submucosal invasion and should retrieve, handle, and submit specimens in ways that support thorough and accurate pathologic assessment, according to new recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer.

"In nonpedunculated lesions with features of deep submucosal invasion, endoscopic biopsy is followed by surgical resection. In cases without features of deep submucosal invasion, en bloc resection and proper specimen handling should be considered (if feasible) for lesions with a high risk of superficial submucosal invasion," wrote Aasma Shaukat, MD, MPH, AGAF, of the Minneapolis Veterans Affairs Health Care System and her fellow experts. The recommendations were published in Gastroenterology.

Malignant colorectal polyps invade the submucosa but do not extend into the muscularis propria. Pedunculated and nonpedunculated polyps should be considered to invade the deep submucosa if they are classified as NICE (NBI International Colorectal Endoscopic) type 3, Kudo type VN (neoplastic and invasive, with an irregular arrangement), or Kudo type VI (an amorphous structure, with a loss of or decrease in pits). "Nonpedunculated lesions with these features should be biopsied (in the area of surface feature disruption), tattooed (unless in or near the cecum), and referred to surgery. Pedunculated polyps with features of deep submucosal invasion should undergo endoscopic polypectomy," according to the MSTFCC recommendations.

Moderate-quality evidence links submucosal invasion with two types of polyp morphology: LST-NG (laterally spreading tumor, nongranular type) showing a depression or sessile shape and LST-G (laterally spreading tumor, granular type) that includes a dominant nodule. According to low-quality evidence, these lesions should be managed with en bloc rather than piecemeal resection. En bloc resection is important for all pedunculated polyps (even if large) and should be considered for LST-G lesions with a dominant nodule. Resected pedunculated polyps should be retrieved through the suction channel – if doing so does not require them to be cut – or with a net or snare during scope withdrawal. Nonpedunculated lesions with suspected submucosal invasion that are removed en bloc should be pinned peripherally around the entire circumference to a hard surface and fixed in 10% formalin. This practice helps pathologists orient specimens to correctly assess depth of invasion and margin involvement.

For both pedunculated and nonpedunculated polyps, features denoting a high risk for residual or recurrent malignancy are poor tumor differentiation, lymphovascular invasion, or more than 1 mm of submucosal invasion.

For both pedunculated and nonpedunculated polyps, features denoting a high risk for residual or recurrent malignancy are poor tumor differentiation, lymphovascular invasion, or more than 1 mm of submucosal invasion. For nonpedunculated polyps, additional high-risk features include tumor budding and tumor involvement of the cautery margin.

The MSTFCC recommends that, when reporting on a malignant colorectal polyp, pathologists follow the structured template of the College of American Pathologists and note the lesion's histologic type, grade of differentiation, extent of tumor extension or invasion, stalk and mucosal margin, and presence or absence of lymphovascular invasion. Specimen integrity, polyp size and morphology, and tumor budding are also useful. To reduce miscommunication and facilitate appropriate management, pathologists should avoid using the terms carcinoma and cancer when describing malignant colorectal polyps, according to the MSTFCC.

The decision to recommend adjuvant surgery "is based on polyp shape, whether there was en bloc resection and adequate histologic assessment, the presence or absence of unfavorable histologic features, the patient's risk for surgical mortality and morbidity, and patient preferences," the recommendations state. Because multidisciplinary management can optimize clinical outcomes for patients with malignant polyps, gastroenterologists, pathologists, oncologists, and surgeons should identify best ways to communicate with each other and share decision-making conjointly and with patients. "Patient values are important in cases where the risk of residual cancer and the risk of surgical mortality are similar," the MSTFCC notes. "In these latter cases, shared decision-making is emphasized."

The authors of the task force recommendations reported having no relevant conflicts of interest since 2016.

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SOURCE: Shaukat A et al. Gastroenterology. 2020 Nov 4. doi: 10.1053/j.gastro.2020.08.050.

CRC rates up in younger adults

USPSTF *from page 1*

Increasing the pressure for change

The move comes after mounting evidence of an increase in CRC among younger adults and mounting pressure to lower the starting age.

Two years ago, the American Cancer Society revised its own screening guidelines and lowered the starting age to 45 years. Soon afterward, a coalition of 22 public health and patient advocacy groups joined the ACS in submitting a letter to the USPSTF asking that the task force reconsider its 2016 guidance (which recommends starting at age 50 years).

The starting age for screening is an important issue, commented Judy Yee, MD, chair of radiology at the Albert Einstein College of Medicine and the Montefiore Health System in New York and chair of the Colon Cancer Committee of the American College of Radiology.

"Right now it is very confusing to physicians and to the public," Dr. Yee said in an interview at that time. "The USPSTF and the ACS differ as far as the age to begin screening, and insurers may not cover the cost of colorectal cancer screening before age 50."

Dr. Barry said that the Task Force took notice of recent data showing an increase in the incidence of CRC among younger adults.

"The risk now for age 45-49 is pretty similar to the risk for people in their early 50s. So in some ways, today's late 40-year-olds are like yesterday's 50-year-olds," he commented.

The task force used simulation models that confirmed what the epidemiologic data suggested and "that we could prevent some additional colorectal cancer deaths by starting screening at age 45," he said.

The rest of the new draft recommendation is similar to the 2016 guidelines, in which the task force says there is convincing evidence that CRC screening substantially reduces disease-related mortality. However, it does not recommend any one screening approach over another. It recommends both direct visualization, such as colonoscopy, as well as noninvasive stool-based tests. It does not recommend serum tests, urine tests, or capsule endoscopy because there is not yet enough evidence about the benefits and harms of these tests.

'The risk now for age 45-49 is pretty similar to the risk for people in their early 50s. So in some ways, today's late 40-year-olds are like yesterday's 50-year-olds.'

"The right test is the one a patient will do," Dr. Barry commented.

Defining populations

CRC in young adults made the news in August 2020 when Chadwick Boseman, known for his role as King T'Challa in Marvel's "Black Panther," died of colon cancer. Diagnosed in 2016, he was only 43 years old.

"The recent passing of Chadwick Boseman is tragic, and our thoughts are with his loved ones during this difficult time," said Dr. Barry. "As a Black man, the data show that Chadwick was at higher risk for developing colorectal cancer."

Unfortunately, there is currently not enough evidence that screening Black men younger than 45 could help prevent tragic deaths such as Chadwick's, he commented. "The task force is calling for more research on colorectal cancer screening in Black adults," he added.

Limiting screening to those at higher risk

In contrast to the USPSTF and ACS guidelines, which recommend

Continued on following page

Statins may lower risk of colorectal cancer

BY WILL PASS
MDedge News

Statin use may significantly lower the risk of colorectal cancer (CRC) in patients with or without inflammatory bowel disease (IBD), based on a meta-analysis and systematic review.

In more than 15,000 patients with IBD, statin use was associated with a 60% reduced risk of CRC, reported lead author Kevin N. Singh, MD, of NYU Langone Medical Center in New York, and colleagues.

"Statin use has been linked with a risk reduction for cancers including hepatocellular carcinoma, breast, gastric, pancreatic, and biliary tract cancers, but data supporting the use of statins for chemoprevention against CRC is conflicting," Dr. Singh said during a virtual presentation at the annual meeting of the American College of Gastroenterology.

He noted a 2014 meta-analysis by Lytras and colleagues that reported a 9% CRC risk reduction in statin users who did not have IBD (World J Gastroenterol. 2014 Feb 21. doi: 10.3748/wjg.v20.i7.1858). In patients with IBD, data are scarce, according to Dr. Singh.

To further explore the relationship between statin use and CRC in patients without IBD, the investigators analyzed data from 52 studies, including 8 randomized clinical trials, 17 cohort studies, and 27 case-control studies. Of the 11,459,306 patients involved, approximately 2 million used statins and roughly 9 million did not.

To evaluate the same relationship in patients with IBD, the investigators conducted a separate meta-analysis involving 15,342 patients from five observational studies, one of which was an unpublished abstract. In the four published studies, 1,161 patients used statins while 12,145 did not.

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'Prospective trials are needed to confirm the risk reduction of CRC in the IBD population, including whether the effects of statins differ between ulcerative colitis and Crohn's disease patients.'

In the non-IBD population, statin use was associated with a 20% reduced risk of CRC (pooled odds ratio, 0.80; 95% confidence interval, 0.73-0.88; *P* less than .001). In patients with IBD, statin use was associated with a 60% CRC risk reduction (pooled OR, 0.40; 95% CI, 0.19-0.86; *P* = .019).

Dr. Singh noted "significant heterogeneity" in both analyses (I2 greater than 75), most prominently in the IBD populations, which he ascribed to "differences in demographic features, ethnic groups, and risk factors for CRC."

While publication bias was absent from the non-IBD analysis, it was detected in the IBD portion of the study. Dr. Singh said that selection bias due to exclusive use of observational studies may also have been present in the IBD analysis.

"Prospective trials are needed to confirm the risk reduction of CRC in the IBD population, including whether the effects of statins differ between ulcerative colitis and Crohn's disease patients," Dr. Singh said.

Additional analyses are underway, he added, including one that will account for the potentially confounding effect of aspirin use.

According to David E. Kaplan, MD, AGAF, of the University of Pennsylvania, Philadelphia, "The finding that statins are associated with reduced CRC in IBD provides additional support for the clinical importance of the antineoplastic effects of statins. This effect has been strongly observed in liver cancer, and is pending prospective validation."

Dr. Kaplan also offered some mechanistic insight into why statins have an anticancer effect, pointing to "the centrality of cholesterol biosynthesis for development and/or progression of malignancy."

The investigators and Dr. Kaplan reported no relevant conflicts of interest.

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Continued from previous page

screening for CRC for everyone over a certain age, a set of recommendations developed by an international panel of experts suggests screening only for individuals who are at higher risk for CRC.

As previously reported, these guidelines suggest restricting screening to adults whose cumulative cancer risk is 3% or more in the next 15 years, the point at which the balance between benefits and harms favors screening.

The authors, led by Lise Helsingen, MD, Clinical Effectiveness Research Group, University of Oslo, said "the optimal choice for each person requires shared decision-making."

Such a risk-based approach is "increasingly regarded as the most appropriate way to discuss cancer screening." That approach is already used in prostate and lung cancer screening, they noted.

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

PERSPECTIVE

Moving the goal posts for colorectal cancer screening


Dr. Shaukat

Clinicians and researchers have actively debated the pros and cons of lowering the screening age to 45 years since 2018, when the American Cancer Society released its colorectal cancer (CRC) screening guidelines. The most compelling argument in support of lowering the screening age is that recent data from Surveillance Epidemiology and End Results (SEER) show that the CRC incidence rates in 45- to 50-year-olds are similar to rates seen in 50- to 54-year-olds about 20 years ago, when the first guidelines to initiate screening at age 50 were widely established. Termed early-onset CRC (EOCRC), the underlying reasons for this increase are not completely understood, and while the absolute numbers of EOCRC cases are smaller than in older-age groups, modeling studies show that screening this age group is both efficient and effective.

Over the last 20 years we have made major strides in reducing the incidence and mortality from CRC in ages 50 years and older, and now we must rise to the challenge of delivering CRC screening to this younger group in order to see similar dividends over time and curb the rising incidence curve of EOCRC. And we must do so without direct evidence to guide us as to the magnitude of the benefit of screening this younger group, the best modality to use, or tools to risk stratify who is likely to benefit from screening in this group. We must also be careful not to worsen racial and geographic disparities in CRC screening, which already exist for African Americans, Native Americans, and other minorities and rural residents. Finally, even though the goal posts are changing, our target remains to get to 80% screening rates for all age groups, and not neglect the currently underscreened 50- to 75-year-olds, who are at a much higher risk of CRC than their younger counterparts.

Aasma Shaukat, MD, MPH, AGAF, is an investigator, Center for Care Delivery and Outcomes Research, section chief and staff physician, GI section, Minneapolis VA Health Care System; staff physician, Fairview University of Minnesota Medical Center, Minneapolis; and professor, University of Minnesota department of medicine, division of gastroenterology, Minneapolis. She has no conflicts of interest.

CGH releases its first GI cancer–themed issue

Articles include guidance on cancer progression in Barrett's esophagus patients (e.g., Association between levels of sex hormones and risk of esophageal adenocarcinoma and Barrett's esophagus), colorectal cancer surveillance (e.g., Risk factors associated with early-onset colorectal cancer), and hepatocellular carcinoma incidence (e.g., High dietary intake of vegetable or polyunsaturated fats is associated with reduced risk of hepatocellular carcinoma) and risk.

Clinical Gastroenterology and Hepatology (CGH) is proud to release its first themed issue on gastroenterological cancers. This "issue within an issue" includes a collection of articles, selected by Editor in Chief Fasiha Kanwal, MD, MSHS, that will provide you with practical research to help guide cancer prevention, surveillance, and treatment decisions for your patients.

View the themed issue on CGH's website and access other curated collections on cghjournal.org.

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DDSEP 9
Digestive Diseases Self-Education Program

Quick Quiz

Q1. You perform a colonoscopy for a patient who underwent sigmoid resection for stage 2 colorectal cancer 1 year ago. The colonoscopy reveals one diminutive adenoma in the cecum, which you remove with a cold snare.

When should you recommend the next colonoscopy?
A. 10 years
B. 5 years
C. 3 years
D. 1 year
E. 6 months

Q2. Patients with celiac disease subscribing to a strict gluten-free diet are at particular risk for which nutrient deficiency?
A. Fiber
B. Protein
C. Folate
D. Thiamine
E. Iron

Answers on following page

Congrats to these five AGA members

We're proud to share the news of two AGA members elected to the prestigious National Academy of Medicine and three honored with the 2020 Sherman Prize.

Congratulations to AGA members Judy H. Cho, MD, and B. Mark Evers, MD, who were recently elected to the National Academy of Medicine.

Judy H. Cho, MD, professor of medicine at Icahn School of Medicine at Mount Sinai, New York, for "establishing that uncommon, loss-of-function variants in the microbial-sensing domain of NOD2 confer risk for Crohn's disease, and identifying a loss-of-function allele in the IL-23 receptor that protects against Crohn's disease and ulcerative colitis, leading to new, approved therapies."

B. Mark Evers, MD, physician in chief of oncology service at University of Kentucky Healthcare, for "his expertise on intestinal hormones and hormonal arcades in oncogenesis. His seminal insights defined the role of gut hormones on normal physiology and metabolism, pioneering innovative understanding of neuroendocrine cell biology and the role of neurohormonal pathways in the development and progression of neuroendocrine tumors."

Being selected to the Academy is one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

In addition, the 2020 Sherman Prize was awarded to the following three AGA members:

David Rubin, MD, AGAF, chief, section of gastroenterology, hepatology and nutrition at University of Chicago Medicine, for his "renown in the IBD community as a brilliant clinician, creative researcher, tireless advocate, and trailblazing educator."

Gary Wu, MD, professor of medicine at University of Pennsylvania, Perelman School of Medicine, for "pioneering the study of the gut microbiome in IBD, publishing seminal research on the relationship between diet and the microbiome — enabling multiple areas of research into dietary interventions for IBD."

Jessica Allegretti, MD, MPH, director of clinical trials at Brigham and Women's Hospital, as a "highly regarded expert in the field of fecal microbiota transplantation (FMT) and microbiome therapeutics, establishing the therapy as an effective treatment in IBD patients with recurrent *C. difficile*."

Presented by the Bruce and Cynthia Sherman Charitable Foundation, the Sherman Prize is awarded to experts in the field of Crohn's disease and ulcerative colitis who have exhibited their commitment to advancing inflammatory bowel disease care and have dedicated their careers to overcome these diseases.

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Experts release new management strategies for malignant colorectal polyps

Early identification and removal of cancerous colorectal polyps is critical to preventing the progression of colorectal cancer and improving survival rates. The U.S. Multisociety Task Force (U.S. MSTF) on Colorectal Cancer has released new guidance for endoscopists on how to assess colorectal lesions for features associated with cancer, discuss how these factors guide management and outline when to advise surgery after malignant polyp removal.

Key recommendations from the U.S. Multisociety Task Force on Colorectal Cancer, which is comprised of leading experts representing AGA, ACG and ASGE, include:

1. Management of malignant polyps must begin with a thorough and knowledgeable endoscopic assessment designed to identify features of deep submucosal invasion.

2. In nonpedunculated lesions with features of deep submucosal invasion, endoscopic biopsy and tattooing should be followed by surgical resection.

3. Nonpedunculated lesions with high risk of superficial submucosal invasion should be considered for en bloc resection and proper specimen handling.

4. When pathology reports cancer in a lesion that was completely resected endoscopically, the decision to recommend surgery is based on polyp shape, whether there was en bloc resection and adequate histologic assessment, the presence or absence of unfavorable histologic features, the patient's risk for surgical mortality and morbidity, and patient preferences.

For more information, review the full publication: Endoscopic Recognition and Management Strategies for Malignant Colorectal Polyps: Recommendations of the US Multi-Society Task Force on Colorectal Cancer. The U.S. MSTF recommendations are published jointly in Gastroenterology, The American Journal of Gastroenterology, and Gastrointestinal Endoscopy.

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AGA Giving Day: Our fight to eradicate disparities in digestive diseases

On Dec. 3, AGA brought together the GI community in an effort to fund health disparity research with the goal of improving care for the patients who rely on us.

We're so proud of how AGA members stepped up to make this campaign a success. With money raised through AGA Giving Day, the AGA Research Foundation will fund research projects that help understand health disparities and create strategies for overcoming them.

AGA Giving Day was the opportunity to do something about this important societal issue as it directly relates to our field. We all have a role to play in creating a just world free of health disparities in digestive diseases and free of inequities in access and effective health care delivery.

The AGA Research Foundation's AGA Giving Day effort help support state-of-the-art research that aligns with the realities of the current multicultural patient population and disease states to achieve health equity for all.

Learn more at gastro.org/aga-givingday.

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Quick Quiz Answers

Q1. Correct answer: C

Rationale
According to the Multi-Society Task Force on Colorectal Cancer, colonoscopy should be performed 1 year after resection, and again 3 years later, in order to decrease the risk of metachronous colorectal cancer.

Reference
Kahi CJ, Boland CR, Dominitz JA. Gastroenterology. 2016. 150(3):758-68.e11.

Q2. Correct answer: D

Rationale
Deficient intake of fiber and folate may originate in the food choice of the individual, whereas some deficiencies of intake, such as thiamine, appear to be celiac specific. The provider should encourage intake of nutrient-dense foods including wholegrain foods, enriched if possible, legumes, fruits, vegetables, lean meat, fish, chicken, and eggs. It is not necessary to prioritize micronutrient supplements over achieving nutritional adequacy through dietary intake. Iron deficiency is an effect of untreated celiac disease.

Reference
Shepherd SJ, Gibson PR. J Human Nutr Dietet. 2012;26:349-58.

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Cirrhosis, Child-Pugh score predict ERCP complications

BY WILL PASS
MDedge News

Cirrhosis may increase the risk of complications from endoscopic retrograde cholangiopancreatography (ERCP), according to a retrospective study involving almost 700 patients.

The study also showed that Child-Pugh class was a better predictor of risk than Model for End-Stage Liver Disease (MELD) score, reported lead author Michelle Bernshteyn, MD, a third-year internal medicine resident at State University of New York, Syracuse, and colleagues.

"There remains a scarcity in the literature regarding complications and adverse effects after ERCP in cirrhotic patients, particularly those incorporating Child-Pugh class and MELD score or type of intervention as predictors," Dr. Bernshteyn said during a virtual presentation at the American College of Gastroenterology annual meeting. "Furthermore, literature review demonstrates inconsistency among results."

To gain clarity, Dr. Bernshteyn and colleagues reviewed electronic medical records from 692 patients who underwent ERCP, of whom 174 had cirrhosis and 518 did not. For all patients, the investigators analyzed demographics, comorbidities, indications for ERCP, type of sedation, type of intervention, and complications within a 30-day period. Complications included bleeding, pancreatitis, cholangitis, perforation, mortality caused by ERCP, and mortality from other causes. Patients with cirrhosis were further analyzed based on etiology of cirrhosis, Child-Pugh class, and MELD score.

The analysis revealed that complications were significantly more common in patients with cirrhosis than in those without cirrhosis (21.30% vs. 13.51%; $P = .015$). No specific complications were significantly more common in patients with cirrhosis than in those without cirrhosis.

In patients with cirrhosis, 41.18% of Child-Pugh class C patients had complications, compared with 15.15% of class B patients and 19.30% of class A patients ($P = .010$). In contrast, MELD scores were not significantly associated with adverse events.

Further analysis showed that, in patients without cirrhosis, diagnostic-only ERCP and underlying chronic obstructive pulmonary disease were associated with high rates of complications ($P = .039$ and $P = .003$, respectively). In patients with cirrhosis, underlying chronic obstructive pulmonary disease and hypertension predicted adverse events ($P = .009$ and $P = .003$, respectively).

"The results of our study reaffirm that liver cirrhosis has an impact on the occurrence of complications during ERCP," Dr. Bernshteyn said. "Child-Pugh class seems to be more reliable as compared to MELD score in predicting complications of ERCP in cirrhosis patients," she added. "However, we are also aware that Child-Pugh and MELD scores are complementary to each other while evaluating outcomes of any surgery in patients with cirrhosis."

In 2017, Udayakumar Navaneethan, MD, a gastroenterologist at AdventHealth Orlando's Center for Interventional Endoscopy, and an assistant professor at the University of Central Florida, Orlando, and colleagues published a national database study concerning the safety of ERCP in patients with liver cirrhosis (Endosc Int Open. 2017 Apr;5[4]:E303-14).

"[The present] study is important as it highlights the fact that ERCP is associated with significant complications in cirrhotic patients compared to those without cirrhosis," Dr. Navaneethan said when asked to comment. "Also, Child-Pugh score appeared to be more reliable than MELD score in predicting complications of ERCP in cirrhotic patients."

He went on to explain relevance for practicing clinicians. "The clinical implications of the study are that a detailed risk-benefit discussion needs to be done with patients with liver cirrhosis, particularly with advanced liver disease Child-Pugh class C, irrespective of the etiology," Dr. Navaneethan said. "ERCP should be performed when there is clear evidence that the benefits outweigh the risks."

The investigators and Dr. Navaneethan reported no conflicts of interest.

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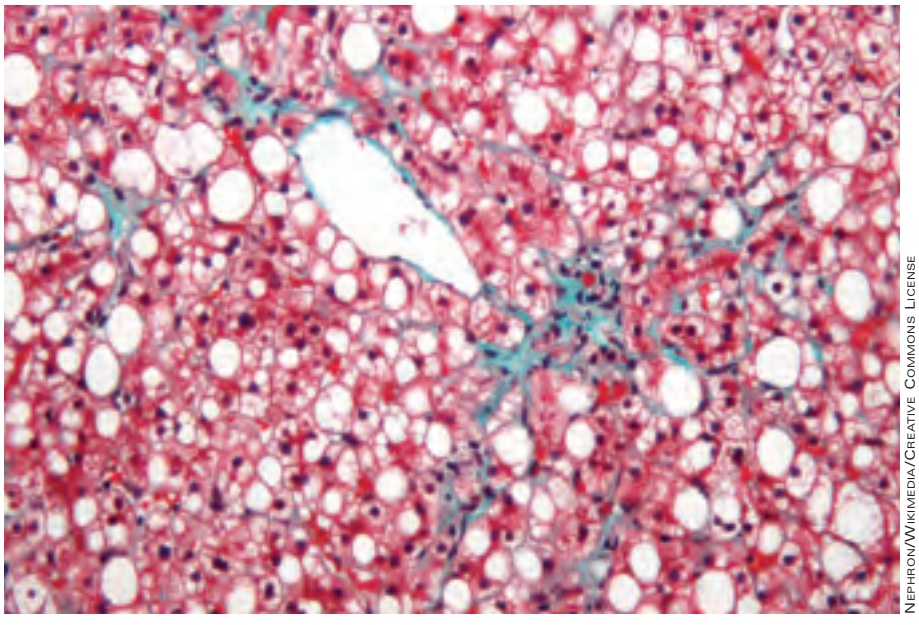
SOURCE: Bernshteyn M et al. ACG 2020, Abstract S0982.

Lipid profiles distinguish obese and nonobese NAFLD patients

BY HEIDI SPLETE
MDedge News



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Both obese and nonobese individuals can develop nonalcoholic fatty liver disease (NAFLD), and lipid profiles were effective predictors in both groups, based on data from a cross-sectional study of 361 individuals.

Given the strong association between obesity and NAFLD, previous research on lipidomic profiles have focused on obese White patients, wrote Youngae Jung, MD, of the Korea Basic Science Institute, Seoul, and colleagues.

"However, there are insufficient data on circulating lipidomics of nonobese NAFLD patients," they added.

In a study published in Alimentary Pharmacology and Therapeutics, the researchers identified 295 adults with NAFLD and 66 controls. Overall, 130 participants were nonobese (body mass index <25 kg/m^2) and 231 were obese (BMI, 25 or higher). The nonobese group included 51 patients with NAFLD, 31 with nonalcoholic steatohepatitis (NASH), and 48 controls; the obese group included 106 patients with NAFLD, 107 with NASH, and 18 controls.

Lipid profiles show predictive promise

Overall, changes in diacylglycerol (DAG) and triacylglycerol (TAG) appeared in both obese and nonobese patients with increases from NAFL to NASH, the researchers noted.

"Levels of DAGs with relatively short chains and a low degree of desaturation significantly increased in NAFL versus no NAFLD, regardless of obesity," the researchers said. "In contrast, levels of DAGs with relatively long chains and a high degree of desaturation significantly decreased in NASH versus NAFL in the obese group, which was not observed in the nonobese group," they noted.

In addition, saturated sphingomyelin (SM) species were significantly associated with visceral adiposity in nonobese NAFLD patients, but not in obese NAFLD patients, and SM levels were significantly associated with both systemic and adipose tissue insulin resistance.

The researchers identified five potential lipid metabolites for nonobese subjects and seven potential lipids for obese subjects that included DAGs, TAGs, and SMs that were distinct between NAFL and NASH patients in order to predict the histologic severity of NAFLD. Overall, these metabolite combinations were effective predictors of NAFLD/NASH in nonobese and obese patients. The areas under the receiver operator characteristic curve were 0.916 versus 0.813 for NAFLD versus non-NAFLD in non-

Continued on following page

Continued from previous page

obese patients, and 0.967 versus 0.812 for NAFLD versus non-NAFLD in the obese patients.

More BMI groups may yield more information

The key study limitation was the cross-sectional study design, the researchers noted. In addition, dividing patients into only two groups based on BMI may not reveal any distinct biology among lean NAFLD patients, who were included with overweight patients in the non-obese group.

However, the results were strengthened by the large amount of data and the confirmed diagnoses of NASH and fibrosis by an expert liver pathologist, they added.

"Therefore, our findings provide new insights that aid in the understanding of pathophysiological mechanisms responsible for the development and severity of non-obese NAFLD, which are relevant to precision medicine and personalized therapy based on various phenotypes of NAFLD," they concluded.

Validation needed in other populations

"Liver biopsy remains the gold standard for diagnosing NAFLD/NASH but has its own limitations and risks, so many researchers in this field are looking for a noninvasive alternative to help with diagnosis," Zachary Henry, MD, of the University of Virginia, Charlottesville, said in an interview. "Imaging methods such as transient elastography and MR-elastography have been introduced and many biochemical markers have been evaluated, yet all have their limitations. In the current study, the authors report a high diagnostic accuracy for evaluating NAFLD using lipidomic profiles, which could introduce a new noninvasive measurement of NAFLD."

Dr. Henry said that he was not surprised by the study findings. However, "I believe they are important as they define a lipid profile that shows differences between patients with NASH versus patients with NAFLD versus patients without NAFLD," he said. "NAFLD is a disease of disordered lipid metabolism in hepatocytes, and although it stands to reason there would be differences in lipid profiles, it is interesting to see the changes between DAGs and TAGs especially as disease progresses from NAFLD to NASH.

"Clinically, I do not think this really changes practice right now since it needs to be validated in other populations of NAFLD. However, it certainly adds to a growing armamentarium of noninvasive testing. Hopefully, we are able to combine some of these noninvasive tests in the future to better predict NAFLD and NASH as well as outcomes such as cirrhosis and hepatocellular carcinoma," he said.

"I think these lipidomic profiles need to be validated in non-Korean populations of patients with NAFLD to determine if these changes are ubiquitous to everyone or if a different profile exists based upon different genetics and environment," Dr. Henry added. "As the authors note in their paper, there have been previously published differences between populations of NAFLD in Asia as compared to Western countries and it is unclear how, if at all, these lipidomic profiles relate to those differences."

The study was funded by the Korea Basic Science Institute, the Korea Health Industry Department Institute, and the National Research Foundation of Korea. The researchers had no financial conflicts to disclose. Dr. Henry had no financial conflicts to disclose.

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SOURCE: Jung Y et al. Aliment Pharmacol Ther. 2020 Sep 6. doi: 10.1111/apt.16066.

Semaglutide shows promise in NASH phase 2 study

BY KATE JOHNSON
MDedge News

Almost 60% of patients with biopsy-confirmed nonalcoholic steatohepatitis and liver fibrosis showed resolution of NASH after treatment with semaglutide, according to a phase 2, double-blind, randomized, placebo-controlled trial published in the New England Journal of Medicine.

"This bodes well for further study of semaglutide and is supported further by marked improvements in weight, glycemic control, and lipid profile," commented the study's senior author Philip N. Newsome, PhD, FRCPE, of the University of Birmingham (England), in an interview.

The highest daily dose (0.4 mg) of the glucagonlike peptide-1 (GLP-1) receptor agonist, semaglutide, which is approved for the treatment of type 2 diabetes, led to levels of NASH resolution "which are higher than any previously demonstrated," noted Dr. Newsome. "This was also accompanied by improvement in noninvasive markers of liver fibrosis and also less fibrosis progression, compared to placebo."

The multicenter study, conducted at 143 sites in 16 countries, included 320 patients, aged 18-75 years, with or without type 2 diabetes, who had histologic evidence of NASH and stage 1-3 liver fibrosis.

They were randomized in a 3:3:3:1:1:1 ratio to receive once-daily subcutaneous semaglutide at a dose of 0.1, 0.2, or 0.4 mg, or placebo for 72 weeks.

The primary endpoint was resolution of NASH and no worsening of fibrosis, with a secondary endpoint being improvement of fibrosis by at least one stage without worsening of NASH.

The study found 40% of patients in the 0.1-mg semaglutide group, 36% in the 0.2-mg group, and 59% in the 0.4-mg group achieved NASH resolution with no worsening of fibrosis, compared with 17% of the placebo group (odds ratio, 6.87; $P < .001$ for the highest semaglutide dose). However, the treatment did not lead to significant between-group differences in the secondary endpoint, which occurred in 43% of patients on the highest semaglutide dose compared to 33% in the placebo group (OR, 1.42; $P = .48$).

Treatment with semaglutide also resulted in dose-dependent reductions in body weight, as well as in glycated hemoglobin levels. Body weight was reduced by a mean of 5% in the 0.1-mg semaglutide group, followed by mean reductions of 9% and 13% in the 0.2-mg and 0.4-mg groups, respectively. This compared to a mean reduction of 1% in the placebo group.


Dr. Zetterman

Similarly, glycated hemoglobin levels among patients with type 2 diabetes dropped by 0.63, 1.07, and 1.15 percentage points in the 0.1-mg, 0.2-mg, and 0.4-mg semaglutide groups, respectively, compared with a drop of 0.01 percentage point in the placebo group.

"The fact that the percentage of patients who had an improvement in fibrosis stage was not significantly higher with semaglutide than with placebo – despite a greater benefit with respect to NASH resolution and dose-dependent weight loss – was unexpected, given that previous studies have suggested that resolution of NASH and improvements in activity scores for the components of nonalcoholic fatty liver disease are associated with regression of fibrosis," wrote the authors. "However, the temporal association among NASH resolution, weight loss, and improvement in fibrosis stage is not fully understood. It is possible that the current trial was not of sufficient duration for improvements in fibrosis stage to become apparent."

The authors also noted that the safety profile of semaglutide was "consistent with that observed in patients with type 2 diabetes in other trials and with the known effects of GLP-1 receptor agonists," with gastrointestinal disorders being the most commonly reported.

Nausea, constipation, and vomiting were reported more often in the 0.4-mg semaglutide group than in the placebo group (nausea, 42% vs. 11%; constipation, 22% vs. 12%; and vomiting, 15% vs. 2%).

The overall incidence of benign, malignant, or unspecified neoplasms was 15% in the treatment groups versus 8% in the placebo group.

Rowen K. Zetterman, MD, who was not involved with the study, noted that "treatment of NASH is currently limited, and no therapies have yet been approved by the Food and Drug Administration."

The findings are "important but not yet exciting," added Dr. Zetterman, who is professor emeritus of internal medicine and associate vice chancellor for strategic planning for the University of Nebraska Medical Center, Omaha.

"Though reversal of liver fibrosis was not noted, the resolution of hepatic inflammation and liver cell injury by semaglutide suggests it may be slowing disease progression," said Dr. Zetterman. This "warrants additional studies where longer treatment with semaglutide may prove reversal of fibrosis and/or prevention of progression to cirrhosis."

The study was sponsored by Novo Nordisk. Dr. Newsome reported disclosures related to Novo Nordisk during the conduct of the study, and to Boehringer Ingelheim, Bristol-Myers Squibb, Echosens, Gilead, Pfizer, Pharmaxis, and Poxel. Several of the other study authors reported receiving fees and grants from various pharmaceutical companies, including Novo Nordisk One author reported pending patents for the use of semaglutide. Dr. Zetterman had no relevant disclosures.

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SOURCE: Newsome PN et al. N Engl J Med. 2020 Nov 13. doi: 10.1056/NEJMoa2028395.

GLIMMER of hope for itch in primary biliary cholangitis

BY EMILY WILLINGHAM

Patients with primary biliary cholangitis (PBC) experienced rapid improvements in itch and quality of life after treatment with linerixibat in a randomized, placebo-controlled trial of the safety, efficacy, and tolerability of the small-molecule drug.

Moderate to severe pruritus "affects patients' quality of life and is a huge burden for them," said investigator Cynthia Levy, MD, AGAF from the University of Miami Health System.

With a twice-daily mid-range dose of the drug for 12 weeks, patients with moderate to severe itch reported significantly less itch and better social and emotional quality of life, Dr. Levy reported at the Liver Meeting, where she presented findings from the phase 2 GLIMMER trial.

After a single-blind 4-week placebo run-in period for patients with itch scores of at least 4 on a 10-point rating scale, those with itch scores of at least 3 were then randomly assigned to one of five treatment regimens – once-daily linerixibat at doses of 20 mg, 90 mg, or 180 mg, or twice-daily doses of 40 mg or 90 mg – or to placebo.

After 12 weeks of treatment, all 147 participants once again received placebo for 4 weeks. During the trial, participants recorded itch levels twice daily. The worst of these daily scores was averaged every 7 days to determine the mean worst daily itch.

The primary study endpoint was the change in worst daily itch from baseline after 12 weeks of treatment. Participants whose self-rated itch improved by 2 points on the 10-point scale were considered to have had a response to the drug.

Participants also completed the PBC-40, an instrument to measure quality of life in patients with PBC, answering questions about itch and social and emotional status.

Reductions in worst daily itch from baseline to 12 weeks were steepest in the 40-mg twice-daily group, at 2.86 points, and in the 90-mg twice-daily group, at 2.25 points. In the placebo group, the mean decrease was 1.73 points.

During the subsequent 4 weeks of placebo, after treatment ended, the itch relief faded in all groups.

Scores on the PBC-40 itch domain improved significantly in every group, including placebo. However, only those in the twice-daily 40-mg group saw significant improvements on the social ($P = .0016$) and emotional ($P = .0025$) domains.

Linerixibat is an ileal sodium-dependent bile acid transporter inhibitor, so the gut has to deal with the excess bile acid fallout, but the diarrhea is likely manageable with antidiarrheals, said Dr. Levy.

Dr. Levy disclosed support from GlaxoSmithKline.
A version of this article originally appeared on Medscape.com.

Black patients found less likely to undergo eradication testing after *H. pylori* treatment

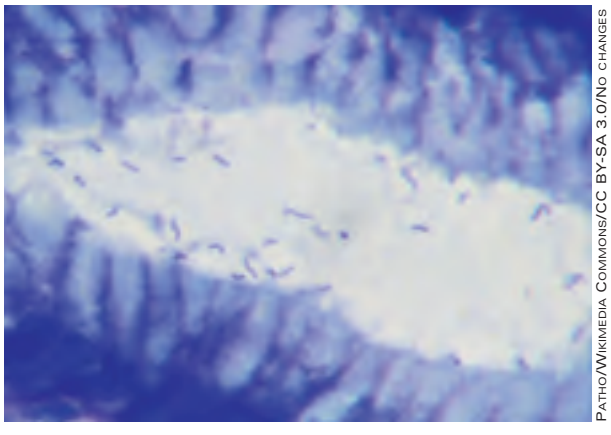
BY WILL PASS
MDedge News

Black patients may be significantly less likely to receive eradication testing after treatment for *Helicobacter pylori* infection than patients of other races/ethnic groups, based on a retrospective analysis of more than 1,700 individuals.

This disparity may exacerbate the already increased burden of *H. pylori* infection and gastric cancer among Black individuals, according to principal author David A. Leiman, MD, MSHP, of Duke University Medical Center in Durham, N.C.

"*H. pylori* infection disproportionately affects racial/ethnic minorities and those of lower socioeconomic status," Dr. Leiman, coauthor Julius Wilder, MD, PhD, of Duke University, and colleagues wrote in their abstract presented at the annual meeting of the American College of Gastroenterology. "ACG guidelines recommend treatment for *H. pylori* infection followed by confirmation of cure. Adherence to these recommendations varies and its impact on practice patterns is unclear. This study characterizes the management of *H. pylori* infection and predictors of guideline adherence."

The investigators analyzed electronic medical records from 1,711 patients diagnosed with *H. pylori* infection through the Duke University Health System between June 2016 and June 2018, most often (71%) via serum antibody test. Approximately two-thirds of those diagnosed were non-White (66%) and female (63%). Out of 1,711 patients, 622 (36%) underwent eradication testing, of whom 559 (90%) were cured.



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Despite publication of the ACG *H. pylori* guideline midway through the study (February 2017), testing rates dropped significantly from 43.1% in 2016 to 35.9% in 2017, and finally 25.5% in 2018 ($P < .0001$).

"These findings are consistent with other work that has shown low rates of testing to confirm cure in patients treated for *H. pylori*," Dr. Leiman said. "There remains a disappointingly low number of patients who are tested for cure."

Across the entire study period, patients were significantly more likely to undergo eradication testing if they were treated in the gastroenterology department (52.4%), compared with rates ranging from 33% to 34.6% for internal medicine, family medicine, and other departments ($P < .001$).

Across all departments, Black patients underwent eradication testing significantly less often than patients of other races/ethnicities, at a rate of 30.5% versus 32.2% for White patients, 35.1% for Asian patients, and 36.7% for patients who were of other backgrounds ($P < .001$). Compared with White patients, Black patients were 38% less likely to undergo eradication testing (odds ratio, 0.62; 95% confidence interval, 0.48-0.79).

Dr. Leiman noted that these findings contrast with a study by Shria Kumar, MD, and colleagues from earlier this year, which found no racial disparity in eradication testing within a Veterans Health Affairs cohort.

"Black patients are significantly less likely to undergo testing for eradication than [patients of other races/ethnicities]," Dr. Leiman said. "More work is needed to understand the mechanisms driving this disparity." He suggested a number of possible

Continued on page 30

Address disparities in care

Minorities *from page 1*

known to worsen outcomes. Compared with Whites, for example, Black patients with Crohn's disease have higher rates of stricture and penetrating lesions and are at greater risk for postsurgical complications and death, even after potential confounders such as age, sex, smoking status, time to operation, and obesity are controlled for. To help close these gaps, Dr. Barnes and his associates recommended enhanced recovery after surgery (ERAS) protocols, which "streamline [the] multidisciplinary management of patients with IBD before surgery, incorporating evidence-based practices focused on nutrition, prevention of postoperative ileus, and use of nonopioid analgesia and goal-directed fluid therapy."

Similar approaches also might improve nonsurgical outcomes in minorities with IBD, the experts said. In the Sinai-Helmsley Alliance for Research Excellence (SHARE) study, Black patients had more complicated IBD at baseline but similar clinical outcomes and patterns of medication use as Whites when they were treated at academic IBD centers. In other studies, race and ethnicity did not affect patterns of medication use, surgery, or surgical outcomes if patients had similar access to care. Such findings "indicate that when patients of minority races and ethnicities have access to appropriate specialty care and IBD-related therapy, many previously identified disparities are resolved or reduced," the experts said.

However, race and ethnicity do affect some aspects of IBD disease activity, genetics, and treatment safety and efficacy. Since White patients have made up the vast majority of research participants, studies of racial and ethnic minorities are needed to improve their IBD diagnosis, prevention, and treatment. Such research is particularly vital because IBD incidence is rising three times faster in racial and ethnic minorities than Whites, said Aline Charabaty, MD, AGAF, clinical director of the gastroenterology division at Johns Hopkins University in Baltimore, and director of the IBD Center at Sibley Memorial Hospital in Washington.

She explained that, when immigrants from countries where IBD is rare adopt the United States' sedentary lifestyle and Western diet (low in fruits and vegetables; high in proinflammatory saturated fats, sugars, and processed foods), their gut microbiome shifts and their IBD risk increases markedly. Studies in other countries have produced similar findings, said Dr. Charabaty, who did not help write the review article.

She also noted that patients from communities with a historically low prevalence of IBD may not understand its chronicity or the need for long-term treatment. However, treatment adherence is a common issue for patients of all backgrounds with IBD, she said. "What is unique is barriers to continuity of care – not being able to get to the treatment center, not being able to afford treatment or take time off work if you live paycheck to paycheck, not being able to pay someone to care for your kids while you see the doctor."

Other potential barriers to seeking IBD treatment include cultural taboos against discussing lower GI symptoms or concerns that chronic disease will harm marriage prospects, Dr. Charabaty said. Such challenges only heighten the need to ascertain IBD symptoms: "Studies show that minorities have less follow-up care and their symptoms tend to be minimized. There is a lot of unconscious bias among providers that factors into this. The barriers are multiple, and it is important to define them and find strategies to overcome them at the level of the patient, the clinician, and the health system."

AGA Resource
AGA applauds researchers who are working to raise our awareness of health disparities in digestive diseases. AGA is committed to addressing this important societal issue head on. Learn more about AGA's commitment through the AGA Equity Project.

The Crohn's and Colitis Foundation supported the work. Dr. Barnes disclosed ties to AbbVie, Gilead, Takeda, and Target Pharmasolutions. Two coauthors also disclosed relevant ties to pharmaceutical companies. Dr. Charabaty disclosed relationships with AbbVie, Pfizer, Janssen, Takeda, and UCB.

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SOURCE: Barnes EL et al. Gastroenterology. 2020 Oct 20. doi: 10.1053/j.gastro.2020.08.064.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Tool predicted vedolizumab nonresponse in practice

BY AMY KARON
MDedge News

Among patients with ulcerative colitis who were treated in routine practice, a point-based clinical scoring tool predicted nonresponse to vedolizumab therapy, according to study findings published online in Clinical Gastroenterology and Hepatology.

A cutoff of 26 points or less was 93% sensitive (95% confidence interval, 79%-98%) for identifying patients who did not reach corticosteroid-free remission during 26 weeks of treatment and was 88% sensitive (95% CI, 83%-92%) for identifying patients who required colectomy, reported Parambir S. Dulai, MBBS, of the University of California, San Diego, and his associates. The tool was less reliable for predicting response to tumor necrosis factor (TNF) antagonists, indicating that it is treatment specific, they noted.

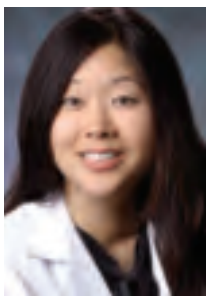
Vedolizumab, an alpha-4-beta-7 anti-integrin that restricts the migration of proinflammatory lymphocytes to the gut, can induce corticosteroid-free remissions and mucosal healing in patients with ulcerative colitis. In clinical practice, 22-week rates of clinical response and remission were approximately 51% and 30%, respectively, in a recent study. Noting the lack of real-world data on predictors of response, the researchers modeled data from 620 patients who received induction and maintenance vedolizumab during the blinded phase 3 GEMINI 1 trial. They used this model to create the clinical scoring tool, which they validated in a cohort of 322 patients with ulcerative colitis who had received vedolizumab (199 patients) or TNF antagonists (123 patients) in routine practice during the Vedolizumab for Health

Continued on following page

PERSPECTIVE

Tool includes variables found in clinical record

The management of moderate to severe ulcerative colitis has become more complex because of the greater number of Food and Drug Administration–approved biologic and small-molecule agents currently available. With more options, practitioners are faced with the challenge of choosing the most appropriate agent based on disease- and patient-specific risk factors. The goals of early intervention are to achieve steroid-free remission with mucosal healing and the associated improvements in quality of life, reduced colectomy, and lower colon cancer risks.


Dr. Ha

Rather than randomly choosing among treatment options, this study by Dulai and colleagues offers a clinical prediction tool that helps clarify which option, vedolizumab versus anti–tumor necrosis factor (TNF), would be more likely, as a first-line agent, to achieve the desired steroid-free clinical remission outcome. In this tool, they included known high-risk factors for colectomy, severe endoscopic activity, and hypoalbuminemia with other variables, such as prior anti-TNF exposure and disease duration. Importantly, this information is readily accessible in a routine clinical record and, therefore, requires no additional tests or studies to calculate.

The value in these types of tools is to assist in early biologic decision-making by providing a numeric cutoff that can be used to recommend one agent versus the other. Another noted feature of this tool is the potential to identify which patients may benefit from dose optimization because lower or intermediate scores tended to respond to dose escalation in vedolizumab partial responders. However, because this tool predominantly assists with the choice of anti-TNF vs. vedolizumab, one may not be able to extrapolate these results to ustekinumab and tofacitinib positioning in ulcerative colitis. Further studies are needed to determine if these variables similarly affect steroid-free remission for these agents.

Christina Ha, MD, FACG, AGAF, is an associate professor of medicine, Inflammatory Bowel Disease Center, Cedars-Sinai, Los Angeles. She is on the advisory board of AbbVie, Janssen, Takeda, Pfizer, Salix, and InDex Pharmaceuticals; has received grant support from Pfizer; and has received research support from Pfizer and Lilly.

Continued from page 28

contributing factors, including provider knowledge gaps, fragmented care, and social determinants of health.

"It is clear that a greater emphasis on characterizing and addressing the social determinants of health, including poverty, education, and location, are needed," Dr. Leiman said. "Although health systems are not solely responsible for the known and ongoing observations of disparities in care, interventions must be identified and implemented to mitigate these issues." Such interventions would likely require broad participation, he said, including policy makers, health systems, and individual practitioners.

"We plan to perform a prospective mixed methods study to contextualize which social determinants are associated with a decreased likelihood of receiving appropriate eradication testing by exploring barriers at patient, practitioner, and health-system levels," Dr. Leiman said. "Ultimately, we aim to leverage these findings to develop an evidence-based intervention to circumnavigate those identified barriers, thereby eliminating the observed disparities in *H. pylori* care."

According to Gregory L. Hall, MD, of Northeast Ohio Medical University, Rootstown, and Case Western Reserve University, Cleveland, and co-director of the Partnership for Urban Health Research, Atlanta, the higher rate of *H. pylori* infection in Black individuals may stem partly from genetic factors. "Studies have shown that African Americans with a higher proportion of African ancestry have higher rates of *H. pylori*, suggesting a genetic component to this increased risk," he said.

Still, Dr. Hall, who is the author of the book Patient-Centered Clinical Care for African Americans, went on to emphasize appropriate *H. pylori* management and recognition of racial disparities in medicine.

"The ability to test for, treat, and confirm eradication of *H. pylori* infections represents a great opportunity to improve quality of life through decreased gastritis, gastric ulcers, and gastric cancer," he said. "[The present findings] show yet another disparity in our clinical care of African Americans that needs increased awareness among providers to these communities."

AGA Resource
AGA applauds researchers who are working to raise our awareness of health disparities in digestive diseases. AGA is committed to addressing this important societal issue head on. Learn more about AGA's commitment through the AGA Equity Project.

Rotonya Carr, MD, of the Hospital of the University of Pennsylvania, Philadelphia, and lead author of a recent publication addressing racism and health disparities in gastroenterology, said the findings of the present study add weight to a known equity gap. Dr. Carr is also an advisory member for the American Gastroenterological Association Equity Project.

"These data are concerning in view of the twofold higher prevalence of *H. pylori* seropositivity and twofold higher incidence of gastric cancer in Black patients, compared with White patients," Dr. Carr said. "These and other data support a comprehensive approach to reduce GI disparities that includes targeted education of both GI specialists and referring providers."

"Clinicians should consider *H. pylori* therapy an episode of care that spans diagnosis, treatment, and confirmation of cure," Dr. Leiman said. "Closing the loop in that episode by ensuring eradication is vital to conforming with best practices, and to reduce patients' long-term risks."

The investigators disclosed relationships with Exact Sciences, Guardant Health, and Phathom Pharmaceuticals. Dr. Hall and Dr. Carr reported no relevant conflicts of interest.

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SOURCE: Reichstein J et al. ACG 2020, Abstract S1332.

Continued from previous page

Outcomes in Inflammatory Bowel Diseases (VICTORY) study.

In the final multivariable model, predictors of steroid-free remission were TNF-antagonist naivety, at least a 2-year history of ulcerative colitis, moderate rather than severe endoscopy activity, and baseline albumin concentration. The resulting clinical scoring tool included these four variables and multiplied them by factors ranging from 0.0647 (for baseline albumin concentration) to 0.2820 (for no prior TNF-antagonist exposure). In the validation cohort, patients were categorized as "high probability" (of response) if they scored 33 points or more on the tool and "low probability" if they scored 26 points or fewer. Rates of corticosteroid-free remissions were substantially different at 32% and 12%, respectively. The tool also predicted responses to vedolizumab more accurately than it predicted responses to TNF antagonists, indicating that it was drug specific.

In the validation cohort, 46% (10 of 22) of low- or intermediate-probability patients showed least a 50% decrease in symptom activity after their vedolizumab infusion interval was shortened to address an insufficient initial response. "However, none of the high-probability patients showed a clinical response to interval shortening," probably because they had higher vedolizumab trough concentrations to begin with, the researchers said. They called for prospective validation of this finding, "ideally in a randomized, controlled trial setting."

The derivation and validation cohorts differed in several important ways. The validation cohort included significantly more females, smokers, patients with moderate endoscopic disease, and patients who had failed prior TNF-antagonist therapy. These patients also had a significantly higher median albumin level and a longer history of disease. "The lower bound of the confidence interval for the [model's] performance reached 0.5, suggesting that model discrimination may not be ideal," the researchers said. "Further validation will therefore be needed to understand external validity on additional cohorts."

An American Gastroenterological Association Research Scholar Award supported the work. Dr. Dulai reported holding a provisional patent for the prediction model and consulting relationships and other ties to Takeda, Janssen, Pfizer, and AbbVie. His coinvestigators reported ties to numerous pharmaceutical companies.

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SOURCE: Dulai PS et al. Clin Gastroenterol Hepatol. 2020 Feb 13. doi: 10.1016/j.cgh.2020.02.010.

Life expectancy gap persists for IBD patients

BY HEIDI SPLETE
MDedge News

Life expectancy increased for adults with inflammatory bowel disease (IBD) over recent decades, but still remained lower than that for individuals without IBD, according to data from a retrospective cohort study using Canadian health databases.

M. Ellen Kuenzig, PhD, of the Children's Hospital of Eastern Ontario and colleagues said, "Most studies evaluating mortality were conducted before the biologic era, and none evaluated life expectancy or health-adjusted life expectancy."

In a study published in the Canadian Medical Association Journal, the researchers used Canadian databases to identify a study population of 32,818 people with IBD matched to 163,284 people without IBD in 1996 that increased to 83,672 people with IBD matched to 418,360 people without IBD in 2011.

Overall, life expectancy for IBD patients increased from 75.5 years to 78.4 years for women and from 72.2 years to 75.5 years for men between 1996 and 2011. However, health-adjusted life expectancy, defined as the number of years a person is expected to live in full health, decreased by 3.9 years for men with IBD between 1996 and 2008, but did not change significantly for women with IBD.

The study was supported by the Institute for Clinical Evaluative Services (Canada). Lead author Dr. Kuenzig received a Post-Doctoral Fellowship Award from the Canadian Institutes of Health Research, Canadian Association of Gastroenterology, and Crohn's and Colitis Canada. The researchers had no conflicts.

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SOURCE: Kuenzig ME et al. CMAJ. 2020 Nov 9. doi: 10.1503/cmaj.190976.

‘Disordered eating’ drops after bariatric surgery in teens

BY MARLENE BUSKO

Among young patients with severe obesity and disordered eating behaviors – continuous eating, overeating, and binge eating – those who had bariatric surgery saw an improvement in the eating behaviors.

Kristina M. Decker, PhD, a postdoctoral fellow at Cincinnati Children’s Hospital Medical Center, presented these findings during the virtual ObesityWeek 2020.

Dr. Decker and associates examined rates of disordered eating in more than 200 adolescents (aged 13-18 years) who were severely obese, of whom 141 underwent bariatric surgery and the remainder did not.

At baseline (presurgery), the teens in both groups had rates of disordered eating ranging from 11% to 50%, with higher rates in those who went on to have bariatric surgery.

Six years later, rates of disordered eating were much lower in those who had bariatric surgery.

The data nevertheless “underscore that young adults with persistent severe obesity are at high risk for poor health and well-being,” Dr. Decker said in an interview.

“This means disordered eating behaviors should be closely monitored” in all such patients, both those who undergo surgery and those who don’t, she stressed.

Robust findings are due to long follow-up and controls

The findings are not unexpected, based on adult bariatric literature, but are “novel because of the age of the patients,” senior author Margaret H. Zeller, PhD, Cincinnati Children’s Hospital Medical Center and professor at the University of Cincinnati, added.

In a comment, psychologist Kajsa Järvholm, PhD, of the Childhood Obesity Unit at Skåne University Hospital, Malmö, Sweden, who has published related work, said that this is “a needed study.”

Notably, it had “long-term follow-up and a control group,” and it “confirms that adolescents are in better control of their eating after surgery.”

However, an important additional takeaway for clinicians is that “disordered eating is associated with other mental health problems and self-worth. Clinicians treating obesity must address problems related to eating disorders to improve outcomes and well-being,” she stressed.

Effects of bariatric surgery impact on overeating, binge eating, in teens questioned

“For teens with severe obesity, metabolic and bariatric surgery is the most effective treatment for improved cardiometabolic functioning, weight loss, and improved quality of life,” Dr. Decker stressed.

However, an important additional takeaway for clinicians is that ‘disordered eating is associated with other mental health problems and self-worth.’

However, pre- and postsurgical disordered eating behaviors have been associated with a lower percentage change in body mass index, although this has not been well studied.

To investigate how disordered eating is affected by bariatric surgery in adolescents with severe obesity, researchers used data from TeenLABS, which enrolled 242 participants aged 19 years and under who mainly underwent Roux-en-Y gastric bypass (67%) or sleeve gastrectomy (28%) from 2007 to 2012 at five adolescent bariatric surgery centers.

The current analysis examined data from 141 participants in TeenLABS who underwent bariatric surgery at a mean age of 16.8 years. Mean BMI was 51.5, most were girls (80%), and they had diverse race/ethnicity (66% were White).

Researchers also identified a control group of 83 adolescents of a similar age and gender who had diverse race/ethnicity (54% White) and a mean BMI of 46.9.

At year 6, data were available for 123 young adults in the surgery group (who by then had a mean BMI of 39.7) and 63 young adults in the nonsurgery group (who had a mean BMI of 52.6).

At baseline and year 6, participants replied to questionnaires that identified three eating disorders: continuous eating (eating in an unplanned and repetitious way between meals and snacks), objective overeating (eating a “large” amount of food without loss of control), and objective binge eating (eating a “large” amount of food with loss of control).

At baseline, rates of continuous eating, overeating, and binge eating were higher in the surgical group (50%, 40%, and 30%, respectively) than the nonsurgical group (40%, 22%, and 11%, respectively).

Six years later, when participants were aged 19-24 years, rates of continuous eating, overeating, and binge eating had declined in the surgical group (to 17%, 5%, and 1%, respectively). In the nonsurgical group, only continuous eating and overeating declined (to 24% and 7%, respectively), and binge eating increased slightly (to 13%).

Disordered eating associated with low self-worth, anxiety, and depression

In young adulthood in both groups, disordered eating was associated with lower self-worth. In the surgical group, it was also associated with lower weight-related quality of life, and in the nonsurgical group, it was also associated with anxiety and/or depression.

“The current findings cannot tell us whether disordered eating is a direct result or caused by anxiety, depression, low self-worth, or poor quality of life,” Dr. Decker said.

“These findings do give us insight about what other areas of clinical concern might present together [in] young adults (e.g., disordered eating, low self-esteem).”

Bariatric surgery affects the amount of food people can eat at one time, she noted in reply to a question from the audience. If people eat too much at a time they can experience vomiting, dumping syndrome (where certain food is “dumped” into the small intestine without being digested, causing nausea and vomiting), and plugging (a sense of food becoming stuck).

The home environment and transition to adulthood might impact disordered eating in young adults, she said in reply to another question, but these issues were not examined in this study.

There are no relevant financial disclosures for Dr. Decker or Dr. Järvholm.

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

Antibody promising in eosinophilic gastritis/duodenitis

BY JIM KLING
MDedge News

In a phase 2 trial in eosinophilic gastritis and duodenitis, an anti–Siglec-8 antibody greatly reduced numbers of eosinophilic cells and led to improved symptoms. The sponsoring company, Alkalos, is currently conducting a phase 3 trial in eosinophilic gastritis or duodenitis.

The news is welcome to clinicians who treat these rare conditions, since the only current treatment is steroids. This is particularly challenging because most patients with these conditions present in their 30s and 40s, according to Carol Semrad, MD, professor of medicine at the University of Chicago, who was asked to comment on the study. She noted that the study's results were impressive, but it will take a phase 3 trial to convince. It's also unclear if the clinical benefit tracks with the impressive reduction seen in eosinophil count. "There's somewhat of a disconnect between symptom reduction and reduction of the eosinophil counts. Sometimes just blocking the inflammation [isn't enough]. Maybe there is other damage to the bowel."

The research, led by Evan S. Dellon, MD, MPH, of the University of North Carolina at Chapel Hill, and Ikuo Hirano, MD, of Northwestern University, Chicago, appeared in the New England Journal of Medicine.

The antibody (lirentelimab) targets sialic acid–binding immunoglobulin-like lectin 8 (Siglec-8), which is an inhibitory receptor found on mature eosinophils and mast cells, and expressed at low levels on basophils. The antibody reduces eosinophil cells through natural killer cell–mediated cellular cytotoxicity and apoptosis, and other antibodies against the same target have been shown to inhibit mast cell activation.

At 22 sites across the United States, researchers randomized 65 adults with active, uncontrolled eosinophilic gastritis or duodenitis, or both, to receive four monthly low- (0.3, 1, 1, and 1 mg/kg) or high-dose lirentelimab (0.3, 1, 3, and 3 mg/kg), or placebo. A total of 10 patients had gastritis, 25 had duodenitis, and 30 had both.

In the intention-to-treat analysis, there was a mean 86% reduction in eosinophil count in patients in the treatment groups, compared with a 9% increase in controls ($P < .001$). In the per-protocol analysis, there was a 95% reduction vs. a 10% increase ($P < .001$). Of treated patients, 95% had a gastrointestinal eosinophil count of 6 or fewer per high-powered field, compared with 0% with placebo.

In the intention-to-treat analysis, 63% of treated patients had a treatment response, defined as at least a 30% reduction in total symptom score and at least a 75% reduction in eosinophil count. About 5% of patients had a response in the placebo group ($P < .001$). The mean percentage change in total symptom score was –48 versus –22 in the placebo group ($P = .004$). In the per-protocol analysis, 69% responded versus 5% ($P < .001$). The mean percentage change in total symptom score was –53 versus –24 ($P = .001$).

About 60% in the treatment group had an infusion-related reaction versus 23% who received placebo; 93% of reactions were mild to moderate. Serious adverse events occurred in 9% of the treatment group and 14% of patients on placebo: 86% of patients in the treatment group experienced transient lymphopenia, as did 47% of the placebo group, but there were no clinical consequences.

The study was funded by Alkalos. Dr. Semrad has no relevant financial disclosures.

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SOURCE: Dellon ES et al. N Engl J Med. 2020 Oct 22. doi: 10.1056/NEJMoa2012047.

Value-based care stunted from delayed Stark, anti-kickback reform

BY JOSEPH LOSURDO, MD, AGAF

Anti-kickback statutes (AKSs) were originally enacted in 1931 to stop Great Depression–era employers from circumventing wage provisions in federal contracts. Since its enactment, AKSs' main focus has changed and is currently aimed at the health care industry. In addition to AKSs, Stark laws were enacted over 30 years ago to address physician self-referral of Medicare patients. Both laws comprise the government's main tools for fighting fraud, waste, and abuse. However, AKSs and Stark laws have not been updated to keep pace with changes in how medical practices do business and care for patients.

Dr. Losurdo

Over the years, additional interpretation and clarification has been issued by the Department of Health & Human Services and the Office of Inspector General. In HHS's June 1, 2012, Advisory Opinion No. 12-06, there is guidance regarding legality of anesthesia services providers' contract with physician-owned professional corporations or limited liability companies to provide anesthesia services. Specifically, it focused on the "company model" where owners of an ambulatory surgery center (ASC) create a separate company for anesthesia services which directly contracts with anesthesia providers and charges for the anesthesia services while the ASC charges for facility fees.

Anyone with specific questions may request an advisory opinion from the OIG about the application of OIG's fraud and abuse authorities and existing or proposed business arrangements. An OIG advisory opinion is legally binding on the requesting party and HHS, but not on any other governmental department or agency. While advisory opinions are specific to the entity that requested it and specifically states, "This opinion may not be relied on by any persons other than [name redacted], the requestor of this opinion. ..."

It captured the attention of the medical community. The AGA has argued that this opinion should not be interpreted to mean that all company model frameworks necessarily violate the AKSs and the OIG's Advisor Opinions FAQ states no person or entity can rely on an advisory opinion issued to someone else. However, Advisory Opinion No. 12-06 has been cited in AKS investigations ever since.

When Congress passed the Medicare Access and CHIP Reauthorization Act (MACRA) in 2015, it changed how physicians would be paid under Medicare and sought to transition physicians to a more value-based payment system. Physicians were incentivized to develop physician-driven payment models to improve efficiency and patient outcomes. However, existing Stark self-referral laws prohibit physicians from referring patients to an entity in which they have a financial interest. As a result, physician practices are unable to participate in many advanced alternative payment models.

S. 2051/H.R. 4206, the Medicare Care Coordination Improvement Act, would allow innovative payment models developed by gastroenterologists to be implemented in the Medicare program. Unfortunately, this legislation has received little traction in Congress.

Stark laws, which have not been updated since their enactment 30 years ago, pose barriers to care coordination since they prohibit payment arrangements that consider volume or value of referrals or other business generated by the parties. These prohibitions stifle innovations in delivering care by inhibiting practices from incentivizing their physicians to deliver patient care more efficiently, because the practices cannot use resources from designated health services in rewarding or penalizing adherence to new clinical care pathways.

Congress recognized that the Stark law was a barrier to new health care delivery models. Congress, therefore, authorized the HHS Secretary to waive Stark self-referral and anti-kickback laws for accountable care organizations (ACOs). This waiver was not extended to physician-driven alternative payment models (APMs), that also need these exceptions to drive innovation in health care and to implement MACRA law as Congress intended.

AGA and the physician community have long sought to update Stark self-referral and AKSs. Last year, Centers for Medicare & Medicaid Services proposed exceptions directed at value-based arrangements that would have allowed providers to participate in value-based arrangements while still protecting the Medicare program from potential abuses. Many of the changes that CMS proposed would have allowed physician practices to engage in value-based arrangements that would improve patient care and AGA provided comments on both the Stark and AKS proposed rules. However, CMS has not yet issued the final rules and has indicated that they will not issue a final rule on Stark which is a lost opportunity to improve health care delivery.

On the legislative front, AGA supports S. 2051/H.R. 4206, the Medicare Care Coordination Improvement Act, which would provide CMS with the regulatory authority to create exceptions under the Stark law for APMs and to remove barriers in the current law to the development and operation of such arrangements. The legislation would allow CMS to waive the Stark laws for physicians seeking to develop and operate APMs similar to what Congress allowed for ACOs. The legislation would allow innovative payment models developed by gastroenterologists to be implemented in the Medicare program. Unfortunately, this legislation has received little traction in Congress.

Until meaningful regulatory and legislative reform updating both Stark and AKSs occur, innovative payment models must wait and gastroenterologists and other providers will remain vulnerable to these outdated regulations. You can help us advance these issues by sharing how they impact your practice. Tell us what types of value-based arrangements you would participate in and how would they improve patient care and efficacy at Lnarramore@gastro.org.

Dr. Losurdo is the AGA's Alternate Advisor to the American Medical Association's CPT Editorial Panel, a member of the AGA Practice Management and Economics Committee's Coverage and Reimbursement Subcommittee and is a partner with Elgin Gastro Endoscopy, who owns an ASC, and Managing Partner and Medical Director of Illinois Gastroenterology Group/GI Alliance, Elgin, Ill.

Obesity increases pneumonia risk, mutation ups contagiousness

BY LUCAS FRANKI
MDedge News

After age and male sex, obesity biggest risk for COVID-19 pneumonia

In a large international study published in The Lancet and presented at ObesityWeek 2020, the likelihood of developing severe pneumonia and requiring mechanical ventilation increased in patients with obesity, independent of age, sex, diabetes, hypertension, dyslipidemia, and smoking.

For each 5-kg/m^2 increase in body mass index, there was a 27% increased risk of mechanical ventilation in the overall cohort and a 65% increased risk in women younger than 50 years after other factors were adjusted for.

However, the study also found an "obesity paradox" for mortality after admission to the ICU, where patients with a BMI of 25-39.9 had a lower risk of death than those with a BMI of less than 25, although patients with a BMI over 40 had the highest mortality rate.

Common mutation making SARS-CoV-2 more contagious

While there was a wide variety of SARS-CoV-2 strains early in the pandemic, 99.9% of circulating SARS-CoV-2 strains in the study feature the D614G mutation on the spike protein, which is associated with increased nasopharynx viral

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loads at diagnosis.

The mutation likely dominates because it increases the spike protein's ability to open cells for the virus to enter, but the mutation is not associated with worse clinical COVID-19 severity and will likely not interfere with the efficacy of any current treatment or vaccine in development.

"As bad as SARS-CoV-2 is, we may have dodged a bullet in terms of how quickly it mutates," said Ilya Finkelstein, PhD, of the Finkelstein Lab at the University of Texas, Austin, adding that the slower mutation rate will give researchers a greater chance to stay one step ahead.

VA joins Pentagon in recruiting volunteers for COVID-19 vaccine trials

According to officials from the Department of Veterans Affairs and Operation Warp Speed, the VA will recruit 8,000 volunteers for phase 3 clinical trials of at least four COVID-19 vaccine candidates at 20 U.S. federal medical facilities.

This announcement follows a September announcement by the Department of Defense that it has partnered with AstraZeneca to recruit volunteers at five of its medical facilities. Since active troops are essential to national security, and veterans are extremely vulnerable to COVID-19, both departments have a vested interest in supporting the development of safe, effective vaccines, said J. Stephen Morrison, senior vice president and director of global health policy at the Center for Strategic and International Studies, a bipartisan think tank in Washington.

COVID exposure risk outside of work increasing for clinicians

One-third of COVID-19 exposures among health care providers (HCPs) in Minnnesota are caused by family or community exposure, not patient care according to a study conducted by the Minnesota Department of Health. Nonwork exposures were more likely to lead to infection.

Between March and July 2020, researchers evaluated 21,406 cases of HCP exposure to confirmed COVID-19 cases.

"Since the time period covered in this report, we've seen a significant increase in the proportion of HCPs who have had higher-risk exposures outside of work due to household or social contacts," said lead author Ashley Fell, MD, MPH, from the Minnesota Department of Health.

AGA Resource

For the latest clinical guidance, education, research and physician resources about coronavirus, visit the AGA COVID-19 Resource Center at www.gastro.org/COVID.

The authors recognize that HCPs, like the rest of the community, are experiencing COVID fatigue and that facilities have to constantly be innovative and vigilant to help HCPs maintain rigorous safety precautions.

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

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