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The goal for I-SEE is to assess EoE severity and have that severity linked to outcomes, said Dr. Evan Dellon.

New EoE severity score may guide treatment

BY THOMAS R. COLLINS
MDedge News

The American Gastroenterological Association has developed a new index to help clinicians gauge the severity of eosinophilic esophagitis (EoE), offering a tool to physicians that experts say has been lacking in the field and should help better guide treatment.

The index – known as I-SEE, for Index of Severity for Eosinophilic Esophagitis – was developed after an exhaustive review of the literature, and allows clinicians to calculate a score based on symptoms, complications, endoscopy findings, and histology and more information is available online at https://eoe.gastro.org/. It was published in Gastroenterology (2022 May 20. doi: 10.1053/j.gastro.2022.03.025) and the Journal of Allergy and Clinical Immunology (2022 May 13. doi: 10.1016/j.jaci.2022.03.015).

In other eosinophilic disorders, such as asthma, there are well-prescribed treatment pathways based on disease severity, said Evan Dellon, MD, MPH,

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AGA issues position statements on CRC reduction

It will 'take a village' to reach goals

BY WILL PASS
MDedge News

The American Gastroenterological Association has published eight position statements aimed at reducing the burden of colorectal cancer (CRC).

The evidence-based statements, published in Gastroenterology (2022 Jun 14. doi: 10.1053/j.gastro.2022.05.011), call for a national approach to CRC screening, outline the elements of a high-quality screening program, and make clear that payers should cover all costs, from bowel prep through pathology, plus follow-up for high-risk patients.

"There is strong evidence that CRC screening is effective [at reducing CRC incidence and mortality] but less than 70% of eligible individuals have been screened," wrote authors led by David Lieberman, MD, AGAF, who is on the AGA Executive Committee on the Screening Continuum and affiliated with Oregon Health & Science University, Portland, noting the recent expansion of eligibility to include individuals in the 45- to 49-year age group.

"CRC screening saves lives, but only if people get screened," Dr. Lieberman

See **CRC** · *page 10*

INSIDE

ESG's metabolic benefits last 5 years

BY JIM KLING
MDedge News

AT DDW 2022

SAN DIEGO – Endoscopic sleeve gastroplasty (ESG) led to sustained weight loss and a reduction of cardiometabolic syndrome comorbidities at 5 years, according to a new retrospective analysis of prospectively collected data.

Improved cardiometabolic outcomes following bariatric surgery have been well documented, but ESG is relatively new, so its outcomes haven't been as well described. The outcomes are encouraging, though not as good as those of bariatric surgery. "It's still better, but only 1% of the patients undergo the surgery, even though they're candidates," said Donevan Westerveld, MD, who presented the study at

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THEN AND NOW

A 'lifetime' of advancement in upper GI tract

BY DAVID KATZKA, MD, AGAF

Fifteen years is a lifetime for the advancement of medical research. This seems particularly true for upper–GI tract disorders.

In 2007, eosinophilic esophagitis was a rare disease; limited clinical data were available describing the symptoms, demographic characteristics, and endoscopic findings. Treatment was guided mostly by uncontrolled patient series for topical steroids and comprehensive diet exclusion therapy. Today, the molecular, genetic, and evolving microbiome's contributions to EoE are being elucidated. EoE is recognized as one of the most common diseases in our practice, and rigorously performed controlled trials of steroids and biologics (including Food and Drug–approved dupilumab) guide our treatment. Diet has also become easier with the identification of a single food antigen as the cause in 40% of EoE patients. The most pressing need is for a test that's reliable and less invasive than endoscopy to assess and monitor treatment.

Dr. Katzka

Barrett's esophagus was of great concern 15 years ago and has surged in importance because of the increasing incidence of Barrett's and esophageal adenocarcinoma, likely emphasized by the obesity epidemic. Sadly, survival with esophageal adenocarcinoma has changed little because most patients present with advanced stages. Multiple studies are questioning guideline recommendations because of their low yield and high expense. Fortunately, a range of easier screening tools are being tested, including sponge on string devices, video capsules, transnasal endoscopy, and the electronic "nose." These can provide more widespread screening in broader populations of patients at risk who may lack heartburn or classic demographics. In 2007 there was little endoscopic therapy; now, the gastroenterologist has a robust armamentarium with multiple methods for mucosal ablation and resection achieving cure and sparing the patient an esophagectomy. Tissue biomarkers continue to be elucidated and are being applied to clinical practice.

For esophageal motility disorders, manometric data were obtained through a primitive water infused system. With high-resolution manometry, the Chicago Classification, and impedance planimetry, our ability to precisely define, understand, and treat these disorders has been greatly enhanced.

In prior decades, the association of *H. pylori* to gastric cancer was noted but landmark trials and meta-analyses have strongly linked eradication of *H. pylori* with reduction in gastric cancer. These include broad population studies from Taiwan and the U.S. Veterans Health Administration, as well as a Cochrane review. These data have reinforced the need to search for and eradicate *H. pylori* infection. Although antibiotic resistance is rampant, newer antibiotic combinations including nitazoxanide, levofloxacin, rifabutin, and tinidazole have been proven effective. Potassium-competitive acid blockers may also augment effective eradication.

Endoscopy itself is one of the greatest areas of advancement in upper GI disease since 2007. What was once limited to biopsy, removal of polyps, and control of gastrointestinal bleeding, now has a breathtaking range of diagnostic and therapeutic capabilities. Who could imagine being able to perform bariatric procedures, create a gastrojejunostomy, treat a Zenker's diverticulum, or drain extraluminal abscesses through an endoscope? With description of the technique of submucosal tunneling, endoscopic mucosal resection has been extended to submucosal dissection for more advanced cancers and benign tumors. This technique has also revolutionized the treatment of achalasia with peroral endoscopic myotomy, a procedure found equivalent to laparoscopic myotomy in controlled trials. Finally, artificial intelligence has taken endoscopic imaging by storm, and the accuracy with which we will diagnose premalignant lesions of the esophagus and stomach should significantly increase our abilities to prevent and treat early cancers. ■

Dr. Katzka is a professor of medicine at Columbia University, New York, and an associate editor of GI & Hepatology News. He reports consulting for Takeda and Celgene.

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Vibrating pill counters constipation

BY JIM KLING
MDedge News

AT DDW 2022

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SAN DIEGO – A swallowable, vibrating capsule improved symptoms among patients with chronic idiopathic constipation in a phase 3 multicenter, randomized, controlled trial. The method represents a mechanical approach to the treatment of constipation.

The swallowable pill acts by vibrating during passage through the gut, where it is thought to augment colonic biorhythm and peristalsis (Am J Gastroenterol. 2018 Oct;133[Supp]:S247). Traditional treatments for constipation generally increase motility or secretion.

"That's how we have been managing constipation since time immemorial. Now we have come up with this novel approach, where there's a pill that is designed to increase local oscillations, and probably induce local contractions of the colon to mimic what happens normally," said Satish Rao, MD, PhD, AGAF, who presented the results of the trial at the annual Digestive Disease Week® (DDW).

"We're now seeing that local stimulation works, and the other neat thing seems to be a lack of side effects, which is really a huge plus. I think it will benefit people with both occasional or chronic constipation," said Dr. Rao, professor of medicine at Medical College of Georgia, Augusta.

The capsules activate for two stimulation cycles, each lasting for about 2 hours. The cycle includes 3 seconds of vibration followed by 16 seconds of rest.

The researchers conducted a study with two active arms and a placebo. It included 312 patients age 22 or older who had an average of between 1 and 2.5 spontaneous bowel movements (SBM) per week.

Treatment lasted for 8 weeks, with patients ingesting a capsule between 9 and 10 p.m. In one treatment group, the device was activated at 6 a.m., and in the other group at about 2 p.m.

The placebo and treatment groups had similar baseline characteristics, except for a longer duration of constipation in the treatment groups (17.9 versus 14.5 years; $P = .0253$). In an intention-to-treat analysis, the treatment groups were more likely to achieve an increase of one complete SBM per week (39.26% versus 22.15%; $P < .0001$) and an increase of two complete SBMs per week (22.7% versus 11.41%; $P < .0006$).

The capsules also improved straining score, stool consistency, and quality of life. There was no significant difference between treatment and placebo groups with respect to bloating or rescue medication use.

The product had few adverse effects. The most common was a vibrating sensation or discomfort (11.0%, versus none in the placebo group).

Another benefit is that the therapy's mimicry of natural cycles appears to grant patients more control of bowel movements. Laxatives and other pharmaceutical interventions may prompt the patient to go to the bathroom within an hour or two, but patients in the trial reported bowel movements at predictable times.

However, he noted that the pill is nondissolvable, which would make it contraindicated for patients who have had previous gut surgeries or narrowing of the gut. He noted that the sponsoring company, Vibrant Gastro, expects to obtain Food and Drug Administration approval by the end of 2022.

The results of the study were well received. "I think it's an exciting new approach for managing patients with chronic constipation. It was a large sample size, and the treatment seems to be well tolerated. It may offer a promising option for patients who have not responded to many other medications," said Adil E. Bharucha, MD, AGAF, who comoderated the session where the research was presented.

However, he pointed out that the presentation did not indicate how many of the patients had previously tried other therapies. "We'd like to see the full paper, which will provide a better understanding of the role of this treatment in practice down the road," said Dr. Bharucha, professor of medicine in the division of gastroenterology and hepatology and director of the office of clinical trials at Mayo Clinic, Rochester, Minn.

The capsule may not work for everyone, said Dr. Bharucha. He suspects that many refractory patients have an issue with pelvic floor muscles, which may restrict stool evacuation. "You wouldn't expect those people to respond optimally to a laxative and I suspect perhaps not to a capsule, either. I think defecatory disorders are substantially underdiagnosed in patients who don't respond to laxatives," said Dr. Bharucha.

Asked why the capsule might benefit patients who don't improve with laxatives, Dr. Bharucha responded: "I think we need more studies to understand how the capsule works."

Dr. Rao consults for Vibrant Gastro. Dr. Bharucha has no relevant financial disclosures. ■

FDA approves first drug for eosinophilic esophagitis

BY MEGAN BROOKS

The U.S. Food and Drug Administration has approved dupilumab (Dupixent, Regeneron) to treat eosinophilic esophagitis (EoE) in adults and children aged 12 years and older weighing at least 40 kg.

EoE is a chronic inflammatory disorder driven by type 2 inflammation that damages the esophagus and causes difficulty swallowing and eating.

"As researchers and clinicians have gained knowledge about eosinophilic esophagitis in recent years, more cases of the disorder have been recognized and diagnosed in the U.S."

Dupilumab is a monoclonal antibody that acts to inhibit part of the inflammatory pathway. It's the first drug to be approved by the FDA for EoE.

In a phase 3 trial, dupilumab 300 mg weekly significantly improved signs and symptoms of eosinophilic esophagitis, compared with placebo, underscoring the role of type 2 inflammation in this disease, Regeneron says in a news release.

According to the company, there are roughly 160,000 patients in the United States living with EoE who are currently using treatments not specifically approved for the disease. Of those patients, about 48,000 continue to experience symptoms despite multiple treatments.

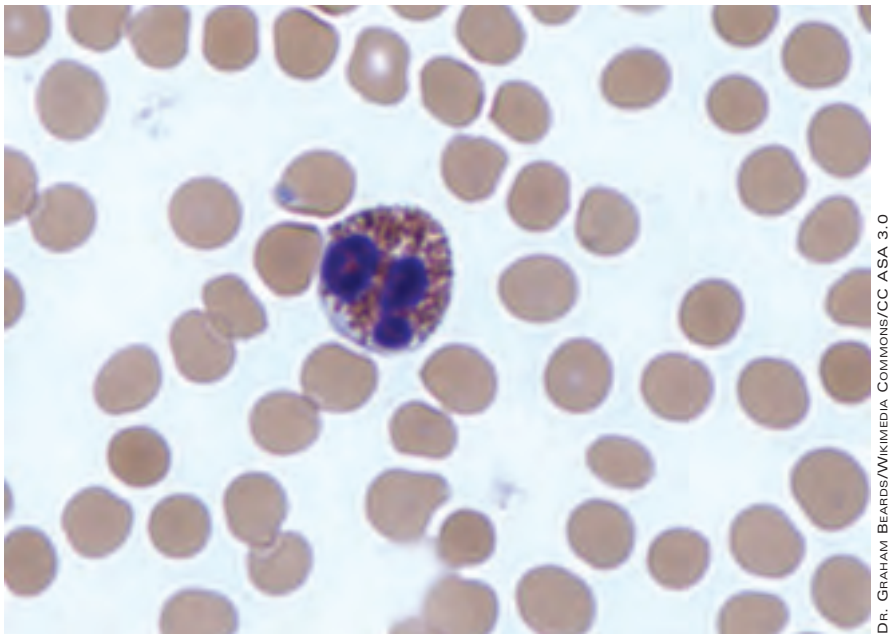
"As researchers and clinicians have gained knowledge about eosinophilic esophagitis in recent years, more cases of the disorder have been recognized and diagnosed in the U.S.," Jessica Lee, MD, director of the division of gastroenterology in the FDA's Center for Drug Evaluation and Research, said in an FDA news release.

The approval of dupilumab will "fulfill an important unmet need for the increasing number of patients with eosinophilic esophagitis," Dr. Lee said.

The efficacy and safety of dupilumab in EoE was demonstrated in a randomized, double-blind, parallel-group, multicenter, placebo-controlled trial that included two 24-week treatment periods (parts A and B) that were conducted independently in separate groups of patients.

In both part A and B, patients received dupilumab 300 mg or placebo every week.

In part A of the trial, 60% of the 42 patients who received dupilumab achieved the predetermined level of reduction of eosinophils in the esophagus, compared with 5% of the 39 patients who received placebo, the FDA said.



Dr. Graham Beards/Wikimedia Commons/CC ASA 3.0

Patients who received dupilumab also experienced an average improvement of 22 points in the Dysphagia Symptom Questionnaire (DSQ) score, compared with 10 points for patients who received placebo.

In part B, 59% of the 80 patients who received dupilumab achieved the predetermined level of reduction of eosinophils in the esophagus, compared with 6% of the 79 patients who received placebo.

Patients who received dupilumab also experienced an average improvement of 24 points in their DSQ score, compared with 14 points for patients who received placebo.

"Assessments incorporating the perspectives from patients with EoE supported that the DSQ score improvement in patients who received Dupixent in the clinical trial was representative of clinically meaningful improvement in dysphagia," the FDA noted.

"Treatment for patients with eosinophilic esophagitis can be challenging, particularly with no previously approved medications," Evan Dellon, MD, principal investigator for the phase 3 trial, said in the company news release.

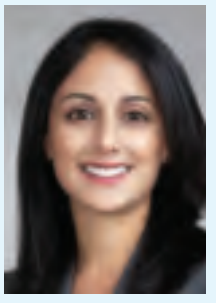
"Now, patients and their doctors have a treatment option available as part of their management plan that has the potential to control symptoms, improve inflammation, and heal the changes in the esophagus caused by this progressive and burdensome disease," added Dr. Dellon, who is professor of medicine in the division of gastroenterology and hepatology at the University of North Carolina at Chapel Hill.

The FDA granted dupilumab priority review and breakthrough therapy designations for EoE.

Dupilumab is already approved in the United States for treatment of moderate to severe atopic dermatitis in adults and children aged 6 years and older whose disease is not adequately controlled by topical prescription therapies or for whom those therapies are not advisable.

The drug is also approved as an add-on maintenance treatment for adults and children aged 6 years and older with certain types of moderate to severe asthma and as an add-on maintenance treatment for adults with inadequately controlled chronic rhinosinusitis with nasal polyposis. ■

Eosinophilic esophagitis (EoE) is a chronic disease requiring long-term treatment for both induction and maintenance of response. For decades, however, Food and Drug Administration–approved therapies for EoE have not been available. Dupilumab is the first drug to receive FDA approval to treat EoE. This human monoclonal antibody directed against the interleukin (IL)-4 receptor–alpha component of the type 2 receptor inhibits signaling of IL-4 and IL-13. Dupilumab has shown efficacy in similar diseases, such as atopic dermatitis and eosinophilic asthma. In 2017 dupilumab was granted Orphan Drug designation for the potential treatment of EoE and in 2020 the FDA granted Breakthrough Therapy designation for EoE. Recent data from the phase 3 trial of dupilumab 300 mg weekly enrolling patients aged 12 years and older demonstrated a significantly greater reduction in disease symptoms, normalization of esophageal eosinophilia, and reduction in endoscopic findings by week 24 compared with placebo.



Dr. Yadlapati

The highly anticipated approval of dupilumab marks a paradigm shift toward biologic medications for treatment of EoE when historical treatments have relied on proton pump–inhibitor therapy or topical swallowed steroids. As we await updates about availability and access of dupilumab for our patients, we can rest assured that a highly efficacious treatment is now approved and will fill an important treatment gap in EoE, particularly for patients not deriving adequate response with traditionally used strategies. With multiple clinical trials underway, this milestone likely represents the beginning of additional effective therapies (nonbiologic and biologic) that will be available for EoE.

Rena Yadlapati, MD, MSHS, FACG, associate professor of clinical medicine in the division of gastroenterology at the University of California, San Diego, medical director of the UCSD Center for Esophageal Diseases, and director of the GI Motility Lab. She has no relevant conflicts of interest.

Understanding EoE severity

Score *from page 1*

AGAF, professor of gastroenterology and hepatology at the University of North Carolina at Chapel Hill.

"That is the ultimate aspiration for I-SEE – assess EoE severity, have that severity linked to certain outcomes and therefore be associated with certain treatment and monitoring recommendations; then reassess the patient severity in a standardized way, and then make additional treatment and monitoring changes if needed," he said in an interview. "However, to get there a lot more research into the use of the tool will be needed."

With support from the AGA, a multidisciplinary group – including adult and pediatric specialists in gastroenterology, asthma and immunology, pathology, epidemiology, and basic and translational research, as well as patient advocates – broke into teams to assess the available literature, developed consensus on the factors to be used, and developed consensus on the scoring system.

New ways have been developed over the years to assess patients' responses to treatments and gauge their disease activity, from patient-reported outcomes to endoscopic assessment platforms and metrics using histology. But all of this information hadn't been synthesized into a tool that clinicians would find practical to use, the expert group said in its paper describing the index.

How it works

The index divides criteria into three main categories: symptoms and complications, inflammatory features, and fibrostenotic features.

In the symptoms and complications category, points are assessed based on whether symptoms are weekly, daily, or several times a day and whether problems such as food impaction or esophageal perforations are present.

Inflammatory features include localized or diffuse edema or furrows on endoscopy and eosinophil counts.

Fibrostenotic scoring items include features such as rings or strictures and how constricting they are, as well as basal zone hyperplasia and lamina propria fibrosis.

Each feature is assigned a score of 1-15. An overall score of 0 points would be considered inactive disease; 1-6 is mildly active disease; 7-14 is moderately active disease; and 15 or more is severely active disease.

Someone with daily symptoms (2 points) and localized edema on endoscopy (1 point) and 15-60 eosinophils per high-power field (1 point) would have a total of 4 points and be considered to have mildly active disease. Someone who is 18 years of age or older with daily symptoms (2 points), food impaction with an ED visit (2 points), diffuse edema on endoscopy (2 points), 15-60 eosinophils per high-power field (1 point), basal zone hyperplasia (2 points), and rings or strictures on endoscopy that don't permit passing a standard upper endoscope (15 points), would have 24 points and be considered to have severely active disease.

The index is only just starting to be tested with patient-level data, but the first results are promising, Dr. Dellon said. He hopes incorporating endoscopic and histologic features into the index will lead to wider evaluation of these indicators of severity because they have been shown to be important clinically.

Dr. Dellon said there is a plan to develop an app that will allow the index's "usability" to be tested across a range of practice settings and disciplines. The index will also be evaluated in existing and prospectively collected datasets.

"This will help us understand the distribution of EoE patient severity in a number of settings, as well as how severity relates to posttreatment outcomes," he said. "Ultimately, it is possible that I-SEE could be incorporated into electronic medical records systems."

Simplifying clinical practice

Philip Katz, MD, AGAF, professor of medicine in the gastroenterology division at Weill Cornell Medicine, New York, said the index could be a step forward in the care of EoE patients.

"The way all of us make choices for these patients and how we judge where they are in terms of the 'severity' of their disease is not ideal, by any means," he said. "[This] appears to be a strong attempt to simplify what we're currently doing now and put it all in one place."

Ease of use will be important and his practice will be evaluating that, he said. He said he hopes that software will make it practical, possibly with the necessary information able to be imported straight from the electronic health record.

"We'll do our best to use the system data in a way that the authors have suggested," he said. "Basically, we'll make our own opinions as data is gathered."

He recommended that clinicians treating EoE try to use the index and assess its performance on their own, in addition to staying aware of data that are collected elsewhere in the field. That way, collectively, the tool will have the maximum impact on improving patient care.

"[The researchers who developed the tool] are people who have dedicated a substantial portion of their professional careers to studying this disease and are comfortable that this is a tool that will offer more value than what we're currently doing," he said. "Chances are, this will be much better than what we currently have."

This new tool was developed as part of AGA's EoE initiative, Eosinophilic Esophagitis: Expand, Optimize, Excel. View additional resources at eoe.gastro.org.

The index was developed as part of a conference that was supported by a grant from Takeda. This conference was also funded in part by the division of intramural research at National Institute of Allergy and Infectious Diseases/National Institutes of Health and supported by CEGIR (U54 AI117804). All activities and products resulting from this conference were independently developed with no involvement or input from the funder. The authors disclosed relationships with various industry entities, including Takeda. None of the other relationships were relevant to this work. Dr. Katz consults with Phathom, Sebela Pharmaceuticals, and AstraZeneca. ■

Alarming increase in esophageal cancer seen

BY PAM HARRISON

FROM DDW 2022

An alarming increase in both esophageal cancer (EC) and the primary precursor lesion for esophageal adenocarcinoma known as Barrett's esophagus (BE) has been observed among middle-aged adults over the past 5 years, and it's not because of better or more frequent screening, warn the authors of a new study from Florida.

The study was highlighted during a press briefing held in advance of the annual Digestive Disease Week® (DDW).

The analysis was carried out by Bashar Qumseya, MD, MPH, and colleagues using EHR from the OneFlorida Clinical Data Research Network, a database that covers over 40% of residents living in Florida. The researchers identified patients who had been diagnosed with EC or BE between 2012 and 2019. The cohort was categorized by age: those aged 18-44 years (young); those aged 45-64 years (middle-aged), and those older than 65 (elderly). Over the study interval, the prevalence of EC remained stable among the elderly but nearly doubled among middle-aged patients, from a rate of 49 per 100,000 in 2012 to a rate of 94 per 100,000 in 2019. Similarly, there was a 50% increase in BE over the same study interval, from 304 per 100,000 in 2012 to 466 per 100,000 in 2019, again in the middle-aged group.

Data from the same cohort also indicated that the great majority of patients with multiple risk factors for EC or BE – obesity, diet, and gastroesophageal reflux disease – had never undergone endoscopy, "so we can definitely do better," Dr. Qumseya said. One simple way to "do better" is to offer patients an endoscopy when they undergo their first colonoscopy at the recommended age of 45 years.

"I am not in a position to make the guidelines," Dr. Qumseya commented. "But we do [already] have guidelines that suggest that patients with multiple risk factors [for EC and BE] be screened, and since we know from our data that this is not happening, I believe that if a patient has multiple risk factors, they should have at least one screening endoscopy at the time of colonoscopy." Dr. Qumseya disclosed having no financial relationships with a commercial interest. ■

Improving access to screening

CRC *from page 1*

said in a press release from the AGA. "Cost sharing is an important barrier to screening, which contributes to racial, ethnic and socioeconomic inequities in colorectal cancer outcomes. The full cost of screening – including noninvasive tests and follow-up colonoscopies – should be covered without cost to patients."

He added: "AGA wishes to collaborate with stakeholders to eliminate obstacles to screening, which disproportionately impact those with low income and lack of insurance."

Eliminating disparities

Among the position statements, Dr. Lieberman and colleagues first called for "development of a national approach to CRC screening" to patch gaps in access across the United States.

"Systematic outreach occurs infrequently," they noted. "CRC screening prevalence is much lower among individuals who do not have access to health care due to lack of insurance, do not have a primary care provider, or are part of a medically underserved community."

According to Dr. Lieberman and colleagues, the AGA is also "working with a broad coalition of stakeholders," such as the American Cancer Society, payers, patient advocacy groups, and others, to create a "national resource ... focused on ensuring high-quality CRC screening and eliminating barriers to CRC screening."

The coalition will work to collectively tackle "disparities created by social determinants of health, which includes lack of access to screening, transportation, and even work hours and child care.

Dr. Lieberman

"The AGA recognizes that moving the needle to achieve a CRC screening participation goal of 80% will take a village," they wrote.

High-quality CRC screening

The investigators went on to describe the key features of a high-quality CRC screening program, including "colonoscopy and noninvasive screening options, patient education, outreach, and navigation support."

Dr. Lieberman and colleagues pointed out that offering more than one type of screening test "acknowledges patient preferences and improves participation."

Noninvasive methods, such as fecal immunochemical testing (FIT), can eliminate "important barriers" to screening, they noted, such as the need for special preparation, time off work, and transportation.

For individuals who have high-risk adenomas (HRAs) or advanced sessile serrated lesions (SSLs), screening should be expanded to include follow-up, the investigators added.

"Evidence from a systematic review demonstrates that individuals with HRAs at baseline have a 3- to 4-fold higher risk of incident CRC during follow-up compared with individuals with no adenoma or low-risk adenomas," they wrote (Gastroenterology. 2020 Aug. doi: 10.1053/j.gastro.2020.04.004.). "There is also evidence that individuals with advanced SSLs have a 3- to 4-fold higher risk of CRC, compared with individuals with nonadvanced SSLs."

Dr. Itzkowitz

Payers should cover costs

To further improve access to care, payers should cover the full costs of CRC screening because "copays and deductibles are barriers to screening and contribute to socioeconomic disparities," that "disproportionately impact those with low income and lack of insurance," according to Dr. Lieberman and colleagues.

They noted that the Affordable Care Act "eliminated copayments for preventive services," yet a recent study showed that almost half of patients with commercial insurance and more than three-quarters of patients with Medicare still share some cost of CRC screening (JAMA Netw Open. 2021 Dec 1. doi: 10.1001/jamanetworkopen.2021.36798).

The investigators made clear that payers need to cover costs from start to finish, including "bowel preparation, facility and professional fees, anesthesia, and pathology," as well as follow-up screening for high-risk patients identified by noninvasive methods.

"Noninvasive colorectal screening should be considered as programs with multiple steps, each of which, including follow-up colonoscopy if the test is positive, should be covered by payers without cost sharing as part of the screening continuum," Dr. Lieberman and colleagues wrote.

Changes underway

According to Steven Itzkowitz, MD, AGAF, professor of medicine and oncological sciences and director of the gastroenterology fellowship training program at the Icahn School of Medicine at Mount Sinai, New York, the AGA publication is important because it "consolidates many of the critical issues related to decreasing the burden of colorectal cancer in the United States."

Dr. Itzkowitz noted that changes are already underway to eliminate cost as a barrier to screening.

"The good news is that, in the past year, the departments of Health & Human Services, Labor, and Treasury declared that cost sharing should not be imposed, and plans are required to cover screening colonoscopy with polyp removal and colonoscopy that is performed to follow-up after an abnormal noninvasive CRC screening test," Dr. Itzkowitz said in an interview. "Many plans are following suit, but it will take time for this coverage to take effect across all plans."

For individual gastroenterologists who would like to do their part in reducing screening inequity, Dr. Itzkowitz suggested leveraging noninvasive testing, as the AGA recommends.

"This publication is the latest to call for using noninvasive, stool-based testing in addition to colonoscopy," Dr. Itzkowitz said. "FIT and multitarget stool DNA tests all have proven efficacy in this regard, so gastroenterologists should have those conversations with their patients. GIs can also make it easier for patients to complete colonoscopy by developing patient navigation programs, direct access referrals, and systems for communicating with primary care providers for easier referrals and communicating colonoscopy results."

Many practices are already instituting such improvements in response to the restrictions imposed by the COVID-19 pandemic, according to Dr. Itzkowitz. "These changes, plus better coverage by payers, will make a huge impact on health equity when it comes to colorectal cancer screening."

The publication was supported by the AGA. The investigators disclosed relationships with Geneoscopy, ColoWrap, UniversalDx, and others. Dr. Itzkowitz disclosed no relevant conflicts of interest. ■

AGA resource

Groups interested in collaborating with AGA should contact Kathleen Teixeira, AGA Vice President, Public Policy and Advocacy, at kteixeira@gastro.org.

American Gastroenterological Association's position statements on reducing the burden of colorectal cancer

1. AGA supports the development of a national approach to CRC screening to ensure accessibility to all individuals in the United States with the goal to eliminate suffering and death from CRC.
2. There is strong evidence from randomized controlled trials, observational clinical studies, and modeling studies that increasing CRC screening rates will reduce CRC incidence and mortality.
3. A screening program should include both colonoscopy and noninvasive screening options, patient education, outreach, and navigation support.
4. Co-pays and deductibles are barriers to screening and contribute to socioeconomic disparities. The full cost of screening should be covered by payers without cost sharing.
5. Screening with high-quality colonoscopy should be covered by payers without cost sharing, consistent with the aims of the Affordable Care Act. These costs include the bowel preparation, facility and professional fees, anesthesia, and pathology.
6. Noninvasive colorectal screening should be considered as programs with multiple steps, each of which, including follow-up colonoscopy if the test is positive, should be covered by payers without cost sharing as part of the screening continuum.
7. AGA supports expansion of the continuum of screening to include the follow-up of patients found to have high-risk adenomas or advanced sessile serrated lesions.
8. AGA, working with a broad coalition of stakeholders, envisions the creation of a national resource to help manage population health focused on ensuring high-quality CRC screening and eliminating barriers to CRC screening.

Source: Gastroenterology. 2022 Jun 14. doi: 10.1053/j.gastro.2022.05.011

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GI & HEPATOLOGY NEWS

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Benefits beyond reducing weight

ESG *from page 1*

the annual Digestive Disease Week® (DDW).

Improvements included weight, hemoglobin A1c percentage, hypertension, and low-density lipoprotein. "I was surprised that the LDL decreased numerically, not so much HbA1c and hypertension. I knew [those] would come down with weight loss," said Dr. Westerveld, a second-year fellow at Weill Cornell Medicine, New York.

He also called for guidelines for ESG. "Given the fact there's an improvement of comorbid conditions, it's something we should look at," said Dr. Westerveld.

"It's fascinating because it tells us two important things about endoscopic sleeve gastroplasty. One, [the benefit] in the majority of cases lasts at least 5 years. The weight loss is durable. And then it tells us that there's improvement in all the cardiometabolic factors that matter, and those effects are seen all the way up to 5 years. So very important findings that support the benefits of the endoscopic gastroplasty in obesity and cardiometabolic risks and metabolic syndrome," said Andres Acosta, MD, PhD, a comoderator of the session in which the study was presented. He is assistant professor of medicine and a consultant in gastroenterology and hepatology at Mayo Clinic in Rochester, Minn.

Continued on following page

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Will ESD replace EMR for large colorectal polyps?

The future standard of care

Dear colleagues,
Resection of polyps is the bread and butter of endoscopy. Advances in technology have enabled us to tackle larger and more complex lesions throughout the gastrointestinal tract, especially through endoscopic mucosal resection (EMR). Endoscopic submucosal dissection (ESD) is another technique that offers much promise for complex colorectal polyps and is being rapidly adopted in the West. But do its benefits outweigh the costs in time, money, and additional training needed for successful ESD? How can we justify higher recurrence rates with EMR when ESD is available? Will reimbursement continue to favor EMR? In this installment of Perspectives, Dr. Alexis Bayudan and Dr. Craig Munroe make the case for adopting ESD, while Dr. Sumeet K. Tewani highlights all the benefits of EMR. I invite you to a great debate and look forward to hearing your own thoughts on Twitter @AGA_GIHN and by email at ginews@gastro.org.

Dr. Ketwaroo

Gyanprakash A. Ketwaroo, MD, MSc, is assistant professor of medicine at Baylor College of Medicine, Houston. He is an associate editor for GI & Hepatology News.

Read more! Please find full-length versions of these debates online at MDedge.com/gihepnews/perspectives.

Endoscopic submucosal dissection (ESD) is a minimally invasive, organ-sparing, flexible endoscopic technique used to treat advanced neoplasia of the digestive tract, with the goal of en bloc resection for accurate histologic assessment. ESD was introduced over 25 years ago in Japan by a small group of innovative endoscopists. After its initial adoption and success with removing gastric lesions, ESD later evolved as a technique used for complete resection of lesions throughout the gastrointestinal tract.

With mounting evidence demonstrating ESD is superior to piecemeal EMR in terms of curative resection and recurrence rates, we think it is time for ESD to be incorporated widely into Western practice. ESD is still evolving and improving; ESD will become both safer and more effective. ESD has revolutionized endoscopic resection, and we are just beginning to see the possibilities and value of these techniques. ■

Dr. Bayudan

Dr. Munroe

Alexis Bayudan, MD, is a second-year fellow, and Craig A. Munroe, MD, is an associate professor, both at the University of California, San Francisco. They have no relevant conflicts of interest.

More investment than payoff

Most large colorectal polyps are best managed by endoscopic mucosal resection (EMR) and do not require endoscopic submucosal dissection (ESD). EMR can provide complete, safe, and effective removal, preventing colorectal cancer while avoiding the risks of surgery or ESD. EMR has several advantages over ESD. It is minimally invasive, low cost, and well tolerated, and allows excellent histopathologic examination. It is performed during colonoscopy in an outpatient endoscopy lab or ambulatory surgery center. There are several techniques that can be performed safely and efficiently using accessories that are readily available. It is easier to learn and perform, with lower risks and fewer resources. Endoscopists can effectively integrate EMR into a busy practice, without making significant additional investments. ■

Dr. Tewani

Sumeet K. Tewani, MD, of Rockford Gastroenterology Associates is clinical assistant professor of medicine at the University of Illinois, Rockford. He has no relevant conflicts of interest

Continued from previous page

The findings should also encourage more innovation. "Doing these endoscopic procedures, having successful results that hold for 5 years, opens the path for new and better procedures, so we have better weight loss," said Dr. Acosta.

Jim Kling/MDedge News

Guidelines should look at ESG because it improves comorbid conditions, said Dr. Donevan Westerveld.

Previous work by Dr. Westerveld's group found benefits of ESG at 12 months, including improvements in mean HbA1c levels in all patients (from 6.1% to 5.5%; P = .05) and those with diabetes or prediabetes (6.6% to 5.6%; P = .02), reduction in mean waist circumference (119.66 to 92.75 cm; P < .001), reduction in systolic blood pressure (129.02 to 122.23 mg/dL; P = .023), triglycerides (131.84 to 92.36 mg/dL; P = .017), and alanine aminotransferase (ALT, 32.26 to 20.68 mg/dL; P < .001).

In the new study, the group followed 255 patients at 1, 3, and 5 years post procedure who were treated consecutively at Weill Cornell Medicine from 2013 to 2021. Among the patients were those who had failed weight loss measures and were either not candidates for surgery or had refused surgery.

The mean age was 45.5 years, 69% were female, and the mean body mass index was 38.6. Overall, 40.3% had prediabetes or diabetes, 26.7% had hypertension, 60.8% had LDL above 100 mg/dL, and 29.3% had elevated ALT. Sixty-six percent had been followed up at 1 year, 78% at 3 years, and 87% at 5 years.

Weight loss averaged 15.7% at 1 year and 15.3% at year 5, and the values were statistically significant. Among patients with diabetes and prediabetes, HbA1c percentage dropped from a baseline value of 6.4% to 5.7% at year 1, 6.1% at year 3, and 5.8% at year 5 (P < .05 for all). For all patients, the value dropped from 5.8% at baseline to 5.6% at year 1, 5.7% at year 3, and 5.4% at year 5. These changes were not statistically significant.

Systolic blood pressure went down among patients with stage 1 hypertension, from 135 mm Hg at baseline to 122 at year 1 and 121 at year 3 (P < .05 or both), but the mean value increased to 129 at year 5 and was not statistically significant. LDL among all patients declined from 136 mg/dL at baseline to 125 at year 1 (nonsignificant), 115 at year 3 (P < .05), and 109 at year 5 (P < .05). Alanine transaminase values declined from about 29 at baseline to 25 at year 1, 26 at year 3, and 24 at year 5 (P < .05 for all).

Serious adverse events were rare, occurring in just two cases (< 1%).

The study was limited by lack of a sham control, and its retrospective data may have included bias because many of the procedures were not paid for by insurance, leading to high rates of self-pay.

Dr. Westerveld has no relevant financial disclosures. Dr. Acosta is a founder of Gila Therapeutics and Phenomix Sciences. Dr. Acosta consults for Amgen, Gila Therapeutics, Rhythm Pharmaceuticals, and General Mills. He has received funding from Rhythm, Novo Nordisk, Apollo Endosurgery, and USGI Medical. ■

Confronting endoscopic infection control

BY BRANDON MAY
MDedge News

The reprocessing of endoscopes following gastrointestinal endoscopy is highly effective for mitigating the risk of exogenous infections, yet challenges in duodenoscope reprocessing continue to persist. While several enhanced reprocessing measures have been developed to reduce duodenoscope-related infection risks, the effectiveness of these enhanced measures is largely unclear.

Rahul A. Shimpi, MD, and Joshua P. Spaete, MD, from Duke University, Durham, N.C., wrote in a paper in Techniques and Innovations in Gastrointestinal Endoscopy (2022 Jan 6. doi: 10.1016/j.tige.2021.12.005) that novel disposable duodenoscope technologies offer promise for reducing infection risk and overcoming current reprocessing challenges. The paper notes that, despite this promise, there is a need to better define the usability, costs, and environmental impact of disposable technologies.

Current challenges in endoscope reprocessing

According to the authors, the reprocessing of gastrointestinal endoscopes involves several sequential steps that require a "meticulous" attention to detail "to ensure the adequacy of reprocessing." Human factors/errors are a major contributor to suboptimal reprocessing quality, and these errors are often related to varying adherence to current reprocessing protocols among centers and reprocessing staff members.

There is a need to better define the usability, costs, and environmental impact of disposable technologies.

Despite these challenges, infectious complications associated with gastrointestinal endoscopy are rare, particularly in relation to end-viewing endoscopes. Many high-profile infectious outbreaks associated with duodenoscopes have been reported in recent years, however, which has heightened the awareness and corresponding concern with endoscope reprocessing. Many of these infectious outbreaks, the authors said, have involved multidrug-resistant organisms.

The complex elevator mechanism, which the authors noted "is relatively inaccessible during the precleaning and manual cleaning steps in reprocessing," represents a paramount challenge in the reprocessing of duodenoscopes. The challenge related to this mechanism potentially contributes to greater biofilm formation and contamination. Other factors implicated in the transmission of duodenoscope-associated infections from patient to patient include other design issues, human errors in reprocessing, endoscope damage and channel defects, and storage and environmental factors.

"Given the reprocessing challenges posed by duodenoscopes, in 2015 the Food and Drug Administration issued a recommendation that one or more supplemental measures be implemented by facilities as a means to decrease the infectious risk posed by duodenoscopes," the authors noted, including ethylene oxide (EtO) sterilization, liquid chemical sterilization, and

repeat high-level disinfection (HLD). They added, however, that a recent U.S. multisociety reprocessing guideline (Gastrointest Endosc. 2021 Jan;93[1]:11-33.e6) "does not recommend repeat high-level disinfection over single high-level disinfection, and recommends use of EtO sterilization only for duodenoscopes in infectious outbreak settings."

New sterilization technologies

Liquid chemical sterilization may be a promising alternative to EtO sterilization because it features a shorter disinfection cycle time and less endoscope wear or damage. However, clinical data for the effectiveness of LCS in endoscope reprocessing remain very limited.

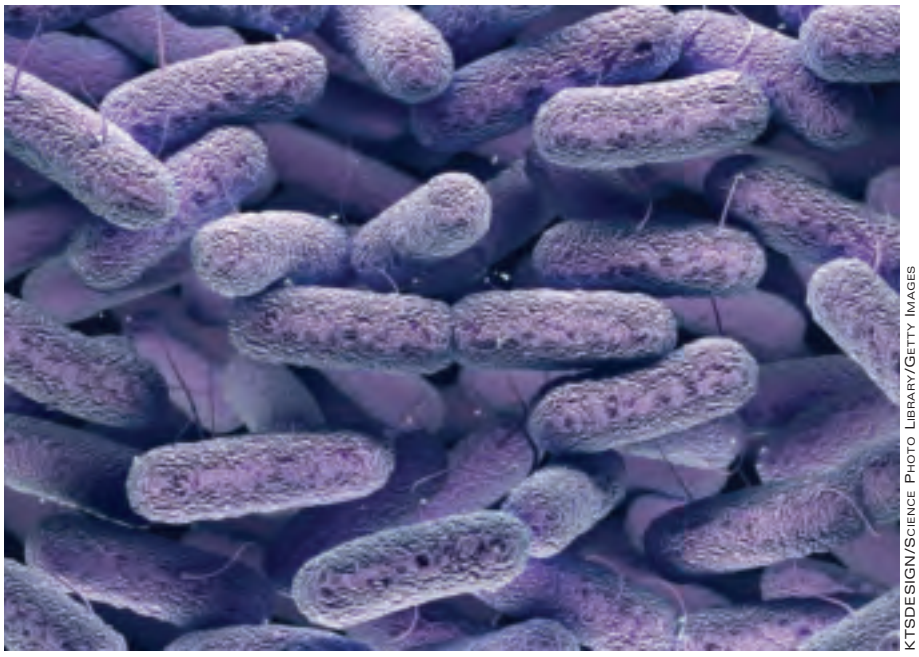
The high costs and toxicities associated with EtO sterilization may be overcome by the plasma-activated gas, another novel low-temperature sterilization technology. This newer sterilization technique also features a shorter reprocessing time, thereby making it an attractive option for duodenoscope reprocessing. The authors noted that, although it showed promise in a proof-of-concept study (Gastrointest Endosc. 2019 Jan;89[1]:105-14), "plasma-activated gas has not been assessed in working endoscopes or compared directly to existing HLD and EtO sterilization technologies."

Quality indicators in reprocessing

Recently, several quality indicators have been developed to assess the quality of endoscope reprocessing. The indicators, the authors noted, may theoretically allow "for point-of-care assessment of reprocessing quality." To date, the data to support these indicators are limited.

Adenosine triphosphate testing has been the most widely studied indicator because this can be used to examine the presence of biofilms during endoscope reprocessing via previously established ATP benchmark levels, the authors wrote. Studies that have assessed the efficacy of ATP testing, however, are limited by their use of heterogeneous assays, analytical techniques, and cutoffs for identifying contamination.

Hemoglobin, protein, and carbohydrate are other point-of-care indicators that have previously demonstrated potential capability of assessing the achievement of adequate manual endoscope cleaning before high-level disinfection or sterilization.



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Novel disposable duodenoscope technologies

Given that consistent research studies have shown the existence of residual duodenoscope contamination after standard and enhanced reprocessing, there has been increased attention placed on novel disposable duodenoscope technologies. In 2019, the FDA recommended a move toward duodenoscopes with disposable components because it could make reprocessing easier, more effective, or altogether unnecessary. According to the authors, there are currently six duodenoscopes with disposable components that are cleared by the FDA for use. These include three that use a disposable endcap, one that uses a disposable elevator and endcap, and two that are fully disposable. The authors stated that, while "improved access to the elevator facilitated by a disposable endcap may allow for improved cleaning" and reduce contamination and formation of biofilm, there are no data to confirm these proposed advantages.

There are several unanswered questions regarding new disposable duodenoscope technologies, including questions related to the usability, costs, and environmental impact of these technologies. The authors summarized several studies discussing these issues; however, a clear definition or consensus regarding how to approach these challenges has yet to be established. In addition to these unanswered questions, the authors also noted that identifying the acceptable rate of infectious risk associated with disposable duodenoscopes is another "important task" that needs to be accomplished in the near future.

Environmental impact

The authors stated that the health care system in the United States is directly responsible for up to 10% of total U.S. greenhouse emissions. Additionally, the substantial use of chemicals and water in endoscope reprocessing represents a "substantial" concern for the environment. One estimate suggested that a mean of 40 total endoscopies per day generates around 15.78 tons of CO_2 per year (Am J Gastroenterol. 2020 Dec;115[12]:1931-2).

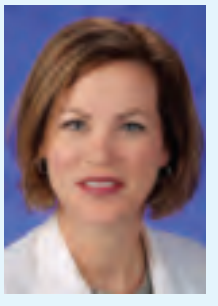
Given the unclear impact disposable endoscopes may have on the environment, the authors suggested that there is a clear need to discover interventions that reduce their potential negative impact. Strategies that reduce the number of endoscopies performed, increased recycling and use of recyclable materials, and use of renewable energy sources in endoscopy units have been proposed.

"The massive environmental impact of gastrointestinal endoscopy as a whole has become increasingly recognized," the authors wrote, "and further study and interventions directed at improving the environmental footprint of endoscopy will be of foremost importance."

The authors disclosed no conflicts of interest. ■

Solutions surrounding proper endoscope reprocessing and infection prevention have become a major focus of investigation and innovation in endoscope design, particularly related to duodenoscopes. As multiple infectious outbreaks associated with duodenoscopes have been reported, the complex mechanism of the duodenoscope elevator has emerged as the target for modification because it is somewhat inaccessible and difficult to adequately clean.

As a result of the challenges associated with duodenoscope reprocessing, the FDA recommended additional measures be implemented by facilities to help mitigate the infectious risk of duodenoscopes. Current research is being conducted on novel sterilization techniques as well as several point-of-care reprocessing quality indicators. Despite improvements in reprocessing quality, residual contamination of duodenoscopes led the FDA to recommend in 2019 that all units using duodenoscopes transition to duodenoscopes with disposable design elements. In addition, fully disposable duodenoscopes have been developed, with two types currently available in the United States.



Dr. Maranki

One of the major considerations related to disposable duodenoscopes is the cost. Currently, the savings from removing the need for reprocessing equipment, supplies, and personnel, does not balance the cost of the disposable duodenoscope. Studies on the environmental impact of disposable duodenoscopes suggest a major increase in endoscopy-related waste.

In summary, enhanced reprocessing techniques and modified scope design elements may not achieve adequate thresholds for infection prevention. Furthermore, while fully disposable duodenoscopes offer promise, questions remain about overall functionality, cost, and the potentially profound environmental impact. Further research is warranted on feasible solutions for infection prevention, and the issues of cost and environmental impact must be addressed before the widespread adoption of disposable duodenoscopes.

Jennifer Maranki, MD, MSc, is professor of medicine and director of endoscopy at Penn State Hershey Medical Center. She reports being a consultant for Boston Scientific.

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GI & HEPATOLOGY NEWS

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AI-based CADe outperforms HDWL colonoscopy

BY BRANDON MAY
MDedge News

An artificial intelligence (AI)–based computer-aided detection (CADe) system missed fewer adenomas, polyps, and sessile serrated lesions and identified more adenomas per colonoscopy than a high-definition white-light (HDWL) colonoscopy, according to findings from a randomized study.

While adenoma detection by colonoscopy is associated with a reduced risk of interval colon cancer, detection rates of adenomas vary among physicians. AI approaches, such as machine learning and deep learning, may improve adenoma detection rates during colonoscopy and thus potentially improve outcomes for patients, suggested study authors led by Jeremy R. Glissen Brown, MD, of the Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, who reported their trial findings in Clinical Gastroenterology and Hepatology (2021 Sep 13. doi: 10.1016/j.cgh.2021.09.009).

The investigators explained that, although AI approaches may offer benefits in adenoma detection, there have been no prospective data for U.S. populations on the efficacy of an AI-based CADe system for improving adenoma detection rates (ADRs) and reducing adenoma miss rates (AMRs).

To overcome this research gap, the investigators performed a prospective, multicenter, single-blind randomized tandem colonoscopy study which assessed a deep learning–based CADe system in 232 patients.

Individuals who presented to four U.S. medical centers for either colorectal cancer screening or surveillance were randomly assigned to the CADe system colonoscopy first (n = 116) or HDWL colonoscopy first (n = 116). This was immediately followed by the other procedure, in tandem fashion, performed by the same endoscopist. AMR was the primary outcome of interest, while secondary outcomes were adenomas per colonoscopy (APC) and the miss rate of sessile serrated lesions (SSL).

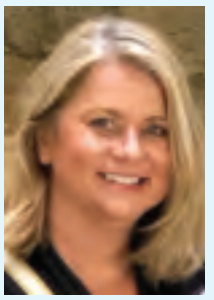
The researchers excluded 9 patients, which resulted in a total patient population of 223 patients. Approximately 45.3% of the cohort was female, 67.7% were White, and 21% were Black. Most patients (60%) were indicated for primary colorectal cancer screening.

Compared with the HDWL-first group, the AMR was significantly lower in the CADe-first group (31.25% vs. 20.12%, respectively; P = .0247). The researchers commented that, although the CADe system resulted in a statistically significantly lower AMR, the rate still reflects missed adenomas.

Additionally, the CADe-first group had a lower

CADe · *Continued on following page*

Several randomized trials testing artificial intelligence (AI)–assisted colonoscopy showed improvement in adenoma detection. This study adds to the growing body of evidence that computer-aided detection (CADe) systems for adenoma augment adenoma detection rates (ADRs), even among highly skilled endoscopists whose baseline ADRs are much higher than the currently recommended threshold for quality colonoscopy (25%).


Dr. Fischer

This study also highlights the usefulness of CADe in aiding detection of sessile serrated lesions (SSL). Recognition of SSL appears to be challenging for trainees and the most likely type of missed large adenomas overall.

Given its superior performance, compared with high-definition white-light colonoscopy, AI-assisted colonoscopy will likely soon become standard of care. Beyond adenoma detection programs such as CADe, there will be systems to aid with the diagnosis and predict histology such as CADx and other AI programs that evaluate the quality of colon examination by the endoscopist. CADe systems are currently quite expensive but expected to be more affordable as new products become available on the market.

AI-based systems will enhance but will not replace the highly skilled operator. As this study pointed out, despite the superior ADR, adenomas were still missed by CADe. The main reason for this was that the missed polyps were not brought into the visual field by the operator. A combination of a CADe program and a distal attachment mucosa exposure device in the hands of an experienced endoscopists might bring the best results.

Monika Fischer, MD, AGAF, is an associate professor of medicine at Indiana University, Indianapolis. She reported no relevant conflicts of interest.

Do myenteric neurons replicate in small intestine?

BY BRANDON MAY
MDedge News

A new study contradicts controversial findings from a 2017 study that had suggested around two-thirds of myenteric neurons replicate within 1 week, which – if true – would have an impact on research into several GI diseases and pathologies.

Previous research had suggested that myenteric nerve cells, which help control peristalsis throughout the digestive tract, do not replicate under normal conditions, wrote Heikki Virtanen, MD, of the University of Helsinki, and colleagues. Their report is in Cellular and Molecular Gastroenterology and Hepatology (2022 Apr 10. doi: 10.1016/j.jcmgh.2022.04.001). However, a study by Subhash

Neurons · *Continued on following page*

The enteric nervous system (ENS) is composed of neurons and glia along the GI tract that are responsible for coordinating its motility, absorption, secretion, and other essential functions. While new neurons are formed during gut development, enteric neurogenesis in adult animals has been a subject of controversy but is of fundamental importance to understanding ENS biology and pathophysiology.

The debate was sparked by a study from Kulkarni and colleagues in 2017 that showed a surprising rate of neuronal turnover, with 88% of all myenteric neurons in the ileum replaced every 2 weeks. Given the complexity of enteric neuronal network formation, the concept of continual neuronal death and rebirth came as a surprise to the field. That finding is in sharp contrast to multiple studies that show essentially no enteric neurogenesis in healthy adult intestine, and to recent transcriptomic studies of the ENS that, while supporting a high turnover of intestinal epithelial cells, have found no significant cycling population of enteric neurons.


Dr. Goldstein

To settle the debate, Virtanen et al. replicated the Kulkarni study using the same methods, with the addition of EdU-based click chemistry, and found no replicating neurons. The bulk of evidence thus supports the concept that enteric neurons in the adult gut are a stable population that undergo minimal turnover. Enteric neuronal progenitors, however, are present in the adult gut and can undergo neurogenesis in response to injury. Further research is needed to identify the signals that activate that neurogenic response and to understand how it can be leveraged to treat neurointestinal diseases.

Allan M. Goldstein, MD, is chief of pediatric surgery at Massachusetts General Hospital, professor of surgery at Harvard Medical School, principal investigator in the Pediatric Surgery Research Laboratories, and codirector of the Massachusetts General Center for Neurointestinal Health, all in Boston. He has no relevant conflicts.

CADe · *Continued from previous page*

SSL miss rate, compared with the HDWL-first group (7.14% vs. 42.11%, respectively; *P* = .0482). The researchers noted that their study is one of the first research studies to show that a computer-assisted polyp detection system can reduce the SSL miss rate. The first-pass APC was also significantly higher in the CADe-first group (1.19 vs. 0.90; *P* = .0323). No statistically significant difference was observed between the groups in regard to the first-pass ADR (50.44% for the CADe-first group vs. 43.64 % for the HDWL-first group; *P* = .3091).

According to the researchers, the study was not powered to identify differences in ADR, thereby limiting the interpretation of this analysis. In addition, the investigators noted that the tandem colonoscopy study design is limited in its generalizability to real-world clinical settings. Also, given that endoscopists were not blinded to group assignments while performing each withdrawal, the researchers commented that "it is possible that endoscopist performance was influenced by being observed or that endoscopists who participated for the length of the study became over-reliant on" the CADe system during withdrawal, resulting in an underestimate or overestimation of the system's performance.

The authors concluded that their findings suggest that an AI-based CADe system with colonoscopy "has the potential to decrease interprovider variability in colonoscopy quality by reducing AMR, even in experienced providers."

This was an investigator-initiated study, with research software and study funding provided by Wision AI. The investigators reported relationships with Wision AI, as well as Olympus, Fujifilm, and Medtronic. ■

Neurons · *Continued from previous page*

Kulkarni, PhD, published in 2017 (Proc Natl Acad Sci U S A. 2017 May 2;114[18]:E3709-18), "challenged this dogma, suggesting that almost 70% of myenteric neurons are replaced within 1 week under normal physiological conditions."

According to the researchers, the difference between the controversial study findings and other research results may be partially explained by differences in methodology. Dr. Virtanen and colleagues initiated the current study because no systematic evaluation of those potential confounding variables had been undertaken.

For example, Dr. Virtanen and colleagues administered the nucleoside analogue 5-iodo-2'-deoxyuridine (IdU) in drinking water with the same concentration and labeling period, DNA denaturation steps, and antibodies as Dr. Kulkarni's 2017 study had used. However, they also examined additional areas of the small intestine, employed paraffin embedding, performed parallel analysis using "click chemistry"–based detection of 5-ethynyl-2'-deoxyuridine (EdU), and more.

The gut's epithelial cells turn over within 1 week "and serve as an internal positive control for DNA replication," the researchers noted. In this study, IdU-positive enteric nerve cells were not revealed in microscopic analysis of immunohistochemically labeled small intestines. In contrast, the researchers wrote that the epithelium demonstrated label retention.

The fact that the repeat of exactly the same experiment with the same reagents and methods did not reproduce the finding, not even partially, supports this interpretation and is further supported by the same conclusion using EdU-based click chemistry data and previous studies."

The authors disclose no conflicts. ■

Esophageal cancer screening isn't for everyone

BY BRANDON MAY
MDedge News

Endoscopic screening for esophageal adenocarcinoma (EAC), may not be a cost-effective strategy for all populations, possibly even leading to net harm in some, according to a comparative cost-effectiveness analysis.

Several U.S. guidelines suggest the use of endoscopic screening for EAC, yet recommendations within these guidelines vary in terms of which population should receive screening, according study authors led by Joel H. Rubenstein, MD, AGAF, of the Lieutenant Charles S. Kettles Veterans Affairs Medical Center, Ann Arbor, Mich. Their findings were published in Gastroenterology (2022 Mar 28. doi: 10.1053/j.gastro.2022.03.037). In addition, there have been no randomized trials to date that have evaluated endoscopic screening outcomes among different populations. Population screening recommendations in the current guidelines have been informed mostly by observational data and expert opinion.

Existing cost-effectiveness analyses of EAC screening have mostly focused on screening older men with gastroesophageal reflux disease (GERD) at certain ages, and many of these analyses have limited data regarding diverse patient populations.

In their study, Dr. Rubenstein and colleagues performed a comparative cost-effectiveness analysis of endoscopic screening for EAC that was restricted to individuals with GERD symptoms in the general population. The analysis was stratified by race and sex. The primary objective of the analysis was to identify and establish the optimal age at which to offer endoscopic screening in specific populations.

The investigators conducted their comparative cost-effectiveness analyses using three independent simulation models. The independently developed models – which focused on EAC natural history, screening, surveillance, and treatment – are part of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network. For each model, there were four cohorts, defined by race as either White or Black and sex, which were independently calibrated to targets to reproduce the EAC incidence in the United States. The three models were based on somewhat different structures and assumptions, but all three assumed EAC develops only in individuals with Barrett's esophagus.

The researchers considered 42 strategies, such as no screening, a single endoscopic screening at six specified ages (between 40 and 65 years of age), and a single screening in individuals with GERD symptoms at the six specified ages.

Primary results were the averaged results across all three models. The optimal screening strategy, defined by the investigators, was the strategy with the highest effectiveness that had an incremental cost-effectiveness ratio of less than $100,000 per quality-adjusted life-year gained.

The optimal screening strategy for White men was one that screened individuals with GERD twice, once at age 45 years and again at 60 years. The researchers determined that screening Black men with GERD once at 55 years of age was optimal.

By contrast, the optimal strategy for women, whether White or Black, was no screening at all. "In particular, among Black women, screening is, at best, very expensive with little benefit, and some strategies cause net harm," the authors wrote.

The investigators wrote that there is a need for empiric, long-term studies "to confirm whether repeated screening has a substantial yield of incident" Barrett's esophagus. The researchers also noted that their study was limited by the lack of inclusion of additional risk factors, such as smoking, obesity, and family history, which may have led to different conclusions on specific screening strategies.

"We certainly acknowledge the history of health care inequities, and that race is a social construct that, in the vast majority of medical contexts, has no biological basis," they wrote.

The study was supported by National Institutes of Health/National Cancer Institute grants. Some authors disclosed relationships with Lucid Diagnostics, Value Analytics Labs, and Cernostics. ■

Over the past decades we have seen an alarming rise in the incidence of esophageal adenocarcinoma, mostly diagnosed at an advanced stage when curative treatment is no longer an option. Esophageal adenocarcinoma develops from Barrett's esophagus that, if known to be present, can be surveilled to detect dysplasia and cancer at an early and curable stage. Therefore, Barrett's esophagus and early esophageal adenocarcinoma would be ideal screening targets since this could prevent significant disease burden and health care costs. However, optimal screening strategies should be personalized, be cost effective, and most importantly, cause no harm to healthy subjects.


Dr. Pouw

Whereas currently screening for Barrett's esophagus focused on White males with gastroesophageal reflux, little was known about screening in non-White and non-male populations. Identifying who and how to screen poses a challenge, and in real life such studies looking at varied populations would require many patients, years of follow-up, much effort and substantial costs. Rubenstein and colleagues used three independent models to simulate many different screening scenarios, while taking gender and race into account. The outcomes of this study, which demonstrate that one size does not fit all, will be very relevant in guiding future strategies regarding screening for Barrett's esophagus and early esophageal adenocarcinoma. Although the study is based around endoscopic screening, the insights gained from this study will also be relevant when considering the use of nonendoscopic screening tools.

R.E. Pouw, MD, PhD, is with Amsterdam University Medical Centers. She discloses having been a consultant for MicroTech and Medtronic and having received speaker fees from Pentax.

Plan a gift that offers a better future for GI

Planned giving provides an opportunity for all who have benefited from digestive disease research to give back to the field in a unique and lasting way.

aga research foundation

Your investment in the AGA Research Foundation will enable the foundation to continue our investment in the future of gastroenterological research and innovation. With donations from AGA members, we can provide young researchers with a secure, ongoing stable source of funding that drives advancement in the diagnosis, treatment, and cure of digestive diseases.

If you make a contribution, it will be because you believe in what we do and because you want to help make a difference in the lives of others. But we'd also like to make sure you benefit from making a gift to the AGA Research Foundation.

Your giving options

There are several gift arrangements to choose from. The chart below summarizes the benefits of some of the main types of charitable gifts. Just think of what you want to accomplish with your gift, and there's probably a way to do it!

Learn more by visiting http://gastro.planmylegacy.org. ■

Options for giving

Your gift	Your goal	How you make the gift	Your benefits
Bequest in will	Defer a gift until after your lifetime.	Name the AGA Research Foundation in your will (designate a specific amount, a percentage, or a share of the residue).	• Control of asset for your lifetime • Donation exempt from future federal estate tax
Outright gift of securities	Eliminate tax on capital gains.	Contribute long-term appreciated stock or other securities.	• Immediate charitable deduction of full fair market value • Elimination of capital gains taxes
Gift of life insurance	Make a large gift with little cost to yourself.	Contribute a life insurance policy you no longer need.	• Current income tax deduction • Possible future deductions through gifts to pay policy premiums
Gift of retirement plan assets	Eliminate the twofold taxation on IRAs or other qualified retirement plans.	Name the AGA Research Foundation as the beneficiary of the balance left after your lifetime using the plan's beneficiary form.	• More assets for family if gift made from most highly taxed assets • Elimination of income and estate taxes
Gift of real estate	Make a gift of an asset no longer needed and generate an income tax deduction.	Donate the property to the AGA Research Foundation, or sell it to us at a bargain price.	• Immediate income tax deduction • Reduction or elimination of capital gains tax
Charitable lead trust	Reduce gift and estate taxes on assets you pass to children or grandchildren.	Create a charitable trust that pays fixed or variable income to us for a specific term of years; thereafter the balance is given to loved ones.	• Reduction of your taxable estate • Property kept by your family, often with reduced gift taxes
Charitable remainder annuity trust	Secure a fixed income and supplement your retirement funds.	Create a charitable trust that pays you a set income annually.	• Fixed payments for life, often at a higher rate of return • Immediate income tax deduction

'The Rock' assumes the presidency of AGA

We're honored to announce that John M. Carethers, MD, AGAF, affectionately nicknamed "The Rock," began his term as the 117th president of the AGA Institute on June 1, 2022.

He currently serves as John G. Searle professor of internal medicine and chair of the department of internal medicine at the University of Michigan Health System, a position he has held since 2009.


Dr. Carethers

Dr. Carethers' research programs focus on familial colon cancer and polyposis syndromes. His research encompasses Lynch syndrome, juvenile polyposis, hyperplastic polyposis, and colorectal cancer. He has published more than 182 articles.

A native of Detroit, Dr. Carethers earned his undergraduate degree in molecular biology and biophysics at Wayne State University. He remained there for medical school, where he graduated at the top of his class. His ability to stay focused on his work earned him the moniker "The Rock." It's a strength that's made him an outstanding role model and exemplary leader.

An active member of AGA for more than 20 years, Dr. Carethers received the AGA Gastrointestinal Oncology Section Research Mentor Award as well as the AGA Distinguished Mentor Award in 2017. He has served on several AGA committees, including the AGA Nominating Committee, AGA Underrepresented Minorities Committee, AGA Research Policy Committee, AGA Institute Council, and the AGA Trainee & Young GI Committee. He has also served as senior associate editor of Gastroenterology.

His academic career began at the University of California, San Diego, preceded by a gastroenterology fellowship at University of Michigan in Ann Arbor and residency at Massachusetts General Hospital in Boston. From the beginning, he has inspired others with his strong work ethic and intense dedication.

Dr. Carethers joined the AGA Governing Board in June 2020 as vice president and served as president-elect prior to assuming the top leadership role. ■

New AGA Research Foundation Executive Board members

We're pleased to share that Michael Camilleri, MD, AGAF, of Mayo Clinic, Rochester, MN, will be taking over the AGA Research Foundation chair role. He has recruited five members to be part of the board.

- Aline Charabaty, MD, AGAF, Johns Hopkins School of Medicine, Washington, D.C.
- Eric Esrailian, MD, MPH, AGAF, David Geffen School of Medicine at UCLA, Los Angeles, CA
- Robert A. Ganz, MD, MASGE, MNGI Digestive Health, Minnetonka, MN
- Aja S. McCutchen, MD, Atlanta Gastroenterology Associates, Hoschton, GA
- Michael L. Kochman, MD, AGAF, University of Pennsylvania, Philadelphia, PA ■

Coding guide for CRC screening

New policies are making colorectal cancer (CRC) screening free to more people and eliminating surprise bills, but only if doctors and facilities submit the correct procedure and diagnosis codes. A new AGA guide can help you identify the correct codes and outline how to help patients who get an unexpected bill after undergoing a colorectal cancer screening.

View the guide for the most common CRC screening tests, how to code for them, and what patients with commercial insurance and Original Medicare can usually expect to pay https://gastro.org/practice-resources/reimbursement/coding-faq-screening-colonoscopy/. ■

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A surprise and a mystery: NAFLD in lean patients linked to CVD risk

BY DAMIAN MCNAMARA

AT DDW 2022

SAN DIEGO – People with nonalcoholic fatty liver disease (NAFLD) and a lean or healthy body mass index are at increased risk for peripheral vascular disease, stroke, and cardiovascular disease, a surprise finding from a new study reveals.

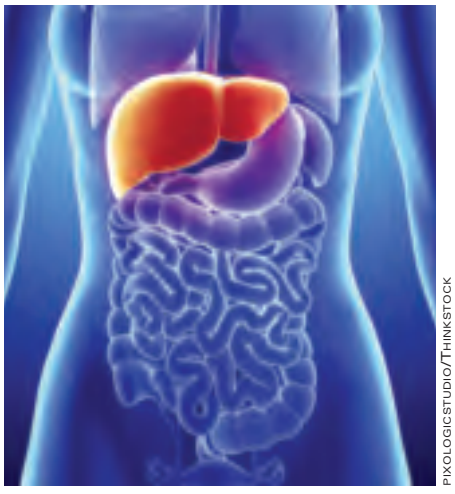
"Our team had expected to see that those with a normal BMI would have a lower prevalence of any metabolic or cardiovascular conditions," lead researcher Karn Wijarnpreecha, MD, MPH, said during a media briefing that previewed select research for Digestive Disease Week® (DDW). "So, we were very surprised to find this link to cardiovascular disease."

The investigators saw this increased risk of cardiovascular disease despite this group having a lower prevalence of atherosclerotic risk factors and metabolic disease.

This first study of its kind suggests physicians should consider the risk of cardiovascular disease in all patients with NAFLD, not just in those who are overweight or living with obesity – groups traditionally thought to carry more risk.

NAFLD in lean individuals is not a benign disease.

"NAFLD patients with a normal BMI are often overlooked because we assume that the risk for more serious conditions is lower than for those who are overweight or obese. But this way of thinking may be putting these patients at risk," added Dr. Wijarnpreecha, who is a transplant hepatology fellow at the University of Michigan, Ann Arbor.



PIXOLOGICSTUDIO/THINKSTOCK

Key findings

Approximately 25% of U.S. adults live with NAFLD, an umbrella term for liver conditions in people who drink little to no alcohol. It is characterized by too much fat stored in the liver. Although most people have no symptoms, the condition can lead to other dangerous conditions, such as diabetes, cardiovascular disease, and cirrhosis of the liver, Dr. Wijarnpreecha said.

The investigators retrospectively studied a cohort of 18,793 adults diagnosed with NAFLD at the University of Michigan Hospital from 2012 to 2021. One aim was to compare the prevalence of cirrhosis, cardiovascular disease, metabolic diseases, and chronic kidney disease in relation to BMI.

They also classified people into four BMI categories: lean, overweight, obesity class 1, and obesity class 2-3.

Compared with non-lean patients, lean patients had a higher prevalence of peripheral arterial disease and stroke and a similar rate of cardiovascular disease based on

identification of ICD codes.

Almost 6% of lean patients had peripheral arterial disease, compared with rates of approximately 4%-5% in overweight people and people with obesity. Similarly, more than 6% of the lean group experienced a stroke compared with 5% or less of the other BMI groups.

"We found that lean patients with NAFLD also had a significant higher prevalence of cardiovascular disease, independent of age, sex, race, smoking status, diabetes, hypertension, and dyslipidemia," Dr. Wijarnpreecha said.

At the same time, compared with non-lean patients, lean patients had a lower prevalence of cirrhosis, diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease in an analysis that adjusted for confounders.

Exploring the unknown

Researchers now have a mystery on their hands: What is causing this unexpected higher risk of cardiovascular disease in lean people with NAFLD?

Loren Laine, MD, AGAF, chief of the section of digestive diseases at Yale University School of Medicine, New Haven, Conn., and moderator of the media briefing, asked Dr. Wijarnpreecha for his leading theory behind this connection.

"We think that could be from a difference in lifestyle, diet, exercise, genetics, or even gut microbiota," Dr. Wijarnpreecha replied. "But these are factors that we did not capture from this current study."

"We are preparing to conduct additional research with longitudinal data to better understand NAFLD in lean patients," Dr. Wijarnpreecha added.

"It's an interesting finding, but there are some questions from this retrospective study," said Arun J. Sanyal, MD, when asked to comment on the study.

Identifying and quantifying any alcohol use, smoking, or hypertension that could also have contributed to increased cardiovascular risk would be useful. Another question relates to how the population with NAFLD was identified. Was NAFLD an incidental finding in their diagnosis, asked Dr. Sanyal, director of the Stravitz-Sanyal Institute for Liver Disease & Metabolic Health at Virginia Commonwealth University, Richmond.

"I'm not dissing the study," he said, "But like all the observations like this, I think we have to kick the tires."

"There's no question it is important to continue to do these types of studies," he added. "Through this kind of research we find new things that lead to the science that can then significantly change how we approach these issues."

Dr. Wijarnpreecha reported no financial relationships with a commercial interest. Dr. Laine and Dr. Sanyal reported financial relationships with a commercial interest, but none were relevant to this coverage. ■

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