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Texas has the highest rate of hepatocellular carcinoma, but it's not evenly distributed across the state or its population.

Neighborhood factors linked to liver cancer disparities

BY MEGAN BROOKS

Factors operating at the community level may help explain disparities in rates of hepatocellular carcinoma (HCC) across Texas.

Researchers found that the risk for HCC is higher in neighborhoods characterized by minority populations, socioeconomic disadvantage, and blue-collar workers from specific industries.

However, these relationships are not uniform across the state, report researchers from Baylor College of Medicine, Houston.

"HCC is a serious health concern in Texas, and our foundational work is a step forward to better prevent this deadly disease," study investigator Hashem El-Serag, MD, PhD, AGAF, said in a news release.

The study was published online in Clinical Gastroenterology and Hepatology (2022 Aug 3. doi: 10.1016/j.cgh.2022.06.031).

HCC is the most common type of liver cancer in the United States, and Texas has the highest rate of HCC. Yet,

See **Neighborhood** · *page 28*

Monitoring UC with noninvasive ultrasound

Reliable alternative to endoscopy?

BY WILL PASS

MDedge News

Intestinal ultrasound (IUS) findings correlate strongly with endoscopy results in patients with ulcerative colitis (UC), with treatment responses detected as soon as 8 weeks after starting tofacitinib, a longitudinal prospective study has found.

IUS accurately detected improvements and remission across a variety of scoring methodologies, suggesting that it may be a cost-effective, noninvasive alternative to endoscopic monitoring, reported lead author Floris de Voogd, MD, of Amsterdam University Medical Centers, and colleagues.

"Endoscopy is generally considered as the gold standard for the diagnosis and follow-up of patients with UC," the investigators wrote in Gastroenterology (2022 Aug 24. doi: 10.1053/j.gastro.2022.08.038). "However, endoscopy is an invasive and costly modality and therefore less attractive to perform frequently during the disease course."

Whereas noninvasive fecal biomarkers are a more economical method of monitoring inflammation and treatment responses,

See **Ultrasound** · *page 21*

Single-donor fecal transplant trial for IBS shows lasting response

BY MARCIA FRELLICK

Fecal microbiota transplantation (FMT) resulted in sustained high response rates in patients with irritable bowel syndrome (IBS) and resulted in only mild side effects after 3 years, new data show.

Nearly three out of four people in a clinical trial experienced fewer symptoms and fatigue and a greater quality of life at both 2 years and 3 years after FMT in Norway. Those FMT-treated patients who relapsed subsequently responded to FMT upon retransplantation,

See **IBS** · *page 18*

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LOOK BACK

Passing the 'baton' with pride

BY JOHN I. ALLEN, MD, MBA, AGAF

I was honored to be the third Editor-in-Chief of GIHN, from 2016 through 2021. GIHN is the official newspaper of the American Gastroenterological Association and has the widest readership of any AGA publication and is one that readers told us they read cover to cover. As such, each EIC and their Board of Editors must ensure balanced content that holds the interest of a diverse readership. I was privileged to work with a talented editorial board who reviewed articles, attended leadership meetings, and offered terrific suggestions throughout our tenure. I treasured their support and friendship.


Dr. Allen

Within each of the 60 monthly issues, we sought to highlight science, practice operations, national trends, and opinions and reviews that would be most important to basic scientists, clinical researchers, and academic and community clinicians, primarily from the United States but also from a worldwide readership. I was given a 300-word section to create editorial comments on pertinent topics that were important to gastroenterologists. Having a background in both community and academic practice, I tried to bring a balanced perspective to areas that often seem worlds apart.

I was privileged to work with a talented editorial board. ... I treasured their support and friendship.

The period between 2016 and 2021 also was a time of political upheaval in this country – something we could not ignore. I attempted to write about current events in a balanced way that kept a focus on patients and AGA's core constituency. Not always an easy task. Sustainability of the Affordable Care Act was very much in question because of judicial and legislative challenges; had the ACA been overturned, our practices would be very different now.

In 2016, the first private equity–backed practice platform was created in south Florida. Little did we know how much that model would change community practice. Then, on Jan. 21, 2020, the first case of COVID 19 was diagnosed in Seattle (although earlier cases likely occurred). By March, many clinics and practices were closing, and we were altering our care delivery infrastructure in ways that would forever change practice. Trying to keep current with ever-changing science and policies was a challenge.

I will always treasure my time as EIC. I was happy (and proud) to pass this baton to Megan A. Adams MD, JD, MSc, my colleague and mentee at the University of Michigan. The partnership between AGA and Frontline Medical Communications has been successful for 15 years and will continue to be so. ■

Dr. Allen, now retired, was professor of medicine at the University of Michigan, Ann Arbor. He is secretary/treasurer for the American Gastroenterological Association, and declares no relevant conflicts of interest.

THEN AND NOW

Endoscopy

BY ZIAD F. GELLAD, MD, MPH, AGAF

In the second issue of GI & Hepatology News in February 2007, an article reviewed the disruptive forces to colonoscopy including CT colonography and the colon capsule. The article stated that "colonoscopy is still the preferred method, but the emerging technology could catch up in 3-5 years."


Dr. Gellad

While this prediction did not come to pass, the field of endoscopy has evolved in remarkable ways over the last 15 years. From the development of high-definition endoscopes to the transformation of interventional endoscopy to include "third space" procedures, previously unimaginable techniques have now become

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Inhibiting adenosine pathways may be key to CRC

BY JIM KLING
MDedge News

Research that could set the stage for future clinical trials explored the potential role of adenosine signaling in altering the immune microenvironment of colorectal cancer (CRC), according to a study appearing in Cellular and Molecular Gastroenterology and Hepatology (2022 Jul 15. doi: 10.1016/j.jcmgh.2022.07.005).

The study in human-derived cells and CRC mouse models suggests that addition of a CD73 inhibitor to the CDK4/6 inhibitor palbociclib may hold promise in the treatment of CRC because CD73 can produce extracellular adenosine. The results hold promise for future research since anticancer therapies often

Adenosine treatment led to changes in the expression levels of genes involved in the cell cycle, cell division, cell cycle phase transition, and DNA repair.

prompt increased expression of PD-L1, and CDK4/6-inhibitor monotherapy can fail because of accumulation of PD-L1 after such treatment.

Previous research has suggested that extracellular adenosine-mediated signaling can lead to accumulation of tumor-associated macrophages (TAMs) and an immunosuppressive tumor microenvironment. TAMs play an important role in the intestinal mucosal immune system in CRC, which mediates tumor-promoting metabolites in the intestine and inflammatory pathways that can lead to and progress CRC. TAMs are also linked to increases in extracellular enzymes like CD39 and CD73 as well as resistance to chemotherapy and anti-PD-1/PD-L1 therapy in CRC. Furthermore, they express PD-L1 and they promote other immunosuppressive molecules.

In normal tissues, CD73 produces adenosine to tamp down excessive immune responses (Curr Opin Pharmacol. 2020 Aug;53:66-76). Some tumors express CD73 or even induce expression in normal cells, leading to immunosuppression in the tumor microenvironment. Previous studies have shown that CD73 expression is a biomarker for poor outcomes in gastric, liver, pancreatic, and colorectal cancer, the authors of this study noted.

To better understand the impact of adenosine, the researchers exposed human macrophages derived from peripheral blood to adenosine, and then analyzed the results using flow cytometry and Western blot. They used RNA sequencing and proteomics to discern changes in the cells that resulted from the exposure.

Adenosine treatment led to changes in the expression levels of genes involved in the cell cycle, cell division, cell cycle phase transition, and DNA repair. The researchers emphasized that extracellular treatment with adenosine led to a reduction in expression of the cell cycle–related gene CCND1, which encodes cyclin D1. Among three genes in the cyclin D family tested, CCND1 was the only one affected by adenosine. Cyclin D1 protein levels also went down.

Cyclin D1 is a known actor in regulating the cell cycle and tumorigenesis, among other roles. Previous reports indicated that cyclin D1 participates in posttranslational regulation of PD-L1, and the current study suggests it plays a similar role in TAMs after exposure to adenosine in the tumor microenvironment. Myeloid cells high in cyclin D1 expression had low levels or even an absence of the immunosuppressive molecule CD39. "Taken together, cyclin D1 may be one of the major orchestrators that trigger the differentiation of pro-tumorigenic TAMs. Our findings suggest a novel immune checkpoint regulatory mechanism of extracellular adenosine signaling, which might be related to the cell cycle of macrophages," the authors wrote.

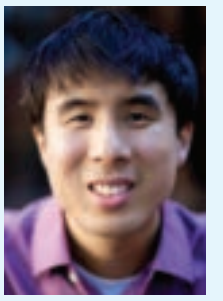
The researchers then introduced a short hairpin RNA directed against CCND1. This led to increases in PD-L1 protein levels. Simultaneous treatment with adenosine led to a slight increase in levels of the PD-L1 protein, which suggests that reduction of CCND1 levels is the primary cause of increased PD-L1, according to the authors.

The CD73 inhibitor AB680, currently in phase 1 clinical trials for castration-resistant prostate cancer and advanced pancreatic cancer and developed by Arcus Biosciences, led to reduced PD-L1 levels in both human and mouse macrophages, and AB680 combined with the CDK4/6 inhibitor palbociclib led to greater inhibition of tumor growth than palbociclib alone in CRC mouse models.

"Thus, the promising effects of CD73 inhibitors might breathe new life for those old drugs and provide potent therapeutic strategies. Given that the therapeutic effects of PD-1/PD-L1 immunotherapy have not been conclusively demonstrated in patients with CRC, our observations should support clinical trials of new combinational therapies for CRC," the authors wrote.

The authors disclose no conflicts. ■

Although cancer immunotherapy has emerged as a powerful treatment modality, its application to colorectal cancer (CRC) is presently restricted to the minor subclass of tumors exhibiting deficient mismatch repair and high microsatellite instability. Programmed death 1 and its ligand, PD-L1, are molecules that typically suppress tumor-killing lymphocytes, yet immune checkpoint inhibitors targeting PD-1 or PD-L1 have limited to no effectiveness in the major form of proficient mismatch repair CRC. Better definition of the immune microenvironment of the different forms of CRC could lead to new treatment regimens.


Dr. Liu

Recent work published by Chang Hoon Lee's group in Cellular and Molecular Gastroenterology and Hepatology illustrates the central role of tumor-associated macrophages in suppressing the immune response to CRC. These macrophages possess biosynthetic enzymes that produce high levels of adenosine. The newly generated adenosine, in turn, alters the cellular protein processing machinery and enhances the expression of PD-L1. Importantly, as treatment of CRC with cell cycle inhibitors such as palbociclib increases expression of PD-L1 and implicates a mechanism of tumor resistance, the new work shows that combined therapy to block adenosine production (with AB680) during palbociclib treatment improves tumor outcomes in mouse models.

This study offers a conceptual advance toward combinatorial therapy that can simultaneously inhibit tumor cell proliferation and activate immune surveillance, providing clear and testable hypotheses for the clinic.

Cambrian Y. Liu, PhD, is research assistant professor in the section of gastroenterology, hepatology, and nutrition in the department of medicine, University of Chicago. He has no relevant conflicts of interest.

Continued from previous page

commonplace. This transformation has changed the nature and training of our field and, even more importantly, dramatically improved the care of our patients.

Just as notably, the regulatory and practice environment for endoscopy has also changed in the last 15 years, albeit at a slower pace. In January of 2007, as the first issue of GI & Hepatology News came out, Medicare announced that it would cover all screening procedures without a copay but left a loophole that charged patients if their screening colonoscopy became therapeutic. That loophole was finally fixed this year as GI & Hepatology News celebrates its 15-year anniversary.

If the past 15 years are any indication, endoscopy practice will continue to change at a humbling pace over the next 15 years. I look forward to seeing those changes unfold through the pages of GI & Hepatology News. ■

Dr. Gellad is associate professor of medicine and associate vice chair of ambulatory services at Duke University Medical Center, Durham, N.C. He is also a staff physician with the Durham VA Health Care system. He disclosed ties with Merck, Novo Nordisk, and Higgs Boson Health.

IBD biomarker may vary based on microbiome

BY JIM KLING
MDedge News

Levels of calprotectin, a biomarker used to detect intestinal inflammation, may vary in fecal samples based on an individual's microbiome composition, according to researchers. The results, if confirmed, might help refine its use in monitoring inflammatory bowel disease (IBD).

Researchers used a new ex vivo functional assay to identify specific bacteria that degrade calprotectin and may play a role in variations found in vivo. "Microbiome-based calibration could improve sensitivity and specificity of fecal calprotectin readouts, thereby facilitating more reliable real-time monitoring and ultimately enabling more timely interventions," the authors wrote in their research letter, which was published in Gastro Hep Advances (2022 May 19. doi: 10.1016/j.gastha.2022.05.007).

The standard for diagnosing ulcerative colitis (UC) and Crohn's disease (CD) is endoscopy and biopsy because it allows both visual and histological examination of the severity and extent of intestinal inflammation, but this cannot be used to monitor patients on an ongoing basis.

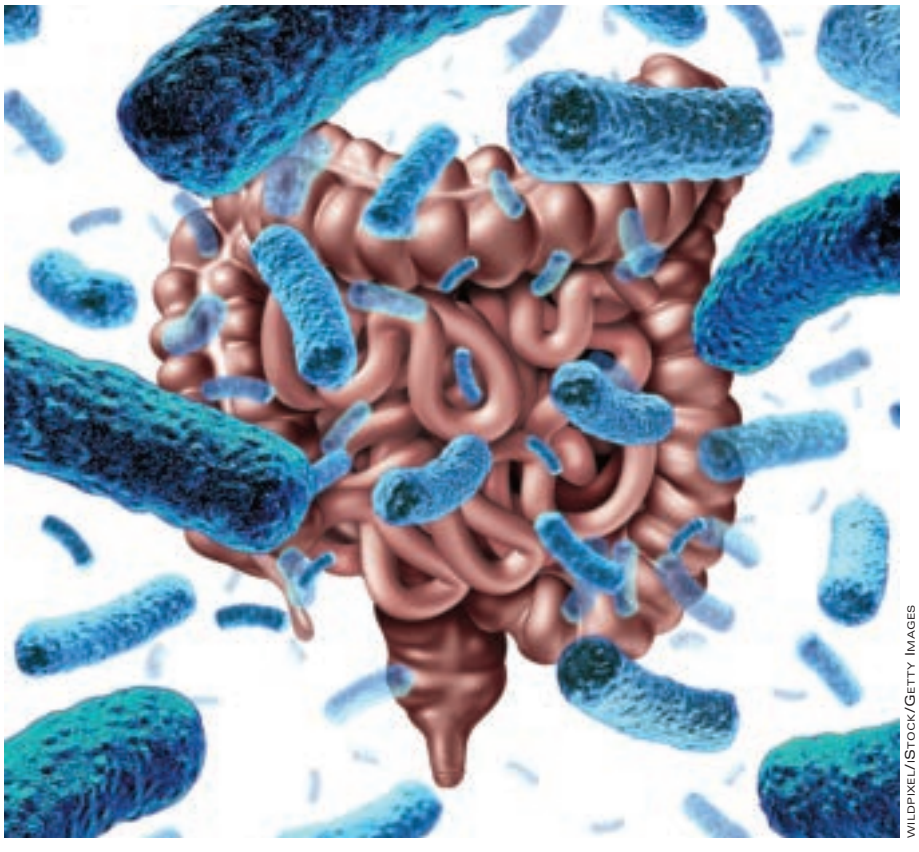
Calprotectin is a promising biomarker for intestinal inflammation, but a meta-analysis found that it has a pooled sensitivity of 85% and a pooled specificity of 75% for the diagnosis of endoscopically active inflammatory bowel disease (J Gastrointestin Liver Dis. 2018 Sep;27(3):299-306).

The researchers investigated whether an individual's microbiome can metabolize calprotectin, which would complicate measurement of fecal calprotectin. They recruited 22 individuals with IBD (64% female, 73% with colonic disease), who provided stool samples. They completed a symptom questionnaire in advance of a colonoscopy. Overall, 64% had endoscopically inactive disease, and 82% had clinically inactive disease.

At a cutoff of 50 mcg/g, 9 patients had normal fecal calprotectin levels, and 13 had elevated levels. Those with clinically or endoscopically active disease had higher levels of fecal calprotectin ($P < .0001$).

There was a significant but poor correlation between disease activity measures and fecal calprotectin levels in CD (r = 0.62; $P = .008$), but there was no statistically significant association for UC (r = –0.29; $P = .6$). Endoscopic disease activity was also significantly correlated with fecal calprotectin in CD (r = 0.83; $P < .001$), but not UC (r = 0.50; $P = .4$).

The researchers created an ex vivo functional assay to measure calprotectin metabolism by the microbiome. They anaerobically cultured fecal samples in the presence of calprotectin and measured levels of calprotectin after 24 hours. Control samples were grown without microbes, without calprotectin, or lacking both. The researchers tested samples in both standard media and in media with low levels of amino acids, reasoning that the latter condition might encourage catabolism of calprotectin. The cultures with low–amino acid content had lower calprotectin levels than those with normal amino acid content ($P < .0007$).



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The researchers found greater calprotectin degradation in the low–amino acid media, and the difference was more pronounced among samples taken from individuals with UC than CD ($P < .02$).

They used metagenomic sequencing data from fecal samples to identify the bacterial species associated with calprotectin metabolism. Similarly to previous reports, the researchers found that Firmicutes was dominant, while Subdoligranulum correlated with calprotectin degradation in low–amino acid media ($P = .04$).

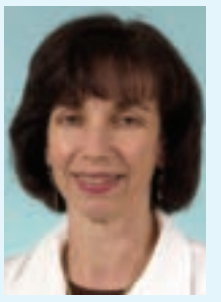
For 5 days, they cultured *Subdoligranulum variabile* in low–amino acid media that also contained calprotectin. Calprotectin levels were lower than a control sample with cultured *Akkermansia muciniphila*, which was previously shown to not be associated with calprotectin degradation in low–amino acid media ($P = .03$). Because Subdoligranulum species were not detectable in 5 of 22 fecal samples, the authors say they are unlikely to be the only species capable of metabolizing calprotectin.

Among IBD patients, only one had both endoscopically active colitis and a low–fecal calprotectin level. The patient's micobiome had Subdoligranulum present, and their fecal sample was able to metabolize calprotectin in the functional assay.

The study was limited by its small sample size, which prevented development of a calibration model for fecal calprotectin, and the researchers called for additional studies among individuals with active colitis. ■

Commentary

The search continues for reliable, noninvasive methods for monitoring disease activity in inflammatory bowel disease (IBD). Noninvasive disease activity measures improve quality of care by facilitating more frequent assessment of therapeutic efficacy, which for IBD otherwise depends on periodic endoscopic evaluation and biopsy. Available tools such as fecal calprotectin are valuable and widely used but are imperfect.



Dr. Rubin

In this report by Kamp et al., the authors provide a potential explanation for variation in fecal calprotectin levels. They make the novel observation that calprotectin can be metabolized by components of the patient's fecal microbiome. The authors generated an ex-vivo functional assay in which they anaerobically cultured fecal samples with or without calprotectin, and showed that Subdoligranulum species (*Subdoligranulum variabile*) when cultured in low–amino acid media, degraded calprotectin, yet another microbiome component, *Akkermansia muciniphilia*, did not. Subdoligranulum species were isolated from 17 of 22 patient microbiomes.

Of note, a patient with endoscopically active colitis and a relatively low fecal calprotectin level harbored Subdoligranulum species, which – when isolated and assayed ex vivo – degraded calprotectin. These studies suggest that individualized, patient microbiome–based calibration assays might help improve the sensitivity and specificity of fecal calprotectin levels for monitoring disease activity. As the authors note, more patients need to be studied, especially focusing on those with active disease and paradoxically low calprotectin levels.

Deborah C. Rubin, MD, AGAF, is the William B. Kountz Professor of Medicine and professor of developmental biology in the division of gastroenterology at Washington University, St. Louis. She had no conflicts of interest to disclose.

Ustekinumab has comparatively low infection risk

BY LAIRD HARRISON

Patients with inflammatory bowel disease (IBD) taking ustekinumab (Stelara) are less likely to have infections as a side effect than those taking tofacitinib (Xeljanz) or anti–tumor necrosis factor–alpha (anti-TNF), researchers say.

Although the risk of infections is not large for any of these drugs, clinicians should nonetheless take it into account, given their similar efficacy, said Ashwin Ananthakrishnan, MBBS, MPH, associate professor of medicine at Massachusetts General Hospital, Boston.

"These findings may not dramatically change prescribing patterns, but in those who may be particularly vulnerable for infection, they could point toward the safer biologic being Stelara," he told this news organization.

The study by Dr. Ananthakrishnan and his colleagues was published in Clinical Gastroenterology and Hepatology (2022 Jan 19. doi: 10.1016/j.cgh.2022.01.013).

Biologic and small-molecule immunosuppressive therapies have emerged as effective treatments for Crohn's disease and ulcerative colitis, the two conditions that comprise IBD.

But the recent proliferation of drugs in these classes with different mechanisms of action has made prescribing decisions complicated. And because the drugs suppress the immune system, they can make patients vulnerable to infection.

Randomized controlled trials, even those comparing the drugs head to head, have not been large enough to compare safety outcomes with statistical accuracy, Dr. Ananthakrishnan and his colleagues found.

Accessing a large, real-world cohort

To help fill this gap, they analyzed data on 89,972,617 people enrolled in Aetna, a nationwide U.S. health insurance plan, from 2008 to 2019.

They identified 19,096 patients whose IBD was treated with anti-TNF agents, 2,420 with ustekinumab, and 305 with tofacitinib. The number of patients taking tofacitinib is small because it is a newer drug, Dr. Ananthakrishnan said.

They found a higher rate of infection and rate of infection-related hospitalization for the patients taking anti-TNF agents (44% and 7%, respectively), compared with those taking ustekinumab (32% and 4%, respectively) over the course of up to a year.

The researchers adjusted for age, sex, IBD duration, prior corticosteroid use, prior immunomodulator use, prior IBD hospitalization, and comorbidities, after which they then compared the risks of infection.

They found that patients taking ustekinumab were 7% less likely to have any infection than patients taking anti-TNF agents (hazard ratio, 0.93), a statistically significant difference (95% confidence interval, 0.86-0.99; $P = .041$). The reduction in the risk of infection-related hospitalizations was similar but not statistically significant.

The advantage with ustekinumab over anti-TNF agents was larger for patients with comorbidities. There was a 25% reduction in the risk of infections for patients taking ustekinumab who had a Charlson comorbidity index score of at least 2 and who were younger than 65 years (HRm, 0.71; 95% CI, 0.58-0.87; $P < .001$).

For patients taking tofacitinib, there were no significant differences in the rate of infection (HR, 0.97; 95% CI, 0.75-1.24) or infection-related hospitalizations (HR, 0.59; 95% CI, 0.27-1.05), compared with TNF antagonists.

The respiratory system and the urinary tract were the most common sites of infections. Bacterial, viral, and fungal infections were similarly distributed in the three groups.

Remaining questions

Further research is needed, said Dr. Ananthakrishnan, as "to understand the comparative safety may be particularly important for vulnerable populations, like those who are older or have other underlying comorbidity, where safety is increasingly an important issue."

The findings are similar to those of other studies comparing infections in association with ustekinumab to anti-TNF medications for related conditions, such as psoriatic arthritis and psoriasis, he said.

Clinicians have seen similar differences among the drugs in clinical practice, said Miguel Regueiro, MD, AGAF, chair of the Digestive Disease and Surgery Institute at Cleveland Clinic, who was not involved in the study.

"It aligns well with what we've thought, but it's nice to see in a publication," he said in an interview.

The implications of the study are limited, because it was not a prospective randomized trial and because the number of patients taking tofacitinib was so small, Dr. Regueiro added.

Another limitation is that the patients who were admitted to the hospital in this database were not necessarily admitted because of their infections, said Stephen Hanauer, MD, AGAF, medical director of the Digestive Health Center at Northwestern University, Chicago, who also was not involved in the study.

Dr. Hanauer told this news organization that comparisons with other agents would be helpful.

"They didn't look at vedolizumab (Entyvio) in this database," he said. "Entyvio is generally considered to be safer than TNF inhibitors or tofacitinib with fairly comparable safety to ustekinumab."

Dr. Ananthakrishnan reported financial relationships with Gilead, Ikena Therapeutics, and Sun Pharma. Dr. Regueiro reported financial relationships with AbbVie, BMS, Janssen, UCB, Pfizer, Takeda, Celgene, Genentech, Gilead, UCB, Miraca Labs, Amgen, Seres, Allergan, Salix, Prometheus, Lilly, TARGET Pharma Solutions, Alfasigigma, and BMS. Dr. Hanauer reported financial relationships with Janssen Pharmaceuticals, AbbVie, Takeda Pharmaceutical, and Pfizer.

Dr. Hou

With our growing armamentarium of effective medical therapies for Crohn's disease (CD) and ulcerative colitis (UC) come increasing decisions for patients and providers for treatments based on comparative effectiveness and safety. One of the most frequent concerns by both patients and providers is risk of infection. While we have partial data on safety from clinical trials, trials are underpowered to compare safety outcomes and also typically compare placebo rather than other active treatments.

This study by Cheng et al. provides further reassurance that ustekinumab and tofacitinib are at least as safe from an infection standpoint as are TNF inhibitors, with UST having a small, but statistically significant lower risk of infection overall compared to TNF inhibitors. While there have been signals that ustekinumab may have lower infection risk compared to TNF inhibitors from clinical trials and real-world analyses of ustekinumab in other disease states, this study is remarkable in that it studies CD and UC specifically. Ustekinumab dosing for CD and UC are higher than that used for other indications, so it's highly relevant to study ustekinumab in CD and UC, specifically for safety. This study is also notable in that no statistically significant difference in infection, particularly herpes zoster, was observed in tofacitinib vs. TNF inhibitors.

This study has limitations as a retrospective administrative dataset, including its inability to determine indication of prescription for CD or UC vs. rheumatologic or dermatologic condition, lack of adjustment for concomitant immunomodulator use, and inability to determine primary indication for hospitalization. However, this study should allow providers to discuss with patients with greater confidence that infection risks of ustekinumab and tofacitinib were overall low and that ustekinumab has lower risks of infections than do TNF inhibitors.

Jason K. Hou, MD, MS, is an investigator in the clinical epidemiology and outcomes program in the Center for Innovations in Quality, Effectiveness, and Safety at the Michael E. DeBakey VA Medical Center and an associate professor at the Baylor College of Medicine, both in Houston. He has no relevant conflicts of interest.

Endoscopy experts review training, assessment evidence to reduce education challenges

BY MARCIA FRELLICK
MDedge News

Endoscopic training is increasingly complex as benchmarks for quality evolve and tools and procedures advance with innovation.

A team of experts, led by Matthew J. Whitson, MD, with Hofstra University/Northwell Health in Hempstead, N.Y., aimed to simplify challenges for educators and clinical endoscopists with a review of tools and techniques for education, as well as assessment methods.

Their review was published in the Techniques and Innovations in Gastrointestinal Endoscopy (2022 Feb 17. doi: 10.1016/j.tige.2022.02.002).

Giving feedback

Key steps to effective feedback include first talking about the goals for the endoscopy session, then careful observation, but minimal feedback during the endoscopy. Most of the feedback should come after the endoscopy, the authors wrote.

One study demonstrated that with beginning endoscopists, giving feedback afterward led to long-term skill development as compared with short-term benefits of frequent feedback in the middle of procedures (Acad Med. 2009 Oct;84[10 Suppl]:S54-7).

Feedback should be constructive and specific with emphasis on goals for the next procedure. It should be delivered in a respectful, nonthreatening way for greatest effectiveness.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Mastery learning

In this model, each trainee must achieve competence in specific skills to progress to the next level.

"For example, the trainee must master retroflexion in the stomach prior to attempting clip hemostasis in the stomach," the authors wrote.

Repetitively practicing the skill is coupled with direct feedback.

Mastery learning is often paired with simulation so trainees can practice in a safe space before working with patients.

Cognitive-load theory

Knowing the challenges of learners can help educators with instruction techniques. An important concept is cognitive-load theory (CLT). CLT is focused on the working memory of a learner and the harm that an overload of information can have on learning. A learner's working memory can process only a few pieces of information at any given time, the theory states.

One mitigation strategy by educators may be to assign a trainee a smaller piece of a specific task appropriate to the trainee's skill level.

"For example, an early trainee endoscopist may be able to inject epinephrine for a bleeding vessel, but not be ready to perform effective Bi-Cap cautery," the authors suggested.

Different learning styles

Learning styles include visual, aural, reading/writing, and kinesthetic styles (when learners need to touch or manipulate to learn a skill).

"A study of surgical trainees demonstrated that kinesthetic learning was the most preferred unimodal learning style of those entering the field," the authors wrote.

Dr. Whitson and coauthors gave examples of working with trainees with different learning styles.

A trainee who learns visually, they say, might need to learn about "loop reduction" by looking at images of alpha or beta loops or using ScopeGuide during endoscopy. A kinesthetic learner may need to feel a successful loop reduction with hands on the endoscope during simulation to understand the skill better.

"There is some suggestion that the millennial generation – the demographic of the current gastroenterology fellows – may have higher preferences for kinesthetic learning," the authors wrote (Gastrointest Endosc. 2019;89[5]:1056-62).

Role of simulation

The Accreditation Council for Graduate Medical Education, which oversees Gastroenterology Fellowship training, mandates simulation in gastroenterology education but does not specify endoscopic simulation. The American Board of Surgeons, however, does require their trainees to complete the flexible endoscopic curriculum, which is simulation based.

Simulator use appears particularly helpful early in training. One study demonstrated that colonoscopy simulation has benefit in the first 30 colonoscopies in depth of insertion, independent completion, and ability to identify landmarks (Am J Gastroenterol. 2004 Jan;99[1]:33-7).

However, another study showed simulation after 50 colonoscopies has shown no benefit, the authors wrote (Clin Gastroenterol Hepatol. 2014;12[10]:1611-23). Finding uses for simulators beyond diagnostics will be important for justifying buying more of them for medical centers given the high cost.

Procedural volume

Dr. Whitson and colleagues wrote that using sheer volume of procedures as a measure of competency is falling out of favor and there is recognition in the field that competency will come at different times and at different volumes for individual trainees.

Continued on following page

Industry payments to GIs, hepatologists now on decline; gender disparities remain

BY TARA HAELLE
MDedge News

Industry payments to U.S. gastroenterologists and hepatologists increased from 2014 to 2016 before beginning to steadily decrease after 2016, according to new research published in Gastroenterology (2022 Jun 14. doi: 10.1053/j.gastro.2022.06.029).

The study aimed to identify trends in these specialties in the years after the Sunshine Act, enacted in 2010, and the federal program Open Payments, established in 2013.

"Although Open Payments launched in September of 2014, all the joinpoints in our study occurred more than a year later in 2016, suggesting a delay in observable changes in behavior on industry physician relationships," wrote Xiaohan Ying, MD, of Weill Cornell Medicine in New York, and colleagues. "Since 2016, we have seen a sustained reduction in general industry payments to physicians while research payments remained stable, which is likely the desired outcome of this program."


Dr. Kosinski

That's also the conclusion of Lawrence Kosinski, MD, MBA, AGAF, Councillor for Development and Growth for the American Gastroenterological Association, who was not involved in the study.

"Most all of us are aware of the Sunshine Act and have reacted accordingly, so I am not surprised that reimbursement per physician has declined over the time period," Dr. Kosinski told this news organization. "Many physicians are very sensitive to their reporting and have decreased their exposures," said Dr. Kosinski, founder of SonarMD and a member of the Health & Human Services Advisory Committee on Value-Based Payment. "What does surprise me is the marked disparity in payments with a very small number of physicians receiving tremendous reimbursement from speaking engagements and promotions."

The researchers retrospectively analyzed industry payments to 26,981 practicing pediatric and adults gastroenterologists and hepatologists using the National Plan and Provider Enumeration System and data from Open Payments between January 2014 and December 2020. The researchers excluded education payments and focused on general payments, which "include charitable contribution, speaker fees, consulting fees, ownership and investments, education, entertainment, food and beverages, gift, honoraria, royalty and license, and travel and lodging," they reported.

Gender disparities seen

The analysis revealed that 87.7% of practicing U.S. gastroenterologists and hepatologists had received at least one payment between 2014 and 2020, totaling $430.8 million. While 78% of the recipients were

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A study assessing competency in esophagogastroduodenoscopy (EGD), for example, demonstrated that, while most trainees will achieve independent intubation rates of the second part of the duodenum by 150 procedures, it will take between 200 and 250 for the average fellow to reach competency of all motor skills for a standard EGD, and 300 to become efficient (Gastrointest Endosc. 2019;90[4]:613-20).

Assessment of skills has evolved from numbers of procedures to competency-based assessments to the development of direct observation tools.

Coaching for the practicing endoscopist

Most studies on coaching have focused on trainees, but coaching can be used with experienced endoscopists as well.

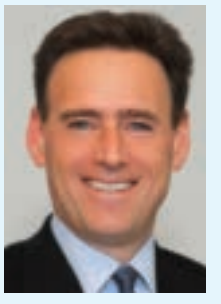
One study investigated use of direct verbal coaching to train experienced practitioners in water immersion colonoscopy "which resulted in shorter cecal intubation times, improved [adenoma detection rate], and less use of sedation during procedures," the authors noted (J Interv Gastroenterol. 2012 Jul-Sep; 2[3]: 122-5). Another study currently underway in the United Kingdom uses electronic feedback coupled with education and training to change behaviors to improve polyp detection performance in colonoscopy (Endosc Int Open. 2020 Nov;8[11]:E1545-52).

The authors noted that using one of these tools or strategies does not preclude using another.

"[I]n fact educators likely will recognize the utility of incorporating multiple of these techniques in the same endoscopy session with a trainee," the authors wrote.

One author holds stock in Boston Scientific. The remaining authors disclose no conflicts. ■

Successful training is the foundation of high-quality endoscopy. Whitson et al. eloquently and thoroughly explore the principles central to successful training and review the latest understanding of best practices to apply them. Beyond fellows, this will have ongoing relevance to practicing endoscopists as they must learn new skills and in turn apply them in teaching others.


Dr. Cohen

Feedback is an essential aspect of deliberative practice in my experience. The art of giving useful feedback requires one to be introspective, interactive, and iterative.

Introspective: The instructor must assess the presession skill level and adjust the learning plan with observation in real time of student performance, taking primary consideration simultaneously for patient safety. From these inputs, the teacher decides a) what helpful information to convey, b) how best to deliver the message, and c) when best to do it.

Interactive: "How best to deliver" will usually entail an approach to stop the action and ask the trainee to consider the present challenge and possible solutions rather than to dictate an action or demonstrate what to do. It is not always best to wait until after the procedure – contrary to what the authors favor in this article – but interruptions must be few and focused.

Iterative: The lessons taught are building blocks that ideally relate to prior challenges and set the agenda for next learning goals.

The authors rightly emphasize the concern for cognitive overload. In practice, a maximum of one or two take-home lessons per mentored training session is a good rule of thumb; the converse should be equally emphasized, that every single proctored training examination ought to be mined for at least one relevant lesson, be it a technical, a cognitive, or another nontechnical pearl related to teamwork, professionalism, and so on.

Much simulator investigation to date, including my own, has focused on technical skills and performance outcomes – more work is needed especially in web, simulator, and even AI-based tools to teach cognitive skills for recognizing abnormalities, identifying them, and making real-time evidence-based decisions. The value of simulator-based teaching of endoscopic nontechnical skills, practice in troubleshooting common mishaps, and teaching by counter example of what not to do are other areas of great promise. There is not yet a prescribed, evidence-based guideline regarding which simulation devices should be used, at what stages of fellowship, and how often; however, the principles described in this paper provide the road map for how simulation ought to be integrated into endoscopic teaching.

Jonathan Cohen, MD is a clinical professor of medicine at New York University. He is the Editor of "Successful Training in Gastrointestinal Endoscopy," 2nd ed. (Hoboken, N.J.: Wiley-Blackwell, 2022) and an investigator in ex vivo and computer endoscopy simulators. He is a consultant for Olympus America and Micro-Tech Endoscopy, receives royalties from Wouters-Kluwer and Wiley, and holds stock in GI Windows, Virtual Health Partners, ROMtech, and MD Medical Navigators.

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men, 90.4% of all payments went to men.

"Despite encouraging trends observed in our study, where total and per-person payments to women have grown, these payments still unacceptably lag far behind those of men and are nowhere near equitable," the authors noted. "One possible explanation for [the disparities] is that while improving, there are still significant gender disparities in authorship and leadership in medicine, and not just in gastroenterology and hepatology."

The gender disparities did not surprise Dr. Kosinski because GI is still a male-dominated field, he said. "The speakers are likely older, which represents a time when it was even more male dominated," added. "Time will change this."

Who gets paid, and how much?

While $27.5 million was going to research and grants, most of the payments ($403.3 million) were general payments; out of the total payments to specialists, $30 million went to hepatology, and $400.8 million went to gastroenterology. Nearly all of the general payments ($398.1 million) were for noneducation purposes; 90.5% of general payments went to men and 9.5% went to women, at an average of $17,167 per person. Nearly half the payments (43.8%) were for speaker fees, totaling $174.3 million, followed by 18.4% going to consulting ($73.1 million) and 12.9% going to food and beverages ($51.5 million).

While most of the payments (81.8%) came from pharmaceutical companies, totaling $325.6 million, medical device companies paid more per payment (average $323.02) than pharmaceutical companies did (average $143.72).

Most of the physicians accepting payments (86.6%) received less than $10,000, but this made up only 8.3% of all payments. Meanwhile, 74% of all the payments, $294.6 million, went to just 3.1% of the physicians, all of whom received more than $100,000.

That breakdown is what most caught Dr. Kosinki's attention.

"It's one thing for a speaker to declare that they are receiving funds from pharma, but they never let us know how much," Dr. Kosinski said. "Some of these speakers are realizing a very significant payment, which could change the opinions of those listening to their presentations."

The authors reported that a group of 50 top earners (0.2%) received more than $1 million between 2014 and 2020. Their payments totaled $94.8 million and accounted for nearly a quarter (23.8%) of all the payments. All but one of these physicians were men, and one physician has received more than $1 million every year since 2014.

"It is likely that these few individuals are highly sought after due to their experiences and expertise," the authors wrote.

Payments for guideline authors explored

The authors noted a similar phenomenon – high payments for experts in specific subject areas – among guideline authors.

The authors examined payments to practicing U.S. gastroenterologists and hepatologists who helped write clinical guidelines for the following organizations:

- American Gastroenterological Association.
- American College of Gastroenterology.
- American Association for the Study of Liver Disease.
- North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.
- American Society for Gastrointestinal Endoscopy.

The 186 guidelines published between 2014 and 2020 had 632 physician authors, 415 of whom were practicing gastroenterologists and hepatologists in the United States. Most of these physicians (85.8%) received at least one industry payment, with payments to guideline authors totaling $43.6 million.

Similar to the lopsided breakdown for total payments across all physicians, the majority of the payments (87.4%, or $38.1 million) went to one-quarter of the authors, who each received more than $100,000 per person. Meanwhile, 38.2% of the guideline authors received less than $10,000.

"However, these numbers are likely to decrease in the future as professional societies, such as AASLD, require a majority of the guideline authors to be free of conflict of interest relevant to the subject matter," the authors explained. They also added that the members selected as part of the AGA's guideline development group must report all conflicts of interest, including indirect and intellectual ones, and they are recused or excluded when appropriate. These guideline–development group participants must also forgo speaking and consulting arrangements until 1 full year after the guideline's publication.

IronHeart/Moment/Getty Images

Trends have been shifting

Total industry payments initially grew at a rate of 11.4% a year between 2014 and 2016 before decreasing at a rate of 5.8% per year after 2016 ($P = .03$). Though a similar trend occurred at the individual level, it did not reach significance.

However, the trend differed slightly between men and women: Payments to men increased 10.4% annually until 2016 then decreased 6.8% per year thereafter, but women's payments increased 11.3% per year until 2019. Between 2014 and 2019, the amount per person payment dropped 3.5% annually to physicians overall, but payments to women initially increased 35.4% a year between 2014 and 2016 before decreasing.

Although not statistically significant, trends for types of payments showed that speaker and food/beverage fees have been declining since 2016 while consulting fees have been declining since 2014.

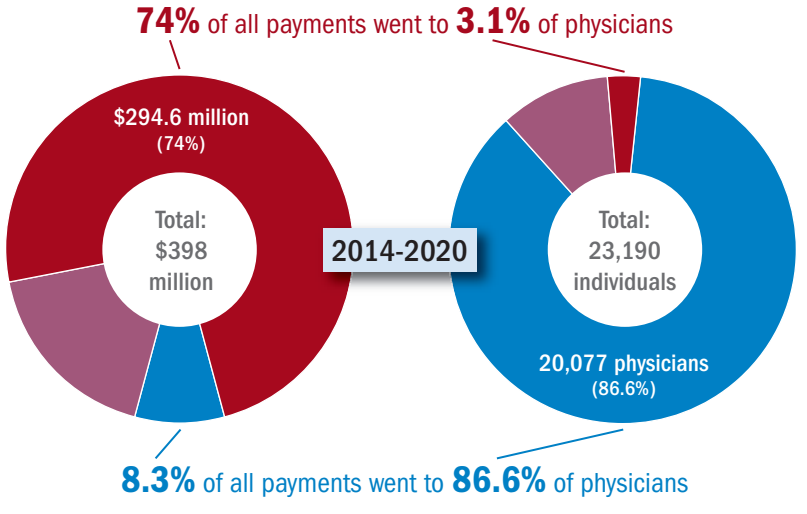
"The reduction in industry payments could be due to the Hawthorne effect, where physicians alter their behavior after becoming aware that their payments were being monitored," the authors wrote. "Although many physicians see themselves as less vulnerable to be biased by industry compensation, studies have shown that even small payments can affect behavior such as prescription pattern. Additionally, studies have found that patients are less likely to trust physicians who have received industry payments."

The authors acknowledged the role of industry payments in funding clinical trials but noted that pharmaceutical companies themselves have been taking on more design and execution of trials in recent decades. Further, only 6% of all payments went to research and grant funding, a little more than half the payments for food and beverages.

"While industry research funding is undeniably crucial, it simply plays a very small role in total industry compensation for physicians," the authors wrote. "While speaker events could be beneficial and educational for physicians and other audiences, these events could also be utilized as means to promote specific products. While it is beneficial to seek input from experienced gastroenterologists for novel therapies and devices, actions should be taken to place limitations on industry payments to physicians, especially for the top earners."

One author reported speaker fees from W.L. Gore and Cook Medical. The other two others had no disclosures. No external funding was noted. Dr. Kosinski reported having no relevant disclosures. ■

Industry payments to gastroenterologists and hepatologists



Note: Based on data from Open Payments, National Plan and Provider Enumeration System.

Source: Gastroenterology. 2022 Jun 14. doi: 10.1053/j.gastro.2022.06.029

MDedge News

Long-term results explored

IBS *from page 1*

reported the authors, who also correlated individual microbial profiles with clinical outcomes.

The study, led by Magdy El-Salhy, MD, PhD, department of medicine, Stord (Norway) Hospital, was published online in Gastroenterology (2022. doi: 10.1053/j.gastro.2022.06.020).

An expert not involved with the study, Brian Lacy, MD, PhD, a gastroenterologist with the Mayo Clinic in Jacksonville, Fla., said that the results of the study are important, but he cautions against treating IBS with FMT outside clinical trials, at least until the protocol is validated, given demonstrated risks.

"I believe that this will help researchers around the world refine their techniques, as we learn more about FMT for the treatment of IBS."

The new study included 125 patients (104 women, 21 men) in three groups: 38 received a placebo, 42 received 30 g of donor feces, and 45 received 60 g of donor feces. The feces – all from one male donor – was administered to the duodenum.

The response rates for those who received FMT were significantly higher than for those who received placebo. Those receiving 30 g of feces had a response rate of 69.1%, and those in the 60-g group had a response rate of 77.8%, whereas the response rate in the placebo group was 26.3%.

Patients provided a fecal sample and completed five questionnaires at the beginning of the study and at 2 and 3 years after FMT.

Patients in both treatment groups had significantly fewer IBS symptoms – such as abdominal pain, abdominal bloating, dissatisfaction with bowel habits, and quality of life interruption – and less fatigue compared with the placebo group, as well as higher quality of life scores at 2 and 3 years.

No long-term adverse effects were reported. The dysbiosis index decreased only in the treatment group at years 2 and 3.

Microbial modifications correlate with IBS symptoms

In addition, the fluorescent signals of 10 bacteria that had changed after FMT were significantly correlated with improved IBS symptoms and fatigue in both treatment groups.

"Of the bacteria markers whose fluorescence signals changed in the 30-g and 60-g groups, but not in the placebo group, at both 2 and 3 years after FMT, nine were significantly correlated with the total IBS-SSS [IBS–Severity Scoring System] scores," the authors wrote. One more bacterium with a changed fluorescence signal in the active treatment group also correlated with total fatigue.

Dr. El-Salhy told this news organization that those findings open the door for the select bacteria to be used, for example, in capsule form to treat IBS and fatigue.

The most surprising finding for the team was that the "majority of IBS patients [who] responded to FMT maintained response up to 3 years" or more, said Dr. El-Salhy, alluding to unpublished data up to 5 years.

"Furthermore, 80% of those who relapsed after 3 years responded to a new FMT," he said.

Women had higher response rates than men at years 2 and 3 after FMT, but there were no differences between complete remission rates of women and men at years 2 and 3.

'Impressive' results, but caution warranted

"The results are impressive," Dr. Lacy said. "I believe that this will help researchers around the world refine their techniques, as we learn more about FMT for the treatment of IBS. It also clearly plays up the importance of the gut microbiome in symptom generation in IBS patients."

However, he said, until the results are replicated, and the protocol validated, FMT should not be used routinely to treat IBS because there are risks with the procedure.

Dr. Lacy pointed out there have been mixed results in the literature regarding FMT and IBS.

He cited a meta-analysis of four studies (n = 254) in 2019 that did not show a benefit for FMT in patients with IBS (Am J Gastroenterol. 2019 Jul;114[7]:1043-50). However, a second meta-analysis of five studies (n = 267) did show some benefit, possibly owing to the type of donor and small-bowel infusion (Aliment Pharmacol Ther. 2019 Aug;50[3]:240-8).

The authors added that, in the seven randomized, controlled trials investigating FMT for IBS, four concluded that FMT eased symptoms and improved quality of life in patients with IBS, whereas treatment was not effective in the other three.

The authors pointed to differences in protocols, donors, the cohort treated, FMT dose, and route of administration.

The longest response time previously studied in the randomized, controlled trials was 1 year, the authors pointed out. The new study was a 3-year follow-up of these authors' previous randomly assigned placebo-controlled trial participants.

The 'super-donor' concept

The authors of the current study described the single chosen donor as "a healthy male aged 36 years with a normal BMI [body mass index] who was born via vaginal delivery, breastfed, a nonsmoker, was not taking any medication, was treated only a few times with antibiotics, exercised regularly, and consumed a sport-specific diet that was richer in protein, fiber, minerals, and vitamins than the average diet."

The donor had high microbial diversity, and his fecal bacteria makeup was different from that of 254 healthy subjects for 14 of the 48 bacterial markers investigators tested.

Dr. Lacy said that the "super-donor" concept is noteworthy and an apparent key to success.

"Other studies have not done this," Dr. Lacy noted.

Among the strengths of the study are that it included a relatively large cohort of patients with IBS, with three IBS subtypes and a single well-defined donor. However, it did not include the fourth IBS subtype, unsubtyped IBS, and it investigated only a part of the intestinal bacterial content, the authors acknowledged.

Most interesting, Dr. Lacy said, is that the IBS subtype did not seem to matter to FMT outcomes at 3 years and that all three subtypes responded better than placebo.

"That's encouraging," Dr. Lacy said.

The investigators received a grant from Helse Fonna. The study authors and Dr. Lacy reported no relevant financial relationships. ■

The treatment of IBS remains a major health care challenge. It is now evident that dysregulation of the microbiota-gut-brain axis is an important contributing factor that may drive and perpetuate the symptoms of IBS.

Dr. Monaghan

This study by El-Salhy et al. highlights the safety and sustained benefit of fecal microbiota transplantation (FMT) in patients with IBS for up to 3 years following transplantation. The authors also identified 10 fecal bacterial markers that correlated with IBS symptoms in patients who underwent FMT. The researchers linked their high response rates to donor selection criteria that were based on specific bacterial species that positively affect the gut microbiota in terms of abundance, diversity, and stability over time.

The positive effects seen in this study may also relate to the use of donor fecal material that was thawed for 2 days at 4 degrees C and manually mixed to preserve strictly anaerobic bacterial viability and growth. However, we should be mindful that caution is required when using FMT to treat gastrointestinal diseases, as the long-term adverse effects of this procedure remain unclear.

Further larger age- and gender-matched studies should be undertaken to validate these important observations, which also focus on deciphering optimal route of administration for FMT. More extensive research is needed to understand the complex multi-kingdom microbial, metabolic, epigenetic, and immunological correlates of FMT treatment response in IBS patients. It will be critical to support longitudinal human observational FMT-based interventional studies with rigorous experimental approaches for addressing causal relationships between altered microbiome and disease phenotype.

Tanya M. Monaghan, PhD, BSc (Hons), BM, FRCP, is clinical associate professor and honorary consultant in gastroenterology, Nottingham (England) Digestive Diseases Centre; NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust, and the University of Nottingham. Dr. Monaghan has no relevant conflicts of interest.

Strictures: Balloon dilation avoids later surgery

BY WILL PASS
MDedge News

Endoscopic balloon dilation (EBD) is an effective treatment option for strictures of the small bowel in patients with Crohn's disease, based on a nationwide Danish cohort study.

Approximately three out of four patients who underwent an EBD were spared subsequent small-bowel surgery. Similar outcomes were seen across primary and postsurgical strictures, reported lead author Mads Damsgaard Wewer, BSc, of the University of Copenhagen, and colleagues.

"Retrospective studies investigating EBD are available with variable follow-up periods; however, a nationwide study to demonstrate more precise durability of EBD in unselected patients is lacking," the investigators wrote in European Journal of Gastroenterology & Hepatology (2022 Aug 1;34[8]:831-7). Their aim was to understand the use of EBD and the need for redilation and surgery. This retrospective study used a cohort of adult patients with Crohn's disease who had strictures of the small bowel during a 19-year period.

The population comprised 9,737 patients with incident Crohn's disease, among whom 90 (1%) underwent EBD during a median 8.2-year follow-up period. Of these 90 patients, 49 had primary strictures, while the remaining 41 had postsurgical strictures.

In the primary stricture group, 59% of patients had one EBD procedure and did not require subsequent small-bowel surgery, 14% of patients required redilation but no further surgery, and 27% of patients required small-bowel surgery after dilation. In this same group, the 1-, 3-, and 5-year cumulative incidence rates of EBD failure were 19%, 21%, and 25%, respectively. Of note, just 8% of patients with primary stricture who were treated with EBD ultimately required enterotomy, compared with 16% of patients with primary stricture who underwent small-bowel resection without first attempting EBD.

In the postsurgical stricture group, 49% of patients underwent one EBD procedure without need for another small-bowel surgery, 27% needed redilation but avoided surgery, and 24% required surgery after dilation; 1-, 3-, and 5-year cumulative incidence rates of EBD failure in this group trended slightly higher than the primary stricture group over time, at 19%, 25%, and 29%, respectively.

The researchers concluded that, "... small bowel–related EBD is an effective treatment option, and one that could be offered to more patients with Crohn's disease in the future."


Dr. Carmichael

'Reassuring study'

David H. Bruining, MD, AGAF, associate professor of medicine and section head of the inflammatory bowel disease interest group at Mayo Clinic, Rochester, Minn., called it a "reassuring study that confirms previous data regarding the efficacy of endoscopic balloon dilation of Crohn's disease strictures."

Dr. Bruining suggested in an interview that the findings, while drawn from Denmark, can be applied to a U.S. population; he also noted the "impressive" size of the study, as well the duration of follow-up, which extended up to 19 years.

EBD is "gaining more traction," Dr. Bruining said, "as far as the belief among both referring physicians, and gastroenterologists, that it is effective, and it is safe. I think that body of literature is growing, and it's more widely established at this point."

Dr. Bruining noted that EBD should be reserved for patients who have short strictures no longer than 4-5 mm "without associated internal penetrating disease."

In the future, such patients may have even more treatment options, Dr. Bruining predicted. New antifibrotic medications are "on the horizon," which could one day be used with or without EBD to address fibrotic strictures in Crohn's disease. Dr. Bruining is a part of the Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium, a group that aims to develop this emerging approach. He and his colleagues recently published a review (Physiol Rev. 2022 Apr 1;102[2]:605-52) of research into antifibrotic therapy to date.

Limiting factors

"This is an important study that really adds something to the literature," noted Joseph Carmichael, MD, chief medical officer and chief of colon and rectal surgery at the University of California, Irvine. "The cohort is a little unusual in this area in that it encompasses a whole country. Yet this is exactly what makes the data stand apart from previous studies, since the patient population was unselected. That's how you get a true incidence of the intervention."

Beyond the generally favorable outcomes associated with EBD, Dr. Carmichael highlighted similar rates of success across both primary and postsurgical strictures. "Some of the previous data suggest postsurgical strictures don't do as well with endoscopic dilation, and this [study] seems to go against that," he said. "Which really deserves a closer look."

Reflecting on the researchers' call for more frequent use of EBD in patients with Crohn's, Dr. Carmichael speculated that several factors may be limiting current utilization in Europe and the United States. For one, there may not be enough interventional gastroenterologists. Also, the procedure "generally requires a high-volume provider who's got surgical backup because these [procedures] have a 2%-4% incidence of technical failure – including perforation or bleeding. These risks may deter patients from undergoing the procedure.

"Patients with Crohn's disease can be pretty remarkable in their ability to endure obstruction," he added. "If someone's feeling their symptoms aren't altering their quality of life, they may choose not to proceed with it."

With all candidate patients, Dr. Carmichael recommended discussing the risks of EBD compared with the risks of declining the intervention, such as complete bowel obstruction, bowel perforation, or fistula. "That's a question that needs to be included with every conversation when we discuss procedures," he explained.

The researchers report that, among others, they have relationships with Janssen-Cilag, AbbVie A/S, and Celgene. Dr. Bruining and Dr. Carmichael reports no relevant conflicts of interest. ■

COVID-19 may trigger irritable bowel syndrome

BY LAIRD HARRISON

COVID-19 can cause disorders of gut-brain interaction, including postinfection irritable bowel syndrome (IBS), researchers say.

Gastrointestinal symptoms are common with long COVID, also known as post–acute COVID-19 syndrome, according to Walter Chan, MD, MPH, AGAF, and Madhusudan Grover, MBBS, AGAF.

Dr. Chan, an assistant professor at Harvard Medical School, Boston, and Dr. Grover, an associate professor of medicine and physiology at Mayo Clinic, Rochester, Minn., conducted a review of the literature on COVID-19's long-term gastrointestinal effects. Their review was published in Clinical Gastroenterology and Hepatology (2022 Aug 6. doi: 10.1016/j.cgh.2022.05.044).

Estimates of the prevalence of gastrointestinal symptoms with COVID-19 have ranged as high as 60%, Dr. Chan and Dr. Grover report, and the symptoms may be present in patients with long COVID, a syndrome that continues 4 weeks after initial infection or longer.

In one survey of 749 COVID-19 survivors, 29% reported at least one new chronic gastrointestinal symptom. The most common were heartburn, constipation, diarrhea, and abdominal pain. Of those with abdominal pain, 39% had symptoms that met Rome IV criteria for irritable bowel syndrome.

People who have gastrointestinal symptoms after their initial SARS-CoV-2 infection are more likely to have them with long COVID. Psychiatric diagnoses, hospitalization, and the loss of smell and taste are predictors of gastrointestinal symptoms.

Infectious gastroenteritis can increase the risk for disorders of gut-brain interaction, especially postinfection IBS, Dr. Chan and Dr. Grover write.

COVID-19 likely causes gastrointestinal symptoms through multiple mechanisms. It may suppress angiotensin-converting enzyme 2, which protects intestinal cells. It can alter the microbiome. It can cause or worsen weight gain and diabetes. It may disrupt the immune system and trigger an autoimmune reaction. It can cause depression and anxiety, and it can alter dietary habits.

No specific treatments for gastrointestinal symptoms associated with long COVID have emerged, so clinicians should make use of established therapies for disorders of gut-brain interaction, Dr. Chan and Dr. Grover recommend.

Beyond adequate sleep and exercise, these may include high-fiber, low-FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols), gluten-free, low-carbohydrate, or elimination diets.

For diarrhea, they list loperamide, ondansetron, alosetron, eluxadoline, antispasmodics, rifaximin, and bile acid sequestrants.

For constipation, they mention fiber supplements, polyethylene glycol, linaclotide, plecanatide, lubiprostone, tenapanor, tegaserod, and prucalopride.

Dr. Chan reported financial relationships with Ironwood, Takeda, and Phathom Pharmaceuticals. Dr. Grover reported financial relationships with Takeda, Donga, Alexza Pharmaceuticals, and Alfasigma. ■

Reducing the burden of UC care

Ultrasound *from page 1*

they fail to characterize disease extent and fall short in detecting early endoscopic responses, the investigators added.

The present study aimed to determine if IUS could offer more clinical insight by measuring bowel wall thickness. Thirty patients were enrolled with moderate to severe UC, all with an endoscopic Mayo score of at least 2. Twenty-seven of these patients were evaluable through follow-up, having undergone both IUS and endoscopy at baseline and 8 weeks after starting tofacitinib.

Dr. Dolinger

At both time points, IUS findings correlated significantly with endoscopic Mayo score (EMS), UC endoscopic index for severity, and Robarts Histopathology Index, with correlation coefficients of 0.68, 0.73, and 0.49, respectively. Remission according to EMS was defined as a score of 0, and improvement was defined as a score of 1 or less.

Patients with EMS improvement showed lower median bowel wall thickness in the sigmoid colon after 8 weeks of treatment than did patients without improvement (1.8 mm vs. 4.5 mm; $P < .0001$); patients who were in EMS remission after 8 weeks also had lower median bowel wall thickness of the sigmoid colon (1.4 mm vs. 4.0 mm; $P = .016$).

The investigators also sought to define cutoff values for bowel wall thickness. The most accurate cutoff values for identifying endoscopic remission and improvement were 2.8 mm (area under the receiver operating curve, 0.87; 95% confidence interval, 0.74-1.00; $P = .006$) and 3.9 mm (AUROC, 0.92; 95% CI, 0.82-1.00; $P < .0001$), respectively. Treatment response was best identified by a 32% threshold reduction in thickness (AUROC, 0.87; 95% CI, 0.74-1.00; $P = .002$).

"Intestinal ultrasound, with bowel wall thickness as the single most important parameter is accurate to determine treatment response to tofacitinib in patients with moderate-severe UC when compared against endoscopy," the investigators concluded.

Michael Dolinger, MD, MBA, assistant professor of pediatrics and the associate pediatric gastroenterology fellowship program director at the Icahn School of Medicine at Mount Sinai, New York, said the study is noteworthy because it is the first of its kind to show that IUS can accurately monitor treatment responses in UC.

"This study is what we're looking for now, and in the future," Dr. Dolinger said in an interview. "We're looking for noninvasive biomarkers to predict early responses so that we know as clinicians ... if our medicines are working or if we need to pivot and switch effectively."

For patients, this can mean feeling better quicker while reducing burden of care, he added.

"We can use this study to predict patient responses without having to potentially rescope them in 8 weeks using a 5-minute point-of-care test in the clinic," Dr. Dolinger said. "It's huge to be able to say that for patients with colitis, and to provide reassurance that not only are they potentially feeling better, but the medicine is working to change and heal their bowel wall really quickly as well."

Dr. Dolinger speaks from clinical experience. Over the past 2 years, he and his colleagues at Mount Sinai have been implementing IUS for patients with both UC and Crohn's disease.

"It's become part of our standard of care," Dr. Dolinger said. "This is now emerging in the United States and will soon take hold. There is a lot of interest."

Dr. Dolinger is one of just a few American physicians credentialed by the International Bowel Ultrasound Group, an organization based out of Europe, Israel, and Canada. Formalized training and certification are necessary, Dr. Dolinger noted, to ensure that this new clinical approach maintains consistency as it is rolled out across the United States.

"We have the unique opportunity to do something from the ground up quickly, but also correctly, meaning that we can train everyone to speak the same language and do the same standardized exams so that all the findings and research are relatable," Dr. Dolinger said.

He advised interested physicians to contact their local inflammatory bowel disease center to find out if training is available, and if it is, devoting "a lot of time" to the learning process.

"If you're going to use this potentially as a clinical decision-making tool without using other invasive procedures, you really want to make sure what you're doing is accurate and correct," Dr. Dolinger said.

The investigators disclosed relationships with AbbVie, Merck, Takeda, and others. Dr. Dolinger disclosed a relationship with NeuroLogica, a subsidiary of Samsung Electronics. ■

CLINICAL CHALLENGES AND IMAGES

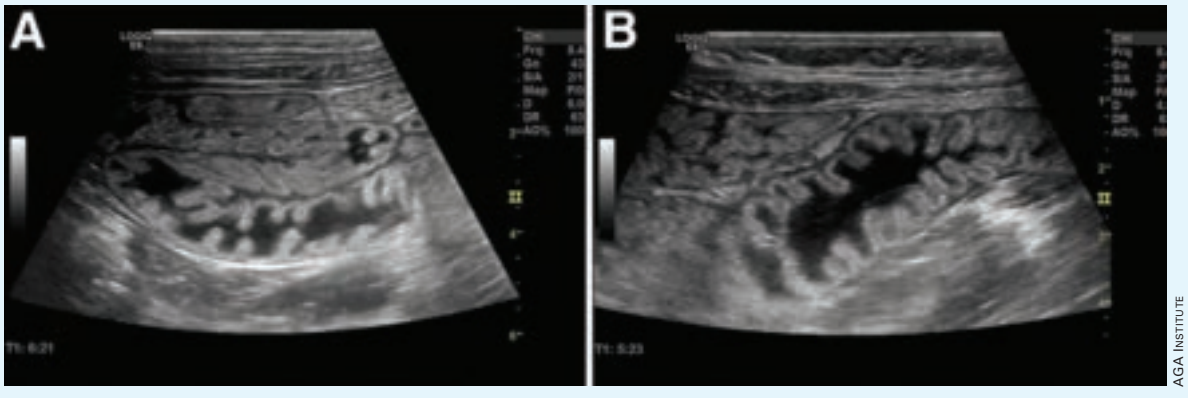
What's your diagnosis?

BY CARLA SERRA, MD, HANA PRIVITERA HRUSTEMOVIC, MD, AND FEDERICO MARIA VERARDI, MD

Previously published in Gastroenterology (2019 Apr 1;156[5]: 1253-4).

A 67-year-old woman presented with a year-long history of general malaise, low-grade fever, diarrhea, and a 20-kg weight loss. She had a history of hypertension and depressive disorder. In the previous 4 years, she had undergone several rheumatologic examinations for polyarthritis, and having been diagnosed with seronegative rheumatoid arthritis, she had been treated with steroids, methotrexate, and etanercept, with little benefit.

Recent laboratory tests showed: hemoglobin, 8.3 g/dL; mean corpuscular volume, 70 fL; erythrocyte sedimentation rate, 78; and C-reactive protein, 6.4 mg/dL. To evaluate the microcytic anemia and the diarrhea, endoscopic investigations had been performed a few months earlier.



AGA Institute

Esophagogastroduodenoscopy showed villous atrophy at the level of DII; histology was compatible with intramucosal xanthoma. There were no pathologic findings at colonoscopy. The situation had not been further investigated.

At presentation, the physical examination revealed lower-limb edema, skin and mucosal pallor, and a body mass index of 17.4 kg/m^2. Laboratory tests showed microcytic anemia (hemoglobin, 10.0 g/dL; mean corpuscular volume, 74 fL), increased acute-phase proteins (erythrocyte sedimentation rate, 59; C-reactive protein, 8.53 mg/dL), and malabsorption (albumin, 2.5 g/dL; multiple electrolytes deficiencies including iron, vitamin A, and vitamin D deficiency).

Abdominal ultrasound examination revealed three small lymph nodes in the periaortic region (maximum diameter, 10 mm), marked mesenteric and ileal wall thickening, mild jejunal wall thickening, an increased number of connivent valves, and a mild amount of peri-intestinal fluid effusion (Figure A, B).

What is the likely diagnosis and the appropriate treatment?

The answer is on page 32.

Rethinking histology as treatment target in UC

BY LIAM DAVENPORT

For patients who experience endoscopic remission of ulcerative colitis (UC), signs of active disease on histology did not affect their risk of clinical relapse, according to a large prospective study that reinforces a low endoscopy score as the treatment target.

In the study of more than 250 patients in endoscopic remission from UC, 19% experienced a clinical relapse within 1 year. The researchers found that a lower baseline endoscopy score was linked to a lower risk of relapse.

"Our findings do not support the use of histology as a target for treatment in patients with ulcerative colitis who already achieved clinical and endoscopic remission," wrote Talat Bessissow, MD, McGill University Health Center, Montreal, and colleagues.

They add that the results "support the use of the Mayo endoscopic subscore of zero as the optimal target for endoscopic remission."

The study was published in the American Journal of Gastroenterology (2022 Jul 21. doi: 10.14309/ajg.0000000000001912).

The natural history of UC is characterized by frequent relapse, the authors wrote, but "treating symptoms alone is not sufficient to prevent long-term complications."

This led to a shift toward using endoscopic healing as a therapeutic goal, a move that was aided by the advent of novel medical therapies, including biologic agents. Crucially, endoscopic healing is associated with improved long-term outcomes, as well as improved quality of life.

The authors continue, however, that a "significant proportion" of patients experience relapse despite achieving endoscopic healing, which "could be explained in part by the fact that up to 40% of patients in endoscopic healing will have ongoing active histologic disease."

However, in studies in which histologic activity was an endpoint, results have conflicted, and questions remain as to which parameters to include when assessing histologic activity.

Measuring the predictive values of endoscopy and histology

To investigate further, the researchers conducted a prospective observational study of consecutive adult patients with confirmed UC who presented to an endoscopy unit for colonoscopy for disease assessment or surveillance.

The study enrolled 253 patients. Almost half (47.4%) were younger than 50 years, and 46.3% were women. They were followed for 12 months, during which time 19% developed clinical relapse, defined as a partial Mayo endoscopic score (MES) of greater than 2.

When compared with patients with an MES of 0, the team found that patients with an MES of 1 or greater than or equal to 2 were at higher risk of relapse, with an adjusted hazard ratio of 2.65 and 2.57, respectively. A lower baseline MES also was associated with a lower risk of relapse, and patients with proctitis were more likely to experience relapse than those with pancolitis.

Active histology was no more common among those who experienced relapse than among those who did not. But with regard to histologic factors, the team found that the presence of basal plasmacytosis was associated with clinical relapse, at an adjusted odds ratio of 2.07.

On the other hand, a Geboes Score of greater than or equal to 3.1, indicating the presence of epithelial neutrophils with or without crypt destruction or erosions, was not significantly associated with the risk of relapse, nor with the time to clinical relapse.

Clinical implications

Approached for comment, Miguel Regueiro, MD, AGAF, chair of the Digestive Disease and Surgery Institute at Cleveland Clinic, said that this is "the largest prospective study assessing histologic activity or remission to predict future disease relapse in ulcerative colitis."

He said that, based on these findings, "patients who achieve an endoscopic and clinical remission are at a low likelihood of clinical relapse," and added that "these should be the 'treat-to-target' endpoints."

"Patients who have biopsy evidence, [such as] histologic activity based on the Geboes Score, do not require an escalation of therapy or a change in inflammatory bowel disease therapy," Dr. Regueiro said.

He noted, however, that one primary question remains: Aside from surveillance of dysplasia, is there a role for biopsy in cases of UC in which the Mayo score is 0?

"In my practice, I still take biopsies from a previously involved colitis segment, even if Mayo 0," he said.

"If there is histologic activity, I would not increase or optimize the current medications, but I also would not deescalate," Dr. Regueiro added. "I would keep the patient on a regular surveillance colonoscopy regimen, too."

No funding for the study has been reported. Dr. Bessissow has relationships with AbbVie, Alimentiv (formerly Robarts), Amgen, Bristol-Myers-Squibb, Ferring, Gilead, Janssen, Merck, Pentax, Pfizer, Roche, Sandoz, Takeda, and Viatris. Other authors have disclosed numerous financial relationships. Dr. Regueiro has disclosed no such relationships.

AGA Clinical Practice Update: Expert Review

How to manage patients with short-bowel syndrome

BY MARCIA FRELLICK

MDedge News

Caring for patients with short-bowel syndrome (SBS) requires a multidisciplinary approach involving dietitians, nurses, surgeons, gastroenterologists or internists, and social workers experienced in SBS care, according to a clinical practice update expert review from the American Gastroenterological Association.

Kishore Iyer, MD, from Mount Sinai Hospital New York; John K. DiBaise, MD, from Mayo Clinic in Scottsdale, Ariz.; and Alberto Rubio-Tapia, MD, from Cleveland Clinic, developed 12 evidence-based best practice advice statements. The items focus on adult patients with SBS; however, there was some overlap with the management of pediatric SBS. The review was published online in Clinical Gastroenterology and Hepatology (2022 Jun 11. doi: 10.1016/j.cgh.2022.05.032).

Defining SBS

One update concerns defining SBS. The authors recommend that surgeons performing massive resections should report the residual bowel length, rather than the length of bowel resected.

"It is only the former that dictates outcome," they wrote.

There is general agreement that a residual small-intestine length of 200 cm or less meets criteria for SBS. Measurement should be taken from "along the antimesenteric border of unstretched bowel, from the duodenojejunal flexure to the ileocecal junction, the site of any small bowel–colon anastomosis, or to the end-ostomy."

Based on the residual bowel length, patients can be classified into three groups: end-jejunostomy, jejuno-colic, and jejuno-ileo-colic.

Assessing nutritional status

A dietitian experienced in SBS should perform a thorough nutritional assessment on all SBS patients. Long-term monitoring should include laboratory studies checking electrolytes and liver and kidney function, fluid balance, weight change, serum micronutrients, and bone density. Bone density should be repeated periodically, every 2-3 years.

Fluid and electrolyte problems may affect outcomes for SBS patients, particularly for those without a colon.

Adjusting diets

Most adult patients with SBS have significant malabsorption, so dietary intake "must be increased by at least 50% from their estimated needs," the authors wrote. It's best if the patient consumes the increased quantity throughout the day in five to six meals, they noted.

An experienced dietitian should counsel the

Continued on page 27

Continued from page 22

patient based on the patient's eating preferences. Incorporating preferences can help increase compliance with the adjustments that may become necessary based on symptoms, stool output, and weight.

Using pharmacologic therapy

Using antisecretory medications, including proton pump inhibitors or histamine-2 receptor antagonists, helps reduce gastric secretions, the damage of acid on the upper-gut mucosa, and the function of pancreatic exocrine enzymes.

Antidiarrheals reduce intestinal motility but also cause a slight reduction in intestinal secretion. Common agents include loperamide, diphenoxylate with atropine, codeine, and tincture of opium. The review authors say loperamide should get preference over opiate drugs because it is not addictive or sedative.

Use of antidiarrheals should be guided by their effect on stool output.

"Loperamide and codeine may have a synergistic effect when used together," the authors wrote.

Clonidine, which can be given transdermally, has also shown some benefit in treating high-output stool losses, presumably because of its effects on intestinal motility and secretion.

Weighing risks and benefits of teduglutide

The glucagonlike peptide–2 teduglutide is of particular interest for its ability to help improve intestinal absorption and hopefully wean patients off parenteral nutrition and some will achieve enteral autonomy, the authors wrote. "The very short half-life of native GLP-2 has been extended to allow daily subcutaneous injection in the recombinant molecule, teduglutide."

However, because teduglutide is a growth factor and can boost the growth of polyps and cancer, it is contraindicated in patients with active gastrointestinal malignancies. Patients should undergo colonoscopy before treatment and periodically thereafter, the authors advised. The benefits of its use in patients with nongastrointestinal malignancy should be weighed carefully with these risks.

"The significant side effects of teduglutide and the cost mandate that teduglutide is employed only after optimizing diet and the more conventional SBS treatments described previously in carefully selected patients with [short-bowel syndrome–intestinal failure]," the authors wrote.

Dosing drugs effectively

Medications in tablet form need to dissolve before being absorbed. Most oral medications are absorbed within the proximal jejunum, so they can be used in patients with SBS.

"However," the authors noted, "sustained- and delayed-release medications should be avoided."

They suggested that, when applicable, alternatives such as liquids and topical medications should be considered, as should the monitoring of medication levels in the blood.

If a patient does not respond, approaches to consider may include increasing a dose, changing dose frequency, or changing drug formulation or route of administration, such as intravenous, subcutaneous, or transdermal.

Including parenteral nutrition and oral rehydration

Almost all patients with SBS will need parenteral nutrition (PN) support following resection, and few will be able to stop it before discharge from the hospital.

"Although more than 50% of adults with SBS are able to be weaned completely from PN within 5 years of diagnosis, the probability of eliminating PN use is less than 6% if not successfully accomplished in the first 2 years following the individual's last bowel resection," the authors wrote.

For long-term PN, tunneled central venous catheters are preferred over peripherally inserted central venous catheters because of the higher risk of thrombosis and issues related to self-administration of PN with the central catheters. Also, tunneled catheters are preferred over totally implanted devices, or ports, for long-term patients because the main benefit of the port is not realized given that the device needs to be continually accessed and exchanged weekly.

"A knowledge of these complications is critical for those caring for these patients to be able to not only identify and treat them when they occur but also to prevent their occurrence whenever possible."

"When calculating PN volume and content, changes in the patient's weight, laboratory results, stool or ostomy output, urine output, and complaints of thirst should be monitored," the authors noted.

The authors also discussed oral rehydration solution because patients lose more water and sodium from their stoma than they take in by mouth. Careful consideration of the glucose and sodium levels in oral fluids is important because inappropriate fluids will exacerbate fluid losses in SBS. For example, hypotonic (including water, tea, coffee, alcohol) and hypertonic (including fruit juices and sodas) solutions should be limited.

"A major misconception on the part of patients is that they should drink large quantities of water; however, this generally leads to an increase in ostomy output and creates a vicious cycle further exacerbating fluid and electrolyte disturbances," they wrote, instead advising glucose–electrolyte rehydration solution to enhance absorption and reduce secretion.

Preventing complications

"A knowledge of these complications is critical for those caring for these patients to be able to not only identify and treat them when they occur but also to prevent their occurrence whenever possible," the authors wrote. Although they considered it beyond the scope of the review to outline every complication, they indicated some complications and management strategies via an included table. These complications can include cirrhosis, osteoporosis, acute kidney disease, and central venous catheter–related infection or occlusion.

Considering further surgery or intestinal transplantation

The authors noted that any further surgery should be carefully considered, with the following three contexts having possible value: "(1) to recruit unused distal bowel, (2) to augment the function of residual bowel through specific lengthening and tapering operations, or (3) to slow intestinal transit."

Surgeons involved in managing SBS may need to confront complex intra-abdominal problems such as massive desmoid tumors, mesenteric ischemia, or complex enterocutaneous fistulae; a multidisciplinary intestinal rehabilitation team may be better able to help these patients. The authors noted that care for patients starts even before the first operation, by taking every measure to avoid massive bowel resection and the resulting SBS.

The authors noted the importance of early referral for intestinal transplantation consideration for patients with refractory dependency on parenteral nutrition or even onset of parenteral nutrition failure, which refers to complications such as intestinal failure–associated liver disease.

"At present, nearly 50% of patients being considered for ITX are also requiring simultaneous liver replacement, indicating late referral for ITX," they wrote, citing a data from a report by the Centers for Medicare & Medicaid (Fed Regist. 2007 Mar 30;72[61]:15197-280).

They also noted that data have shown short- and medium-term outcomes are steadily improving (Am J Transplant. 2019 Jul;19[7]:2077-91); however, long-term outcomes have been challenged by opportunistic infections, long-term graft attrition, and other impediments that may be preventing early referral for intestinal transplantation.

Educating patients, caregivers

Long-term PN may restrict activity for patients, but patients and caregivers should know about some modifications.

One is to cycle the PN over 10-14 hours overnight to allow freedom from the infusion pump during the day. Infusion pumps can be programmable, and some can be carried in a backpack for infusing during the day.

Authors recommend patient support groups, such as the Oley Foundation, which can help with issues surrounding body image and travel.

Because of the relative rarity of SBS, nonspecialist physicians may care for patients without a dedicated multidisciplinary team and may need education support in managing patients with complex care needs. One source the authors recommend is the Learn Intestinal Failure Tele-ECHO (Expanding Community Healthcare Outcomes) (LIFT-ECHO) project. The LIFT-ECHO project has become an online educational community with case-based learning in SBS, intestinal failure, and PN.

The authors disclose relationships with Takeda, Zealand, VectivBio, Napo, and Hanmi. ■

No evidence that NSAIDs cause IBD flares: Study

BY MEGAN BROOKS

A new study has found no convincing evidence to suggest a causal relationship between NSAID use and inflammatory bowel disease (IBD) exacerbations.

Rather, the study suggests that observed associations between IBD exacerbation and NSAID exposure may be explained by preexisting underlying risks for IBD flares, residual confounding, and reverse causality.

"We hope these study findings will aid providers in better directing IBD patients on their risk for IBD exacerbation with NSAID use," write Shirley Cohen-Mekelburg, MD, with University of Michigan Medicine, Ann Arbor, and colleagues.

"This may guide therapy for both IBD and non-IBD related pain management, and the comfort of patients with IBD and the clinicians who treat them when considering NSAIDs as a non-opioid treatment option," they add.

The study was published online in the American Journal of Gastroenterology (2022 Aug 12. doi: 10.14309/ajg. 0000000000001932).

Taking a second look

To see whether an association exists, Dr. Cohen-Mekelburg and colleagues conducted a series of studies that involved roughly 35,000 patients with IBD. First, they created a propensity-matched cohort of 15,705 patients who had received NSAIDs and 19,326 who had not taken NSAIDs. Findings from a Cox proportional hazards model suggested a higher likelihood of IBD exacerbation in the group that had taken NSAIDs (hazard ratio, 1.24; 95% confidence interval, 1.16-1.33), after adjusting for age, gender, race, Charlson comorbidity index, smoking status, IBD type, and use of immunomodulator or biologic medications.

However, those who received NSAIDs were already at increased risk of experiencing a disease flare. And the prior event rate ratio for IBD exacerbation, as determined by dividing the adjusted HR after NSAID exposure by the adjusted HR for pre-NSAID exposure, was 0.95 (95% CI, 0.89-1.01).

The researchers used a self-controlled case series to verify their findings and to adjust for other immeasurable patient-level confounders. In this analysis, which involved 3,968 patients, the risk of IBD flare did not increase in the period from 2 weeks to 6 months after exposure to an NSAID.

The incidence of IBD exacerbations was higher in the 0- to 2-week transition period after an NSAID was prescribed, but it dropped after the 2-week "risk" window. This suggests that these short-term flares may be secondary to residual confounding related to reverse causality, rather than the NSAIDs themselves, the researchers say.

While NSAIDs represent the most common first-line analgesic, their use for patients with IBD is variable, in part due to the suspected risk of IBD exacerbation "despite inconclusive evidence of harm to date," Dr. Cohen-Mekelburg and colleagues note.

They also note that about 36% of patients with IBD in their cohort received at least one NSAID prescription, and three-quarters of these patients did not experience an IBD exacerbation during an average of 5.9 years of follow-up.

Good study, reassuring data

"This is a good study trying to understand the potential sources of bias in associations," Ashwin Ananthakrishnan, MBBS, MPH, with Massachusetts General Hospital and Harvard Medical School in Boston, who wasn't involved in the study, told this news organization.

Overall, he said the study "provides reassurance that cautious, short-duration or low-dose use is likely well tolerated in most patients with IBD. But more work is needed to understand the impact of higher dose or more frequent use."

Also weighing in, Adam Steinlauf, MD, with Mount Sinai Health System and Icahn School of Medicine at Mount Sinai in New York, noted that patients with IBD experience pain throughout the course of their disease, both intestinal and extraintestinal.

"Treating the underlying IBD is important, but medications used to treat joint pain and inflammation specifically are few," said Dr. Steinlauf, who wasn't involved in the new study.

"Sulfasalazine has been used with success, but it does not work in everyone, and many are allergic to the sulfa component, limiting its use. Narcotics are often reluctantly used for these issues as well. Medical marijuana has emerged on the scene to control both types of pain, but to date, there is inconclusive evidence that it significantly treats both pain and underlying inflammation," Dr. Steinlauf pointed out.

NSAIDs, on the other hand, are "excellent" choices for treating joint pain and inflammation, but gastroenterologists often try to avoid these medications, given the fear of triggering flares of underlying IBD, Dr. Steinlauf told this news organization.

In his view, this new study is "important in that it quite elegantly challenges the notion that gastroenterologists should avoid NSAIDs in patients with IBD."

Although more data are clearly needed, Dr. Steinlauf said this study "should give practitioners a bit more confidence in prescribing NSAIDs for their patients with IBD if absolutely necessary to control pain and inflammation and improve quality of life when other standard treatments fail.

"The association of NSAIDs with subsequent flares, of which we are all so well aware of and afraid of, may in fact be related more to our patients' underlying risks for IBD and reverse causality rather than the NSAIDs themselves. Future studies should further clarify this notion," Dr. Steinlauf said.

The study received no commercial funding. Dr. Cohen-Mekelburg, Dr. Ananthakrishnan, and Dr. Steinlauf have disclosed no relevant financial relationships. ■

Characterizing locales

Neighborhood *from page 1*

within Texas, incidence rates vary by race, ethnicity, and geographic location.

The Baylor team examined these disparities at the neighborhood level, with a focus on measures of social determinants of health and the industries where most neighborhood residents work.

They identified 11,547 Texas residents diagnosed with HCC between 2011 and 2015, at a mean age of 63 years. Roughly three-quarters were men, and 44% were non-Hispanic White, 14% non-Hispanic Black, 37% Hispanic, and 5% other.

The researchers used demographics, socioeconomic status, and employment provided by the U.S. Census Bureau to characterize the neighborhoods where these people lived when they were diagnosed with HCC.

Among their key findings, the risk for HCC among African American and Hispanic residents was highest in West Texas, South Texas, and the panhandle. However, some factors, like age and socioeconomic status, were not affected by location.

Across the entire state, however, people older than 60 years and those of low socioeconomic status had a higher relative risk for HCC.

Two areas of employment – construction and service occupations – also stood out as being associated with a higher risk for HCC, whereas employment in agriculture was associated with lower risk.

The authors caution that the ecological nature of the study precludes any firm conclusions regarding a causal link between working in these industries and HCC.

"Further research, including longitudinal studies, [is] needed to clarify the roles of specific occupations in HCC risk," corresponding author Abiodun Oluyomi, PhD, said in the news release.

"Our findings validate factors previously associated with HCC, and our geographic analysis shows areas of Texas where specific intervention strategies may be most relevant," Dr. Oluyomi added.

This research was supported by the Cancer Prevention & Research Institute of Texas. The authors have no relevant disclosures. ■

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 (https://gastro.org/aga-leadership/initiatives-and-programs/aga-equity-project/).

New blood test could reshape early CRC screening

BY TARA HAELLE

A simple blood test that looks for a combination of specific RNA snippets may become a novel way to screen for early-onset colorectal cancer, suggests a new study published online in Gastroenterology (2022 Jul 15. doi: 10.1053/j.gastro.2022.06.089).

Researchers identified four microRNAs that together compose a signature biomarker that can be used to detect and diagnose the presence of colorectal cancer from a liquid biopsy in a younger population (Curr Genomics. 2010 Nov;11[7]:537-61).

MicroRNAs, or miRNAs, are small RNA molecules that do not encode proteins but are used instead to regulate gene expression. The study authors developed and validated a panel that detects four miRNAs occurring at higher levels in plasma samples from patients with early-onset colorectal cancer, with high sensitivity and specificity.

"The point would be to use this test as a routine part of annual health care, or for people in high-risk families every 6 months."

"The point would be to use this test as a routine part of annual health care, or for people in high-risk families every 6 months," study senior author Ajay Goel, PhD, MS, AGAF, chair of the department of molecular diagnostics and experimental therapeutics at the City of Hope Comprehensive Cancer Center, Duarte, Calif., said in an interview.

"It's affordable, it can be done easily from a small tube of blood, and as long as that test stays negative, you're good," Dr. Goel said, because even if patients miss a test, the next one, whether it's 6 months or a year later, will catch any potential cancer.

"Colon cancer is not going to kill somebody overnight, so this should be used as a precursor to colonoscopy. As long as that test is negative, you can postpone a colonoscopy," he said.

Andrew T. Chan, MD, MPH, AGAF, a professor of medicine at Harvard Medical School and vice chair of gastroenterology at Massachusetts General Hospital, both in Boston, who was not involved in the research, said in an interview that the findings are exciting.

"It would be really value-added to have a blood-based screening test," Dr. Chan said, adding that researchers have pursued multiple different avenues in pursuit of one. "It's very nice to see that area progress and to actually have some evidence that microRNAs could be a potential biomarker for colorectal cancer."

Screening now insufficient for early-onset disease

The U.S. Preventive Services Task Force recently lowered the recommended age to 45 years to begin screening for colorectal cancer. Part of the rationale for the change came from the rising rates of early-onset colorectal cancer, a distinct clinical and molecular entity that tends to have poorer survival than late-onset disease, the authors noted.

Early-onset disease, occurring primarily in people under 50 without a family or genetic history of colorectal cancer, now makes up

Continued on following page

Continued from previous page

about 10%-15% of all new cases and continues to rise, they write.

"Early-onset colorectal cancer patients are more likely to exhibit an advanced stage tumor at initial presentation, distal tumor localization, signet ring histology, and a disease presentation with concurrent metastasis," the authors wrote. "This raises the logistical clinical concern that, since the tumors in early-onset colorectal cancer patients are often more aggressive than those with late-onset colorectal cancer, a delayed diagnosis could have a significant adverse impact and can lead to early death."

Yet current screening strategies are insufficient for detecting

YakobchukOlena/iStock/Getty Images

enough early-onset cases, the authors assert.

Colonoscopies are invasive, carry a risk for complications, and are cost- and time-prohibitive for people at average risk. Meanwhile, existing fecal and blood tests "lack adequate diagnostic performance for the early detection of colorectal cancer, especially early-onset colorectal cancer, as these assays have yet to be explored or developed in this population," they wrote.

The ideal "diagnostic modality should preferably be acceptable to healthy individuals, inexpensive, rapid, and preferably noninvasive," they note.

Finding and validating miRNA

The researchers therefore turned to the concept of a liquid biopsy, focusing on identifying miRNAs associated with colorectal cancer, because their expression tends to be stable in tissues, blood, stool, and other body fluids.

They first analyzed an miRNA expression–profiling dataset from 1,061 individuals to look for miRNAs whose expression was higher in colorectal cancer patients. The dataset included 42 patients with stage 1-2 early-onset colorectal cancer, 370 patients with stage 1-2 late-onset colorectal cancer, 62 patients younger than 50 years without cancer, and 587 patients aged 50 years or older without cancer.

The researchers found a total of 28 miRNAs that were significantly unregulated in early-onset colorectal cancer tissue samples, compared with cancer-free samples and 11 miRNAs unregulated specifically in only the early-onset colorectal cancer samples. Four of these 11 miRNAs were adequately distinct from one another and were detectable in the plasma samples that the researchers would use to train and validate them as a combination biomarker.

The researchers used 117 plasma samples from Japan, including 72 from people with early-onset colorectal cancer and 45 from healthy donors, to develop and train an assay detecting the four miRNAs. They then validated the assay using 142 plasma samples from Spain, including 77 with early-onset colorectal cancer and 65 healthy donors.

In the Japan cohort, the four-miRNA assay had a sensitivity of 90% and a specificity of 80%, with a positive predictive value (PPV) of 88% and a negative predictive value (NPV) of 84%. In the Spain cohort used for validation, the assay performed with a sensitivity of 82%, a specificity of 86%, a PPV of 88%, and an NPV of 80%.

"Taken together, the genome-wide transcriptomic profiling approach was indeed robust, as it identified the biomarkers that were successfully trained and validated in plasma specimens from independent cohorts of patients with early-onset colorectal cancer, hence highlighting their translational potential in the clinic for the detection of this malignancy in early stages," the authors wrote.

By disease stage, the four-miRNA panel identified both early-stage (stage 1-2; sensitivity, 92%; specificity, 80%) and late-stage (stage 3-4; sensitivity, 79%; specificity, 86%) early-onset colorectal cancer in the validation cohort.

Clinical benefit of blood test

The researchers also assessed the benefit-harm trade-off of this liquid biopsy assay compared with other screening modalities, taking into consideration the risk for false positives and false negatives.

A decision curve analysis "revealed that the miRNA panel achieved a higher net benefit regardless of threshold probability in comparison to intervention for all patients or none of the patients," the researchers reported. "These findings suggest that this miRNA panel might offer more clinical benefit with regards to the avoidance of physical harm and misdiagnosis."

They also found that expression levels of these four miRNAs significantly decreased after surgical removal of the colorectal cancer, strongly suggesting that the miRNAs do originate with the tumor.

"To have a relatively inexpensive and noninvasive means of screening a younger population is a very important unmet need," said Dr. Chan.

It's not feasible to recommend colonoscopies in people younger than 45 years because of resource constraints, he said, so "this is a wonderful new development to actually have the possibility of a blood-based screening test for younger individuals, especially given that rising incidence of young-onset colorectal cancer."

Dr. Goel pointed out that only half of those recommended to get screened for colorectal cancer actually undergo screening, and a large reason for that is the desire to avoid colonoscopy, a concern echoed in the findings of a recent study by Christopher V. Almario, MD, MSHPM, and colleagues.

Dr. Goel expects that this strategy would increase compliance with screening because it's less invasive and more affordable, particularly for younger patients. He estimates that a commercial assay using this panel, if approved by the Food and Drug Administration, should cost less than $100.

Dr. Almario, an assistant professor of medicine at the Cedars-Sinai Karsh Division of Gastroenterology and Hepatology in Los Angeles,

The ideal "diagnostic modality should preferably be acceptable to healthy individuals, inexpensive, rapid, and preferably noninvasive."

agreed that an FDA-approved blood-based screening test would be a "game-changer," as long as it's accurate and effective.

Though Dr. Almario did not review the data in Goel's study, he said in an interview that a blood test for colorectal cancer screening would be "the holy grail, so to speak, in terms of really moving the needle on screening uptake."

Next steps

Dr. Chan noted that one caveat to consider with this study is that it was done in a relatively small population of individuals, even though the test was validated in a second set of plasma samples.

"Additional validation needs to be done in larger numbers of patients to really understand the performance characteristics because it is possible that some of these signatures may, when they're using a broader group of individuals, not perform as well," Dr. Chan said.

Dr. Goel said he is working with several companies right now to develop and further test a commercial product. He anticipates it may be shelf-ready in 2-5 years.

"The take-home message is that clinicians need to be more cognizant of the fact that incidence of this disease is rising, and we need to do something about it," Dr. Goel said, particularly for those younger than 45 years who currently don't have a screening option.

"Now we have at least a sliver of hope for those who might be suffering from this disease, for those for whom we have zero screening or diagnostic tests," he said.

The research was funded by the National Cancer Institute and Fundación MAPFRE Guanarteme. Dr. Goel, Dr. Chan, and Dr. Almario reported no conflicts of interest. ■

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After index colonoscopy, what's the CRC risk by age?

BY PAM HARRISON

New data suggest that, for individuals who do not have an adenoma detected on an index colonoscopy, the risk of developing an advanced neoplasia (AN) and colorectal cancer (CRC) is lower in those who are aged 40-49 years, compared with those who are 50-59 years old.

However, there is no difference between the two age groups in detection rates of nonadvanced adenoma (NAA) or advanced adenoma (AA), the same study found.

"The primary goal of this study was to investigate the risk of metachronous AN associated with conventional adenoma detected on the index colonoscopy," explain the authors, led by Gene Ma, MD, Kaiser Permanente Northern California, San Jose.

"The lack of good-quality evidence to inform surveillance in the 40-49 year old population has resulted in inconsistent surveillance patterns in clinical practice, leading to variation in the quality of care, including both inadequate and excessive colonoscopic surveillance," Dr. Ma and colleagues observe.

The findings from this study "expand our understanding of the risk of AN and CRC in younger individuals and suggest that the current multi-society guidelines for surveillance may be applicable for individuals 40-49 years of age," the authors conclude.

The study was published online Aug. 12 in the American Journal of Gastroenterology (2022. doi: 10.14309/ajg.0000000000001946), and included 2,396 individuals between 40 and 49 years of age and 8,978 individuals between 50 and 59 years of age.

The colonoscopy was carried out for screening in 40.2% in the younger age group versus 34.8% in the older age group and was prompted by a positive fecal immunochemical test in 3.3% of the younger age group versus 32% of the older age group.

The median follow-up for both age groups was roughly 7 years.

"When comparing the 40-49 years group to the 50-59 years group, index colonoscopy detected no adenoma in 62.9% versus 40.1% ($P < .0001$); NAA in 25.4% versus 39.0% ($P < .001$), and AA in 11.6% versus 21.0% ($P < .0001$), respectively," Dr. Ma and colleagues report.

When the two age groups were compared for surveillance colonoscopy, no adenoma was detected in 67% of the younger age group versus 54.7% of the older age group ($P < .0001$), whereas NAA was detected in 25.4% of the 40- to 49-year-olds versus 38.4% of the 50- to 59-year-olds ($P < .0001$). AA was detected in 3.5% versus 6.95 ($P < .0001$) of persons in each of the two age groups, respectively.

AN was detected on surveillance colonoscopy after index colonoscopy in 2.2% of the younger age group and twice that percentage, at 4.4%, in the older age group ($P = .0003$). On surveillance colonoscopy, NAA was found in 4.6% of the younger age group, compared with 7% of the older age group ($P = .03$), whereas AA was found in 7.9% of the 40- to 49-year-olds, compared with 11.7% of the 50- to 59-year-olds ($P = .06$).

The median time until surveillance colonoscopy was similar in both age groups when either NAA or AA was found on index colonoscopy, the authors note. In addition, the median time until the detection of AN was similar whether NAA or AA was detected on index colonoscopy, they add.

The overall crude cumulative incidence of AN was lower in the younger age group when no adenoma was detected on index colonoscopy ($P = .0003$) as well as when NAA was detected, which would be consistent with recommendations from current guidelines for surveillance colonoscopy after adenoma detection. However, there was no difference between the two age groups in the overall cumulative incidence of AN when AA was detected on index colonoscopy.

Overall, the risk for metachronous AN in persons aged 40-49 years was lower when no adenoma was detected on index colonoscopy, but there was no difference between the two age groups when NAA or AA was detected again on index colonoscopy. Similarly, those aged 40-49 years of age had a lower risk for AA or CRC when no adenoma was detected on index colonoscopy – but again, there was no difference in the risk for AA or CRC when either NAA or AA was detected on index colonoscopy.

The authors have no conflicts of interest to report.

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What's your diagnosis?" on page 21: Whipple's disease.

The ultrasound features were highly suggestive of malabsorption, a hypothesis that was supported by the laboratory findings. Celiac disease, one of the most common causes of malabsorption, was excluded by serology tests. Esophagogastroduodenoscopy was therefore repeated: The mucosa of the distal first part and second part of the duodenum appeared completely covered with tiny white spots (Figure C). Histologic examination revealed that the mucosal architecture of the villi was altered by the presence of infiltrates of macrophages with wide cytoplasm filled with round periodic acid-Schiff (PAS)–positive inclusions, associated to aggregates of neutrophils attacking the epithelium (Figure D). These histologic findings are consistent with Whipple's disease.

Whipple's disease is a chronic infectious disease caused by a gram-positive ubiquitous bacterium named *Tropheryma whipplei*. In predisposed subjects with an insufficient T-helper response, for example, those undergoing treatment with tumor necrosis factor–alpha inhibitors as in our patient, *T. whipplei* is able to survive and replicate inside the macrophages of the intestinal mucosa and to spread to other organs.[1] Whipple's disease can thus manifest as a multisystemic disease or as a single-organ disease with extraintestinal involvement (e.g., central nervous system, eyes, heart, or lung). The classic form is characterized by weight loss, diarrhea, abdominal pain, and signs of malabsorption, typically preceded by a history of arthralgia. The arthralgia is often misdiagnosed as a form of rheumatoid arthritis and therefore treated with immunosuppressant therapy, which favors the onset of the classic intestinal symptoms.

In the literature, few case reports describe the ultrasound findings in patients with Whipple's disease. The most frequent sonographic features include small-bowel dilatation with wall thickening, the presence of peri-intestinal fluid effusion and mesenteric and retroperitoneal lymphadenopathy.[2,3]

The final diagnosis relies on intestinal biopsy and the histologic finding of foamy macrophages containing large amounts of diastase-resistant PAS-positive particles in the lamina propria of the duodenum, jejunum, ileum, or gastric antral region. The diagnosis, particularly in cases of extraintestinal involvement, can be confirmed by polymerase chain reaction positivity for *T. whipplei* in the examined tissue.

Therapy consists of the administration of ceftriaxone (2 g IV once daily) for 2 weeks followed by oral therapy with trimethoprim-sulfamethoxazole for 1 year.

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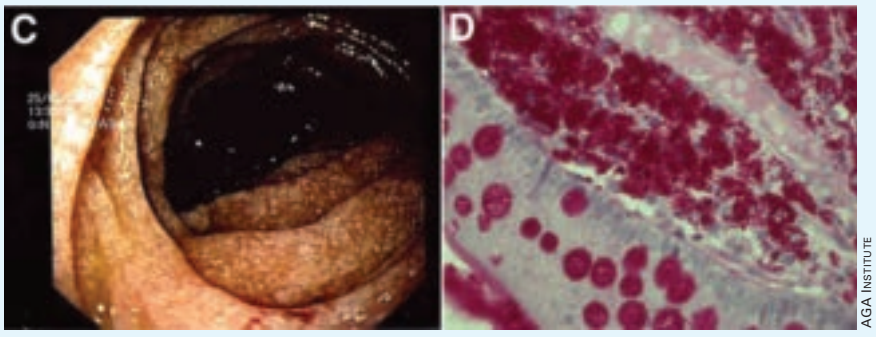


AGA INSTITUTE

A third of adults worldwide may have NAFLD

BY MEGAN BROOKS

The global prevalence of fatty liver disease not caused by alcohol is considerably higher than previously estimated and is continuing to increase at an alarming rate, report researchers from Canada.

Their analysis suggests nearly one-third of the global general adult population has nonalcoholic fatty liver disease (NAFLD), with men much more likely to have the disease than women.

"Greater awareness of NAFLD and the development of cost-effective risk stratification strategies are needed to address the growing burden of NAFLD," wrote Abdel-Aziz Shaheen, MBBCh, MSc, and colleagues with the University of Calgary (Alta.) in Lancet Gastroenterology and Hepatology (2022 Jul 4. doi: 10.1016/S2468-1253[22]00165-0).

High-quality reports on the epidemiology of NAFLD at a global level are scarce and temporal trends of the NAFLD burden, including by gender, have not been described, until now.

The Calgary team identified reports on NAFLD incidence and prevalence in study populations representative of the general adult population published between the date of database inception to May 25, 2021. In total, 72 publications, with a sample population of more than 1 million adults from 17 countries, were included in the prevalence analysis, and 16 publications, with a sample population of nearly 382,000 individuals from 5 countries, were included in the incidence analysis.

"Greater awareness of NAFLD and the development of cost-effective risk stratification strategies are needed to address the growing burden."

By their estimates, the overall global prevalence of NAFLD is 32.4%, with prevalence increasing steadily and significantly over time, from 25.5% in or before 2005 to 37.8% in 2016 or later. The overall prevalence is significantly higher in men than in women (39.7% vs. 25.6%).

These figures contrast with recent meta-analyses and systematic reviews that put the global prevalence of NAFLD at between 25.2% and 29.8%. However, these studies had "considerable" limitations with "potentially biased inferences," Dr. Shaheen and colleagues noted.

By region, their data put the prevalence of NAFLD at 31.6% in Asia, 32.6% in Europe, 47.8% in North America, and 56.8% in Africa.

Dr. Shaheen and colleagues said the rise in NAFLD prevalence "should drive enhanced awareness of NAFLD at the level of primary care physicians, public health specialists, and health policy makers to encourage the development of more effective preventive policies."

Funding for the study was provided by the Canadian Institutes of Health. Dr. Shaheen has received research grants from Gilead and Intercept, and honoraria from SCOPE Canada.

Degree of PPG reduction linked with ascites control after TIPS

BY CAROLYN CRIST
MDedge News

A reduction in portal hepatic pressure gradient (PPG) soon after implantation of a transjugular intrahepatic portosystemic shunt (TIPS) greater than 60% was associated with improved ascites control at 6 weeks in a study published in Hepatology (2022 July 23. doi:10.1002/hep.32676).

"The probability of ascites resolution is much higher if PPG reduction exceeded 60% of PPG before TIPS," wrote the researchers, led by co–first authors Alexander Queck, MD, a postdoctoral researcher in the department of internal medicine at University Hospital Frankfurt (Germany) and Goethe University Frankfurt, and Louise Schwierz, MD, of the department of internal medicine in the University Hospital Bonn (Germany). "This study suggests that, even in patients with uncomplicated TIPS insertion, a short-term follow-up 6 weeks after TIPS should be scheduled to be able to predict their course of disease."

The authors investigated the decrease of PPG in a single-center, retrospective analysis of 341 patients with liver cirrhosis undergoing TIPS insertion for recurrent or refractory ascites between March 1994 and July 2015. During each procedure, portal and inferior vena cava pressures were invasively measured and correlated with patients' outcomes and ascites progression over time. In 241 patients, or 71%, chronic alcohol consumption was the reason for cirrhosis development, followed by 13% with chronic viral hepatitis (n = 43). Median survival after TIPS insertion was 102 weeks, and 19 patients received liver transplants over time.

Median portal pressure before TIPS placement was 28 mm Hg, which decreased to a median of 21 mm Hg after TIPS. Median PPG levels were 19 mm Hg before TIPS and 8 mm Hg immediately after TIPS placement.

At the time of TIPS placement, 65 patients, or 19%, had hepatic encephalopathy, and 9 had severe hepatic encephalopathy. Six weeks after TIPS, two had episodes of hepatic encephalopathy.

After 6 weeks, ascites significantly improved through TIPS insertion. About 47% had a complete resolution of ascites at 6 weeks, whereas 29% had ascites detectable only by ultrasound and 24% of patients still needed large-volume paracentesis. There was an association between extent of PPG reduction and ascites resolution: Median PPG reduction was 55% of initial PPG in patients with persistence of severe ascites, 58% in patients with ascites detected by ultrasound, and 65% in patients with complete resolution of ascites at 6 weeks after TIPS.

Hispanolistic/Getty Images

Ascites resolved in 54% of patients with higher PPG reduction (60% or above), compared with 39% of patients with lower PPG reduction (below 60%). Ascites was detected by ultrasound in another 27% of patients with higher PPG reduction, compared with 31% of patients with lower PPG reduction. In addition, persistent severe ascites was seen in 19% of patients with higher PPG reduction, compared with 30% of patients with lower PPG reduction.

The authors also noted the importance of timing follow-up evaluation: They noted that post-TIPS follow-up is a frequent question and not yet standardized; in this study, they found that, with follow-up at 6 weeks, they could "clearly stratify the course post TIPS" and this could "detect patients at high risk of unstable course of disease."

PPG reduction of more than 60% after TIPS correlated with

Continued on following page

Substantial benefit seen with living-donor transplants

BY CAROLYN CRIST
MDedge News

Living-donor liver transplant recipients gained an additional 13-17 years of life, compared with patients who remained on the wait list, according to a retrospective case-control study.

The data suggest that the life-years gained are comparable to or greater than those conferred by either other lifesaving procedures or liver transplant from a deceased donor, wrote the researchers, led by Whitney Jackson, MD, assistant professor of gastroenterology and medical director of living-donor liver transplantation at the University of Colorado Anschutz Medical Campus.

"Despite the acceptance of living-donor liver transplant as a lifesaving procedure for end-stage liver disease, it remains underused in the United States," the authors wrote in JAMA Surgery (2022 Aug 3. doi: 10.1001/jamasurg.2022.3327). "This study's findings challenge current perceptions regarding when the survival benefit of a living-donor transplant occurs."

"Despite the acceptance of living-donor liver transplant as a lifesaving procedure for end-stage liver disease, it remains underused in the United States."

Dr. Jackson and colleagues conducted a retrospective, secondary analysis of the Scientific Registry of Transplant Recipients database for 119,275 U.S. liver transplant candidates and recipients from January 2012 to September 2021. They assessed the survival benefit, life-years saved, and the Model for End-Stage Liver Disease incorporating sodium levels (MELD-Na) score at which the survival benefit was obtained, compared with those who remained on the wait list.

The research team included 116,455 liver transplant candidates who were 18 and older and assigned to the wait list, as well as 2,820 patients who received a living-donor liver transplant. Patients listed for retransplant or multiorgan transplant were excluded, as were those with prior kidney or liver transplants.

The mean age of the study participants was 55 years, and 63% were men. Overall, 70.2% were White, 15.8% were Hispanic or Latinx, 8.2% were Black or African American, 4.3% were Asian, 0.9% were American Indian or Alaska Native, and 0.2% were Native Hawaiian or Pacific Islander. The most common etiologies were alcoholic cirrhosis (23.8%) and nonalcoholic steatohepatitis (15.9%).


Dr. Jackson

Compared with patients on the wait list, recipients of a living-donor liver transplant were younger, more often women, more educated, and more often White. A greater proportion of transplant recipients had a primary etiology of nonalcoholic steatohepatitis (19.8%) and cholestatic liver disease (24.1%). At wait list placement, one-third of candidates had a MELD-Na score of 14 or higher.

The research team found a significant survival benefit for patients receiving a living-donor liver transplant based on mortality risk and survival scores. The survival benefit was significant at a MELD-Na score as low as 11, with a 34% decrease (95% confidence interval, 17.4%-52.0%) in mortality compared with the wait list. In addition, mortality risk models confirmed a survival benefit for patients with a MELD-Na score of 11 or higher at 1 year after transplant (adjusted hazard ratio, 0.64; 95% CI, 0.47-0.88; $P = .006$). At a MELD-Na score of 14-16, mortality decreased by about 50% (aHR, 0.47; 95% CI, 0.34-0.66; $P < .001$).

The probability of death from a living-donor liver transplant for patients with very low MELD-Na scores (between 6 and 10) was greater than that for patients on the wait list for the first 259 days, at which point the risk of death for both groups was equal. At 471 days, the probability of survival in both groups was equal. As the MELD-Na score increased, both the time to equal risk of death and the time to equal survival decreased, demonstrating that the survival benefit occurs much earlier for patients with a higher MELD-Na score.

Analysis of life-years from transplant showed living-donor transplant recipients gained 13-17 life-years compared to those who didn't receive one.


Dr. Dhanasekaran

"Living-donor liver transplantation is a valuable yet underutilized strategy to address the significant organ shortage and long waiting times on the transplant list in the U.S.," said Renu Dhanasekaran, MD, PhD, assistant professor of gastroenterology and hepatology at Stanford (Calif.) University.

Dr. Dhanasekaran, who wasn't involved with this study, also welcomed the finding that living-donor liver transplantation can benefit patients with low MELD-Na scores, even below the expected cutoff at 15. According to the study authors, previous research had suggested benefit would be seen only at MELD-Na 15 and above (Am J Transplant. 2005;5(2):307-13).

"In my practice, I have several patients whose symptoms are out of proportion to their MELD score, and data like this will convince them and their potential donors to avail a transplant at an earlier stage," she said.

The findings challenge the current paradigm around the timing of referral for a liver transplant and may have ramifications for allocation policies for deceased donors, the study authors wrote. The data can also help to contextualize risk-benefit discussions for donors and recipients.

"Donating a part of one's liver to save a patient suffering from end-stage liver disease is an incredible act of selfless love," Dr. Dhanasekaran said. "I hope strong positive data from studies like this one encourage more donors, patients, and transplant centers to expand the use of [living-donor liver transplant]."

The authors reported no grant support or funding sources for this study. One author disclosed being married to the current chair of the United Network for Organ Sharing's Liver and Intestinal Organ Transplantation Committee. No other conflicts of interest were reported. Dr. Dhanasekaran reported no relevant disclosures. ■

Continued from previous page

resolution of severe ascites 6 weeks after TIPS, the study authors concluded.

"This is one of the first studies that highlights the optimal goal for a portal pressure gradient in the setting of refractory ascites post TIPS procedure," said Neeral Shah, MD, AGAF, an associate professor of gastroenterology and hepatology and transplant hepatology specialist at the University of Virginia, Charlottesville.

"It is exciting to see some data from patients examining a question we have always thought to be true but have never quantified," he said. "As a clinician who refers patients for TIPS, one of my biggest concerns is that significant shunting of blood past liver tissue through a TIPS can lead to the development of confusion."


Dr. Shah

Dr. Shah, who wasn't involved with the study, pointed to ongoing questions about hepatic encephalopathy around TIPS. The study authors didn't find an issue with this among their study population, and some patients had improvements in their mental status after TIPS.

"This has not been my experience in those patients with hepatic encephalopathy at baseline pre-TIPS," Dr. Shah said. "This point will need to be clarified further, especially if we are aiming for portal pressure gradients of 10 mm Hg or less in all patients with refractory ascites."

The study authors declared that the research was conducted without commercial or financial relationships that could be construed as a potential conflict of interest. The authors were supported by the German Research Foundation, the German Federal Ministry of Education and Research, the European Union's Horizon 2020 research program, and Goethe University Frankfurt. Dr. Shah reported no relevant disclosures. ■

AGA Clinical Practice Update: Expert Review

Endoscopic management for recurrent pancreatitis

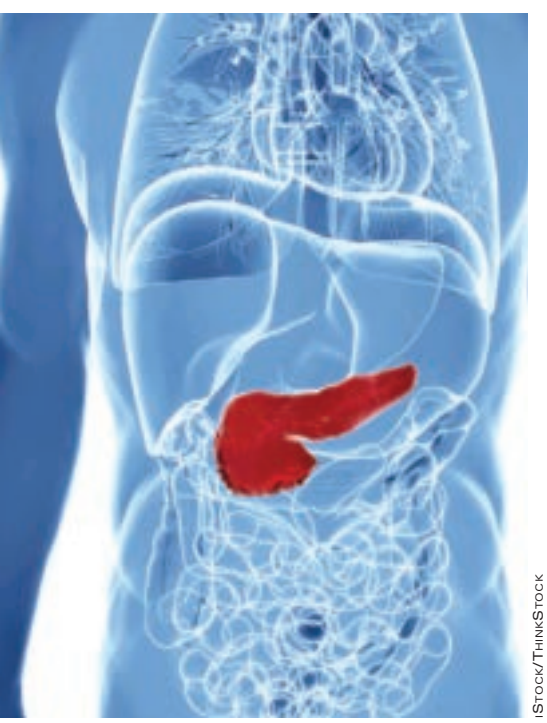
BY CAROLYN CRIST
MDedge News

Endoscopy plays an integral role in the evaluation and management of patients with recurrent acute pancreatitis and chronic pancreatitis, according to a new American Gastroenterological Association clinical practice update published in Gastroenterology (2022 Aug 22. doi: 10.1053/j.gastro.2022.07.079).

Acute pancreatitis remains the leading cause of inpatient care among gastrointestinal conditions, with about 10%-30% of patients developing recurrent acute pancreatitis, wrote co–first authors Daniel Strand, MD, from the University of Virginia Health System, Charlottesville, and Ryan J. Law, MD, from the Mayo Clinic, Rochester, Minn., and colleagues. About 35% of patients with recurrent acute pancreatitis will progress to chronic pancreatitis. Both conditions are associated with significant morbidity and mortality.

"Interventions aimed to better evaluate, mitigate the progression of, and treat symptoms related to [acute pancreatitis] and [chronic pancreatitis] are critical to improve patients' quality of life and other long-term outcomes," the authors of the expert review wrote.

The authors reviewed randomized controlled trials, observational studies, systematic reviews and meta-analyses, and expert consensus in the field to develop eight clinical practice advice statements.



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First, when the initial evaluation reveals no clear explanation for acute or recurrent pancreatitis, endoscopic ultrasound is the preferred diagnostic test. The authors noted that, although there isn't a concretely defined optimal timing for EUS defined, most experts advise a short delay of 2-6 weeks after resolution of acute pancreatitis. MRI with contrast and

Continued on following page

Progress of the AGA Equity Project

BY SANDRA QUEZADA, MD, MS, AGAF, AND BYRON CRYER, MD

In May 2022, the Digestive Disease Week (DDW) conference was held in person again for the first time in 3 years. Two years prior in July 2020 AGA launched the Equity Project, a six-point strategic plan to achieve equity and eradicate health disparities in digestive diseases.

President John Inadomi elected to focus his AGA Presidential Plenary session on updates in gastrointestinal and hepatic health disparities, and opened with a powerful testimony on his personal experiences encountering racism, and recognizing the need to translate spoken intentions into action.

Concrete action items were identified by a coalition of AGA members with diverse representation across specialties, practice settings, and identities. AGA staff and constituency programs have been critical in the execution of each action item.

This served as the perfect segue to the second plenary presentation in which an update was given on the progress of the Equity Project by co-chairs Byron Cryer, MD, and Sandra Quezada, MD, MS. Dr. Cryer described the vision of the Equity Project, including a just world, free of inequities in access and health care delivery; state-of-the-art and well-funded research of multicultural populations; a diverse physician and scientist workforce and leadership; recognition of achievements of people of color; membership and staff committed to self-awareness and eliminating unconscious bias; and an engaged, large, diverse, vocal, and culturally and socially aware early career membership.

Dr. Quezada

Dr. Cryer

Concrete action items were identified by a coalition of AGA members with diverse representation across specialties, practice settings, and identities. AGA staff and constituency programs have been critical in the execution of each action item. Key performance indicators were selected to gauge progress and hold the organization accountable in implementation of project tactics. These metrics demonstrate that the first 2 years of the Equity Project have been very productive. Salient accomplishments include three congressional briefings on health disparities topics, increased education and dialogue on diversity, equity, and inclusion (DEI) through podcasts, career development workshops and DDW sessions, fundraising of over $300,000 to support health disparities research, dedicated DEI sections and section editors for Gastroenterology and Clinical Gastroenterology and Hepatology, and the creation of a guide for GI fellowship program directors to promote equity and mitigate bias in the fellowship selection process.

Although the Equity Project is entering its third and final implementation year, the spirit and values of the Equity Project will live on. Excellence in equity requires ongoing, focused dedication – AGA is committed to ensuring that equity, diversity, and inclusion are inherently embedded through the fabric of the organization, and continuously integrated and assessed in all of the organization's future strategic initiatives. ■

Dr. Quezada is an associate professor of medicine in the division of gastroenterology and hepatology at the University of Maryland, Baltimore. She reports being on the People of Color Advisory Board for Janssen. Dr. Cryer is chief of internal medicine and the Ralph Tompsett Endowed Chair in Medicine at Baylor University Medical Center, Dallas, and a professor of internal medicine at Texas A&M School of Medicine, Bryan. He has no relevant conflicts of interest.

Continued from previous page

cholangiopancreatography can be a reasonable complementary or alternative test, based on local expertise and availability.

Second, the role of ERCP remains controversial for reducing the frequency of acute pancreatitis episodes in patients with pancreas divisum, the most common congenital pancreatic anomaly, the authors wrote. However, minor papilla endotherapy may be useful, particularly for those with objective signs of outflow obstruction, such as a dilated dorsal pancreatic duct or santorinicele. However, there is no role for ERCP in treating pain alone in patients with pancreas divisum.

Third, ERCP remains even more controversial for reducing the frequency of pancreatitis episodes in patients with unexplained recurrent acute pancreatitis and standard pancreatic ductal anatomy, according to the authors. It should only be considered after a comprehensive discussion of the uncertain benefits and potentially severe procedure-related adverse events. When used, ERCP with biliary sphincterotomy alone may be preferable to dual sphincterotomy.

Fourth, for long-term treatment of patients with painful obstructive chronic pancreatitis, surgical intervention should be considered over endoscopic therapy, the study authors wrote. Pain is the most common symptom and important driver of impaired quality of life in patients with chronic pancreatitis, among whom a subset will be affected by intraductal hypertension from an obstructed pancreatic duct. The authors noted that endoscopic intervention remains a reasonable alternative to surgery for suboptimal operative candidates or patients who want a less-invasive approach, as long as they are clearly informed that the best practice advice primarily favors surgery.

The role of ERCP remains controversial for reducing the frequency of acute pancreatitis episodes in patients with pancreas divisum.

Fifth, when using ERCP for pancreatic duct stones, small main pancreatic duct stones of 5 mm or less can be treated with pancreatography and conventional stone extraction maneuvers. For larger stones, however, extracorporeal shockwave lithotripsy or pancreatoscopy with intraductal lithotripsy can be considered, although the former is not widely available in the United States and the success rates for the latter vary.

Sixth, when using ERCP for pancreatic duct strictures, prolonged stent therapy for 6-12 months is effective for treating symptoms and remodeling main pancreatic duct strictures. The preferred approach is to place and sequentially add multiple plastic stents in parallel, or up-sizing. Emerging evidence suggests that fully covered self-expanding metal stents may be useful in this case, but additional research is needed. For example, one study suggested that patients treated with these self-expanding stents required fewer ERCPs, but their adverse event rate was significantly higher (39% vs. 14%) (Pancreatology. 2021 Aug;21[5]:854-61).

Seventh, ERCP with stent insertion is the preferred treatment for benign biliary stricture caused by chronic pancreatitis. Fully covered self-expanding metal stents are favored over placing multiple plastic stents when feasible, given the similar efficacy but significantly lower need for stent exchange procedures during the treatment course.

Eighth, celiac plexus block shouldn't be routinely performed for the management of pain caused by chronic pancreatitis. Celiac plexus block could be considered in certain patients on a case-by-case basis if they have debilitating pain that hasn't responded to other therapeutic measures. However, this should only be considered after a discussion about the unclear outcomes and its procedural risks.

"Given the current lack of evidence, additional well-designed prospective comparative studies are needed to support a more unified diagnostic and therapeutic pathway for the treatment of these complex cases," the authors concluded.

The authors reported no grant support or funding sources for this report. Several authors disclosed financial relationships with companies such as Olympus America, Medtronic, and Microtech. ■

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Do you want to support the AGA Research Foundation, but feel overwhelmed by everyday living costs, such as the latest home repair, food expenses, and escalating gas prices?

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Your gift directly supports the talented young researchers working to advance our understanding of digestive diseases. Make a tax-deductible donation to help spur innovation. Donate today at www.gastro.org/donateonline.

AGA to host women's regional workshops across the U.S. this fall

The AGA Women in GI Regional Workshops – four separate events across the U.S. beginning in October – will provide women physicians and scientists with effective and accessible career development and networking to support professional success and work-life balance.

Registration is now open for the Midwest and Northeast workshops.

Each workshop is an opportunity to gain new knowledge from a unique lineup of experts and various topics. Select attendees also have the opportunity to participate in the Women's Leadership Collaboration Conference at AGA Headquarters (Dec. 2-3, 2022) to advance the work from the regional events nationally.

To register and for more information on the regional workshops, please visit www.gastro.org/AGAWomensRegional. ■

Now accepting applications for summer undergraduate research award

AGA is accepting applications for the third annual AGA-Aman Armaan Ahmed Family Summer Undergraduate Research Fellowship (SURF).

Eight undergraduate students from groups traditionally underrepresented in biomedical research will have the opportunity to perform 10 weeks of research related to digestive diseases alongside an established investigator. Recipients will also receive a $5,400 stipend and funding to offset travel and meal expenses.

Students may independently secure support from an AGA member mentor or choose from our list of participating mentors. Past recipients are eligible to apply!

Additional information about the award, including application requirements and a downloadable preview, are available in the request for applications. Please see important dates below.

- Dec. 14, 2022 - Online applications close at 11:59 p.m. ET.
- March 2023 - Applicants are notified of their status.
- May-August 2023 - Recipients perform summer research with mentors. ■

AGA gratefully acknowledges the Aman Armaan Ahmed Family for supporting this program.

➤ POSTGRADUATE COURSE

Updates in eosinophilic gastrointestinal diseases

BY KATHRYN A. PETERSON, MD, MSCI

Eosinophilic gastrointestinal diseases (EGIDs) are characterized by GI signs or symptoms occurring with tissue eosinophilia. Eosinophilic esophagitis (EoE) is the more commonly recognized EGID as endoscopic and histopathologic diagnostic criteria have long been established. Because of a lack of consensus on biopsy protocols, poorly understood histopathologic diagnostic criteria, and vague, nonspecific gastrointestinal complaints, patients with non-EoE EGIDs go unrecognized for years. Because of this, there is increasing emphasis on better defining rare, distal eosinophilic gastrointestinal diseases (i.e., eosinophilic gastritis, enteritis, and colitis).

EGID nomenclature was standardized in 2022 in part to minimize vague terminology (i.e., eosinophilic gastroenteritis) and to provide more specific information about the location of eosinophilic disease. The 2022 nomenclature suggest that EGID be used as the umbrella term for all GI luminal eosinophilia (without a known cause) but with emphasis on the site of specific eosinophilic involvement (i.e., eosinophilic gastritis or eosinophilic gastritis and colitis). Importantly, there is much work to be done to adequately identify patients suffering from EGIDs. Symptoms are variable, ranging from abdominal pain, bloating, and nausea seen in proximal disease to loose stools and hematochezia in more distal involvement. Signs of disease, such as iron or other nutrient deficiencies and protein loss, may also occur. Endoscopic findings can vary from erythema, granularity, erosions, ulcerations, and blunting to even normal-appearing tissue. In eosinophilic gastritis, Ikuo Hirano, MD, and colleagues demonstrated that increasing endoscopic inflammatory findings in the stomach correlate with assessment of disease severity. Regardless of endoscopic findings, numerous biopsies are needed for diagnosis of EGIDs because, as already established in EoE, eosinophil involvement is patchy. Nirmala Gonsalves, MD, and Evan Dellon, MD, found that a minimum of four biopsies each in the gastric antrum, gastric body, and small bowel are needed to detect disease. Optimal biopsy patterns have not yet been determined for eosinophilic ileitis or colitis.

Dr. Peterson

Despite these advances, there is more work to be performed. Although these disease states are termed "eosinophilic," the immunopathology driving these diseases is multifactorial, involving lymphocytes and mast cells and creating different phenotypes of disease in a similar fashion to inflammatory bowel disease. Current therapies being studied include eosinophil-depleting medications along with others targeting T2 immune pathways. Patients may need multiple therapeutic options and personalized medicine will soon play a larger role in defining treatments. For now, researchers are fervently working on improved methods to identify, phenotype, and treat these morbid disorders. ■

Dr. Peterson is associate professor of gastroenterology at University of Utah Health, Salt Lake City. She has no relevant conflicts of interest.

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10-year delay in one-third of eosinophilic esophagitis diagnoses has persisted for decades

BY TARA HAELLE

It takes at least 10 years for one-third of patients with eosinophilic esophagitis (EoE) to receive a diagnosis and a median of 4 years for patients overall to get their diagnosis – numbers that haven't budged in 3 decades, according to a study published online in the American Journal of Gastroenterology (2022 Aug 12. doi: 10.14309/ajg.0000000000001950).

This delay has persisted despite more than 2,000 publications on the condition since 2014 and a variety of educational events about it, reported Fritz R. Murray, MD, of the department of gastroenterology and hepatology at University Hospital Zurich and his colleagues.

"Bearing in mind that eosinophilic esophagitis is a chronic and progressive disease, that, if left untreated, leads to esophageal structuring ultimately causing food impaction, the results of our analysis are a cause for concern," the authors wrote.

"Substantial efforts are warranted to increase awareness for eosinophilic esophagitis and its hallmark symptom, solid-food dysphagia, as an age-independent red-flag symptom … in order to lower risk of long-term complications," they added.

The researchers retrospectively analyzed prospectively collected data from 1,152 patients in a Swiss database. The patients (74% male; median age, 38 years) had all been diagnosed with EoE according to established criteria. The authors calculated the diagnostic delay from 1989 to 2021 and at three key time points: 1993 – first description of the condition, 2007 – first consensus recommendations, and 2011 – updated consensus recommendations

The median diagnostic delay over the 3 decades studied was 4 years overall and was at least 10 years in nearly one-third (32%) of the population. Diagnostic delay did not significantly change throughout the study period, year by year, or at or after any of the milestones included in the analysis, retaining the minimum 10-year delay in about one-third of all patients.

The median age at symptom onset was 30 years, with 51% of patients first experiencing symptoms between 10 and 30 years of age.

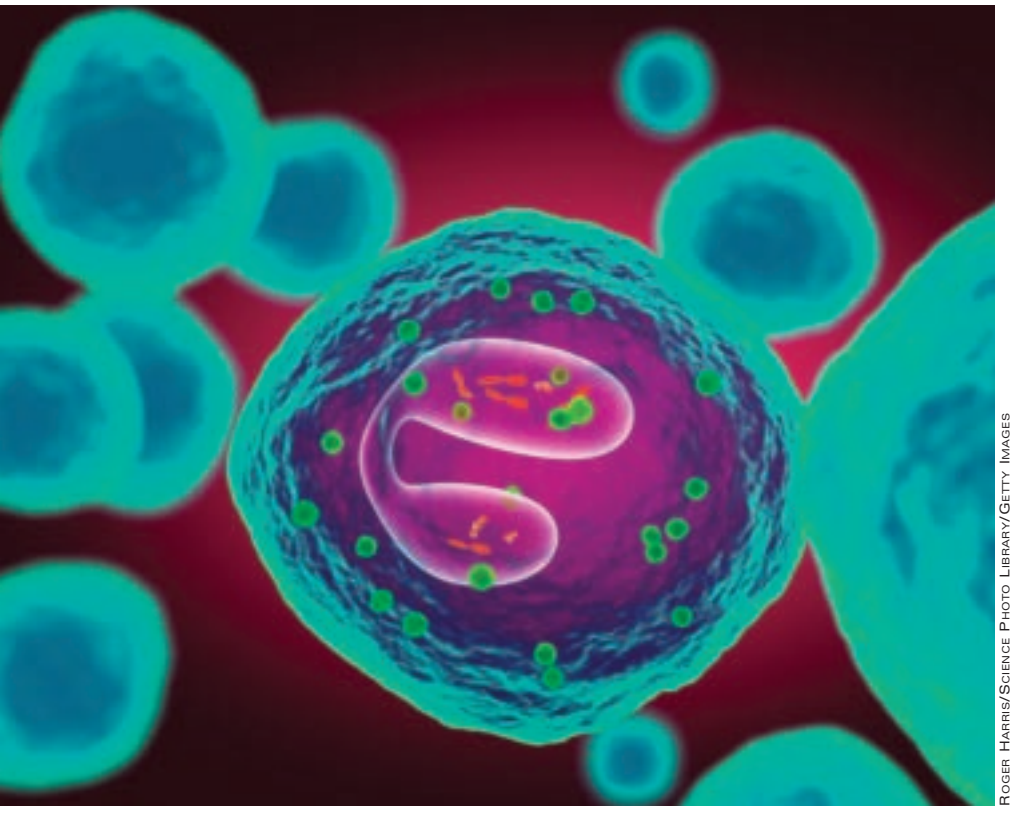
"Age at diagnosis showed a normal distribution with its peak between 30 and 40 years with 25% of the study population being diagnosed with EoE during that period," the authors reported.

Although diagnostic delay did not differ between sexes, the length of time before diagnosis did vary on the basis of the patient's age at diagnosis, increasing from a median of 0 years for those aged 10 years or younger to 5 years for those aged 31-40 years.

"When examining variation in diagnostic delay based on age at symptom onset, we observed an inverse association of age at symptom onset and diagnostic delay, with longest diagnostic delay observed in children," they wrote.

Diagnostic delay was longer in those who needed an endoscopic disimpaction – a median of 6 years – before being diagnosed, compared with those who did not require this procedure, who had a median delay of 3 years. Nearly one-third (31%) of participants had at least one food impaction requiring endoscopic removal before receiving their diagnosis.

Three in four participants (74%) had a confirmed atopic condition besides eosinophilic esophagitis, with 13% not having an atopic comorbidity and another 13% lacking information on whether they did or didn't. Those with atopic conditions were younger (median age, 29 years) when symptoms began than were those without atopic conditions (median age, 34 years).



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Similarly, those with atopic conditions were younger (median age, 38 years) than those without these conditions (median age, 41 years) at the time of diagnosis. Diagnostic delay was a median 2 years shorter – 3 years vs. 5 years – for patients with concomitant atopic conditions.

"Importantly, the length of diagnosis delay (untreated disease) directly correlates with the occurrence of esophageal strictures," the authors wrote, citing previous research finding that the prevalence of strictures rose from 17% in patients with a delay of up to 2 years to 71% in patients with a delay of more than 20 years.

"Future efforts should target the general population, and potentially primary physicians, to strengthen the awareness for eosinophilic esophagitis as a potential underlying condition in patients with dysphagia."

"Esophageal strictures were present in around 38% of patients with a delay between 8-11 years" in that study (Gastroenterology. 2013 Aug 13. doi: 10.1053/j.gastro.2013.08.015), "a delay that is prevalent in about one third of our study population," the authors wrote. "However, even a median delay of 4 years resulted in strictures in around 31% of untreated patients."

Other research (Am J Gastroenterol. 2018 Jun. doi: 10.1038/s41395-018-0052-5) has found that the risk for esophageal strictures increases an estimated 9% each year that eosinophilic esophagitis goes untreated.

The authors suggested that patients' denying symptoms or attempting to address their symptoms with changes in diet or eating behavior may be one reason for the long diagnostic delay, given other findings showing that patient-dependent delay was 18 months, compared with 6 months for physician-dependent delay. Although the authors didn't have the information in their dataset to assess patient- vs. physician-dependent delay, a subgroup analysis revealed that patients and nongastroenterologist doctors combined made up the largest proportion of diagnosis delay.

"This fact indicates that future efforts should target the general population, and potentially primary physicians, to strengthen the awareness for eosinophilic esophagitis as a potential underlying condition in patients with dysphagia," the authors wrote.

"A change in eating behavior, especially in cases with prolonged chewing, slow swallowing or even the necessity of drinking fluids after swallowing of solid food, should raise suspicion also in the general population," they added.

Dr. Murray received travel support from Janssen, and 9 of the other 11 authors reported consulting, speaking, research, and/or travel fees from 23 various pharmaceutical and related companies. ■

MERIT: Endoscopic sleeve gastroplasty shows 'very impressive' outcomes in randomized clinical trial

BY JIM KLING
MDedge News

In a randomized, controlled trial, endoscopic sleeve gastroplasty (ESG) combined with lifestyle modifications was safe and effective for weight loss among individuals with class I and class II obesity, compared with lifestyle modifications alone.

"Lifestyle modifications and pharmacological therapy have several limitations, and the use of bariatric surgery is hampered by its invasive nature and patient perceptions," the study authors wrote. ESG is a minimally invasive, reversible, organ-sparing bariatric procedure that might be able to fill those care gaps, they explained.

Previous retrospective studies have suggested that ESG is effective, and a meta-analysis of 1,772 patients found an average total body weight loss of 15.1% at 6 months (95% confidence interval, 14.3%-16.0%) and 16.5% at 12 months (95% CI, 15.2%-17.8%) (Clin Gastroenterol Hepatol. 2020 May;18[5]:1043-53.e4.). However, according to the authors of the current study, known as MERIT and published in The Lancet (2022 Aug 6;400[10350]:441-51), there have been no randomized, clinical trials investigating ESG's efficacy to date.

"[This is] the kind of study that we have been looking forward to. The outcomes were very impressive," said Danny Issa, MD, who was asked to comment on the study. He is a clinical assistant professor of medicine at the University of California, Los Angeles.

Understanding the study and its results

Between December 2017 and June 2019, the researchers randomized 209 participants to ESG plus lifestyle modification or lifestyle modification only, which served as the control. The mean age was 47.3 in the ESG group (88% female) and 45.7 in the control group (84% female). The mean body mass index was 35.5 kg/m^2 in the ESG group and 35.7 among controls.

After 1 year, the intervention group had a mean percentage of excess weight loss (EWL) of 49.2%, compared with 3.2% for the control group ($P < .0001$). The mean percentage of total body weight lost was 13.6% in the ESG group and 0.8% in the control group ($P < .0001$). After adjustment for age, sex, type 2 diabetes, hypertension, and baseline BMI, the ESG group had a mean difference of excess weight loss of 44.7% (95% CI, 37.5%-51.9%) and a mean difference of total weight loss of 12.6% (95% CI, 10.7%-14.5%), compared with the control group at 52 weeks. At 52 weeks, 77% of the ESG group had at least a 25% excess weight loss, which was the secondary endpoint, compared with 12% of the control group ($P < .0001$).

Overall, 80% of the ESG group had an improvement in at least one metabolic comorbidity, while 12% experienced a worsening. Among the control group, 45% had an improvement and 50% worsened. Among 27 patients in the treatment group with diabetes, 93% experienced an improvement in hemoglobin A1c levels, compared with 15% of patients with diabetes in

the control group. Similarly among patients with hypertension, 60% in the intervention group had an improvement, compared with 40% of controls. Of those with metabolic syndrome, 83% improved after undergoing surgery, compared with 35% of controls.

At 2 years, 68% of the ESG group who achieved a 25% EWL continued to have at least 25% EWL; 2% in the treatment group had a serious ESG-related adverse event, but there was no mortality or need for intensive care or follow-up surgery.

Aiming for level I evidence

"The results are very encouraging, so I think it's good news for the field of bariatric endoscopy. I think it's going to provide more confidence to patients and physicians, and for new trainees who are interested in this field, I think it's going to inspire them," said Shailendra Singh, MD, who was asked to comment on the study. Dr. Singh is an associate professor of medicine and director of bariatric medicine at West Virginia University, Morgantown.

"I think this study will help us reach out to the payers and give them the data behind this. ... ESG is a relatively new endoscopic procedure; I think this is a step forward in that direction."

The study could also improve insurance coverage of the procedure, said Dr. Singh. "I think this study will help us reach out to the payers and give them the data behind this because they always look for level I evidence. ESG is a relatively new endoscopic procedure; I think this is a step forward in that direction," he said.

The study underlines the applicability of the procedure to patients who don't want more invasive surgery, or who can't tolerate some of the higher efficacy medications that are increasingly available.

It is also just one of various options for obesity treatment, which are increasingly being used in combination, according to Avlin Imaeda, MD. "Just like we see in hypertension, where you progressively add more and more medications, I think we're going to see obesity treatment go that way too. I see this as adding choice for patients and adding to this potentially multimodal approach," said Dr. Imaeda, an associate professor of medicine at Yale University, New Haven, Conn., who was not involved in the study.

The study authors report various financial relationships, including some with Apollo Endosurgery, which funded this study. Dr. Issa and Dr. Imaeda have no relevant financial disclosures. Dr. Singh is a consultant for Apollo Endosurgery. ■

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