aga American Gastroenterological Association

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Brian Strickland/University of North Carolina

Dr. Anne F. Peery, of University of North Carolina, Chapel Hill, recommends against surgery in certain patients.

AGA Clinical Practice Update

Medical management of colonic diverticulitis

BY AMY KARON
MDedge News

A new clinical practice update from the American Gastroenterological Association seeks to provide gastroenterologists with practical and evidence-based advice for management of colonic diverticulitis.

For example, clinicians should consider lower endoscopy and CT scans of the abdomen and pelvis with oral and intravenous contrast to rule out chronic diverticular inflammation, diverticular stricture or fistula, ischemic colitis, constipation, and inflammatory bowel disease, Anne F. Peery, MD, MSCR, of the University of North Carolina, Chapel Hill, and associates wrote in Gastroenterology.

"In our practice, patients are reassured to know that ongoing symptoms are common and often attributable to visceral hypersensitivity," they wrote. "This conversation is particularly important after a negative workup. If needed, ongoing abdominal pain can be treated with

See **Diverticulitis** · *page 5*

COVID-19 vaccines: Are they safe for immunocompromised patients?

BY ROXANNE NELSON, RN, BSN
MDedge News

Coronavirus vaccines have become a reality, as they are now being approved and authorized for use in a growing number of countries including the United States. The U.S. Food and Drug Administration has issued emergency authorization for the use of the COVID-19 vaccine produced by Pfizer and BioNTech. Close behind was the vaccine developed by Moderna.

The efficacy of a two-dose administration of the vaccine has been pegged at 95.0%, and the FDA has said that the 95% credible interval for the vaccine efficacy was 90.3%-97.6%. But as with many initial clinical trials, whether for drugs or vaccines, not all populations were represented in the trial cohort, including individuals who are immunocompromised. As of December 2020, it is largely unknown how safe or effective the vaccine may be in this large population, many of whom are at high risk for serious COVID-19 complications.

See **Vaccines** · *page 19*

AGA Clinical Practice Update

How diet and exercise can help manage NAFLD

BY AMY KARON
MDedge News

Exercise and a hypocaloric, Mediterranean-style diet remain first-line interventions that can benefit all patients with nonalcoholic fatty liver disease (NAFLD), according to a clinical practice update from the American Gastroenterological Association.

"[W]eight loss is associated with a reduction in liver fat, which provides a potential for reversal of disease progression," wrote Zobair M. Younossi, MD, MPH, of Inova Fairfax Medical Campus in Falls Church, Va., with his associates.

See **Diet, exercise** · *page 6*

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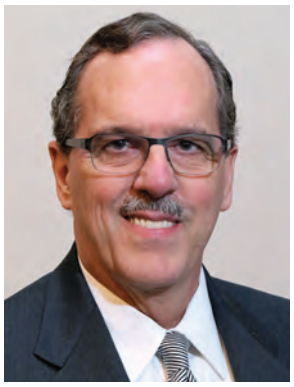
LETTER FROM THE EDITOR

Finding common purpose, or else

I am composing this editorial 4 days after the U.S. Capitol was invaded and 10 days before the presidential inauguration. It is impossible to ignore what is happening in our country, but I hesitate to add my thoughts to the overwhelming sea of opinions circulating in standard media, social media, and the dark web. I hope, as do many, that we return to a civil discourse, recognize the voices of all people, respect each other, and return to a belief in science and facts.


Dr. Allen

I hope, as do many, that we return to a civil discourse, recognize the voices of all people, respect each other, and return to a belief in science and facts.

SARS-CoV-2 has devastated the world and will continue to cause preventable deaths until we adopt stricter mitigation measures, vaccinate most people, and develop widespread immunity. We are gaining immense knowledge about this virus, and as gastroenterologists, we are on the front lines in many aspects. A recent article in American Journal of Gastroenterology (Am J Gastroenterol. 2020 Jun;115[6]:916-23), among others, emphasized that mild GI symptoms may be the only presenting complaint for people with COVID-19. Responses to COVID-19, such as limits on elective procedures and social distancing, have upended our endoscopic processes and even altered the business models of GI practice. We will never go back to pre-COVID models.

The front page of this month's GI & Hepatology News features important articles for our practice. One article delves into an extensive guideline from the American Gastroenterological Association on medical management of colonic diverticulitis. In another article, they also describe how efforts to encourage our patients with nonalcoholic fatty liver disease to exercise and manage their diet can make a real difference in their health. Finally, another explores how and why your immunocompromised patients (including those with inflammatory bowel disease) should and can be safely vaccinated for COVID-19.

Meanwhile, we need civility, science, and community. Without common purpose, we will experience the William Forster Lloyd's Tragedy of the Commons. Incivility has economic and emotional costs, according to the Harvard Business Review (Porath C and Pearson C. "The Price of Incivility." 2013 Feb). "Weathering," the deterioration of Black women's health over time that's related to continued socioeconomic disadvantage, has multigenerational impacts; for example the Department of Health & Human Services reports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that infant mortality among African American women is 2.3 times that of non-Hispanic Whites (https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=23). Late effects of redlining continue to cause economic, health, and emotional harms (Badger E. "How Redlining's Racist Effects Lasted for Decades." The New York Times. 2017 Aug 24).

"If Men were angels, no government would be necessary," James Madison wrote. "In framing a government which is to be administered by men over men, the great difficulty lies in this: you must first enable the government to control the governed; and the next place, oblige it to control itself."

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

Correction

The perspective for "Bariatric surgery resolved NASH long term" that ran on pages 4-5 of the October 2020 issue should read "Cirrhosis regressed to F3 in two out of three patients" instead of "in two-thirds of patients."

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GI&Hepatology News

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Senior Director of Classified Sales Tim LaPella, 484-921-5001, tlapella@mdedge.com
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Study reveals how aspirin may inhibit CRC

BY AMY KARON
MDedge News

Aspirin "rescued" a cystic intestinal phenotype driven by the Wnt pathway, reduced stem cell expression and function, and increased the expression of Dickkopf (DKK)-1, a Wnt antagonist that is frequently lost as colorectal cancer (CRC) progresses, according to recent study findings.

"Dysregulated Wnt signaling, [which is] primarily driven by adenomatous polyposis coli (APC) gene mutations, is fundamental to cancer initiation in both sporadic CRC and familial adenomatous polyposis (FAP). ... Our observations reveal a novel mechanism of aspirin-mediated Wnt inhibition through DKK-1 increase and potential 'pheno-markers' for chemoprevention and adjuvant aspirin human trials," wrote Karen Dunbar, PhD, and her associates in Cellular and Molecular Gastroenterology and Hepatology.

Aspirin shows benefits in sporadic and familial adenoma, significantly reduces CRC incidence, and may delay disease progression while improving survival. "Understanding the biology responsible for this protective effect is key to developing biomarker-led approaches for rational clinical use," wrote Dr. Dunbar, now with the University of Dundee (Scotland) and colleagues.

They found aspirin promoted the wild-type (budding, noncystic) phenotype in intestinal organoids derived from APC-deficient mice and humans with FAP. The same effect was seen in live APC-deficient mice. With the RNAscope protocol, they confirmed that aspirin significantly reduced RNA transcripts for Lgr5 and TROY, which are stem cell markers in CRC. Aspirin also reduced Lgr5 expression in APC-deficient mice and in human organoids derived from normal colonic mucosa, sporadic colorectal tumors, and colorectal tumors from patients with FAP.

In wound-closure models, aspirin inhibited Wnt and epithelial-mesenchymal transition (EMT) while decreasing migration and invasion by colorectal cancer cells. Aspirin accomplished this by increasing the phosphorylation of GSK-3beta and beta-catenin. Notably, aspirin increased the production of E-cadherin, which buffers excess beta-catenin and thereby limits overactivated Wnt to promote an epithelial, rather than mesenchymal, phenotype. "The novel observation that the aspirin-mediated E-cadherin increase is paralleled by greater E-cadherin–beta-catenin binding further supports the hypothesis that aspirin promotes an epithelial phenotype through Wnt inhibition," the researchers wrote.

In colorectal cells and FAP organoids, aspirin also increased the expression of the Wnt antagonist DKK-1, which in turn correlated

Continued on following page

AGA provides 14 recommendations

Diverticulitis *from page 1*

a low to modest dose of a tricyclic antidepressant."

The update from the AGA includes 13 other recommendations, with noteworthy advice to use antibiotics selectively, rather than routinely, in cases of acute uncomplicated diverticulitis in immunocompetent patients. In a recent large meta-analysis, antibiotics did not shorten symptom duration or reduce rates of hospitalization, complications, or surgery in this setting (Dis Colon Rectum. 2019 Dec;62[12]:1533-47). The clinical practice update advises using antibiotics if patients are frail or have comorbidities, vomiting or refractory symptoms, a C-reactive protein level above 140 mg/L, a baseline white blood cell count above 15 × 10^9 cells/L, or fluid collection or a longer segment of inflammation on CT scan. Antibiotics also are strongly advised for immunocompromised patients, who are at greater risk for complications. Because of this risk, clinicians should have "a low threshold" for cross-sectional imaging, antibiotic treatment, and consultation with a colorectal surgeon.

The authors recommend CT if patients have severe symptoms or have not previously been diagnosed with diverticulitis based on imaging. Clinicians also should consider imaging if patients have had multiple recurrences, are not responding to treatment, are immunocompromised, or are considering prophylactic surgery.

Colonoscopy is advised after episodes of complicated diverticulitis or after a first episode of uncomplicated diverticulitis if no high-quality colonoscopy has been performed in a year. This colonoscopy is advised to rule out malignancy, which can be misdiagnosed as diverticulitis, and because diverticulitis (particularly complicated diverticulitis) has been associated with colon cancer in some studies, the update notes. Unless patients have "alarm symptoms" – that is, a change in stool caliber, iron-deficiency anemia, bloody stools, weight loss, or abdominal pain – colonoscopy should be delayed until 6-8 weeks after the diverticulitis episode or until the acute symptoms resolve, whichever occurs later.

The decision to discuss elective segmental resection should be based on disease severity, not the prior number of episodes. Although elective surgery for diverticulitis has become increasingly common, patients should be aware that surgery often does not improve chronic gastrointestinal symptoms, such as abdominal pain, and that surgery reduces but does not eliminate the risk for recurrence.

The authors recommended against surgery to prevent complicated diverticulitis in immunocompetent patients with a history of uncomplicated episodes. "In this population, complicated diverticulitis is most often the first presentation of diverticulitis and is less likely with recurrences," the update states. For acute complicated diverticulitis that has been effectively managed without surgery, patients are at heightened risk for recurrence, but "a growing literature suggest[s] a more conservative and personalized approach" rather than the routine use of interval elective resection, the authors noted. For all patients, counseling regarding surgery should incorporate thoughtful discussions of immune status, values and preferences, and operative risks versus benefits, including effects on quality of life.

Dr. Peery and another author were supported by grants from the National Institutes of Health. The other authors reported having no conflicts of interest.

ginews@gastro.org

SOURCE: Peery AF et al. Gastroenterology. 2020 Dec 3. doi: 10.1053/j.gastro.2020.09.059.

DDSEP 9
Digestive Diseases Self-Education Program

Quick Quiz

Q1. Which of the following settings is associated with an increase in the frequency of transient lower esophageal sphincter relaxations (TLESRs)?

A. Baclofen administration
B. Esophageal outflow obstruction
C. Gastric acid hypersecretion
D. Lean body mass
E. Obstructive sleep apnea

Q2. A 26-year-old female who is 7 weeks pregnant presents with nausea and vomiting. She describes nausea that lasts most of the day with vomiting. She has tried rest and hydration, ginger supplementation, and a wrist band she purchased over the counter. However, she comes to clinic to request further management.

The most appropriate next step is:

A. Gastric-emptying study
B. Upper endoscopy
C. Ondansetron
D. A diet high in carbohydrates, low in protein
E. Doxylamine with vitamin B_6 (pyridoxine)

Answers on page 7

Continued from previous page

with lower stem cell function. "In humans, high serum DKK-1 correlates with increasing colorectal cancer stage, whereas tissue DKK-1 expression is lost with cancer progression," the researchers explained. "Here, we demonstrate that aspirin robustly increases DKK-1 expression in CRC models, which contributes to EMT and [cancer stem cell] inhibition observed with aspirin."

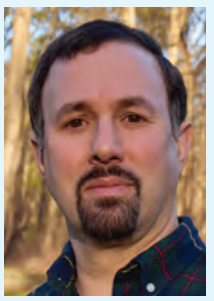
Taken together, the findings "highlight two novel phenotypic indicators of aspirin response, the cystic-phenotype rescue and reduced stem cell marker expression, which may serve as enhanced biomarkers, compared with individual Wnt components," they concluded. "Through targeting Wnt signaling at multiple levels, aspirin enhances commitment to differentiation, and hence, phenotypic markers of Wnt inhibition represent better targets [for] therapeutic exploitation."

Dr. Dunbar and her associates reported having no relevant conflicts of interest. The work was supported by Cancer Research UK and the Chief Scientist Office of Scotland, the MRC Centre, and the CRUK.

ginews@gastro.org

SOURCE: Dunbar K et al. Cell Mol Gastroenterol Hepatol. 2020 Sep 21. doi: 10.1016/j.jcmgh.2020.09.010.

It is well known that aspirin protects against colorectal polyps and cancers, but the molecular mechanisms by which aspirin confers this protection remain obscure. By developing new models and identifying the molecular targets of aspirin, researchers may develop therapies that prevent colorectal polyps and cancers but avoid the negative effects of aspirin. Most colorectal cancers (CRC), both spontaneous and familial, arise from abnormal activation of an important molecular pathway known as the Wnt-signaling pathway. Specific mutations in a key member of this pathway, the tumor suppressor APC, are an early event in spontaneous cancers and are the cause of a condition known as familial adenomatous polyposis (FAP). Wnt signaling also drives CRC by regulating cancer stem cells and a process known as epithelial-mesenchymal transition (EMT).



Dr. Katz

With use of established CRC cell lines, mouse models of FAP, and organoids – three-dimensional models of colonic epithelium – from mice and from human FAP patients, Dunbar and colleagues performed a comprehensive study to define the mechanisms by which aspirin acts to prevent the development and progression of CRC. Here, Dunbar and colleagues found that aspirin limits cancer stem cell populations and the development of EMT, which together are important for tumor cell propagation, invasion, and dissemination. Importantly, they also showed that aspirin increases the expression of a natural Wnt pathway antagonist known as DKK-1, providing a mechanism by which aspirin inhibits Wnt signaling in the context of CRC. Future studies can build on this work by exploring these findings to develop targeted approaches to Wnt inhibition and to prevent colorectal polyps and cancers.

Jonathan P. Katz, MD, is an associate professor of medicine in the division of gastroenterology, department of medicine at the University of Pennsylvania, Philadelphia. He has no conflicts of interest.

Bezafibrate eased pruritus in cholangiopathies

BY AMY KARON
MDedge News

Once-daily treatment with the lipid-lowering agent bezafibrate significantly reduced moderate to severe pruritis among patients with cholestasis, according to the findings of a multicenter, double-blind, randomized, placebo-controlled study (Fibrates for Itch, or FITCH).

Two weeks after completing treatment, 45% of bezafibrate recipients met the primary endpoint, reporting at least a 50% decrease in itch on a 10-point visual analog scale (VAS), compared with 11% of patients in the placebo group (P = .003). There was also a statistically significant decrease in serum alkaline phosphatase (ALP) levels from baseline (35% vs. 6%, respectively; P = .03) that corresponded with improved pruritus, and bezafibrate significantly improved both morning and evening pruritus.

Bezafibrate was not associated with myalgia, rhabdomyolysis, or serum alanine transaminase elevations but did lead to a 3% increase in serum creatinine that "was not different from the placebo group," wrote Elsemieke de Vries, MD, PhD, of the department of gastroenterology & hepatology at Tytgat Institute for Liver and Intestinal Research, Amsterdam, and of department of gastroenterology & metabolism at Amsterdam University Medical Centers, and associates. Their report is in Gastroenterology.

Most patients with cholangitis experience pruritus, but guideline-recommended treatments can have sub par efficacy and tolerability, the investigators wrote. For example, in a recent study (Lancet. 2017 Mar 18;389[10074]:1114-23), a selective inhibitor of an ileal bile acid transporter reduced pruritus in primary biliary cholangitis but frequently was associated with diarrhea.

Lysophosphatidic acid (LPA) has been implicated in cholangiopathy-associated pruritus but is not found in bile. However, biliary drainage rapidly improves severe itch in patients with primary biliary cholangitis. Therefore, Dr. de Vries and associates hypothesized that an as-yet-unknown factor in bile contributes to pruritus in fibrosing cholangiopathies and that bezafibrate reduces itch by "alleviating hepatobiliary cholestasis and injury and, thereby, reducing formation and biliary secretion of this biliary factor X."

The FITCH study, which was conducted at seven academic hospitals in the Netherlands and one in Spain, enrolled 74 patients 18 years and older with primary biliary cholangitis or primary or secondary sclerosing cholangitis who reported having pruritus with an intensity of at least 5 on the 10-point VAS at baseline (with 10 indicating "worst itch possible"; median, 7; interquartile range, 7-8). Patients with hepatocellular cholestasis caused by medications or pregnancy were excluded. Ages among most participants ranged from 30s to 50s, and approximately two-thirds were female. None had received another pruritus treatment within 10 days of enrollment, and prior treatment with bezafibrate was not allowed. Patients received once-daily bezafibrate (400 mg) or placebo tablets for 21 days, with visits to the outpatient clinic on days 0, 21, and 35.

There were no serious adverse events or new safety signals. One event of oral pain was considered possibly related to bezafibrate, and itch and jaundice worsened in two patients after completing treatment. In the 24-month BEZURSO study (N Engl J Med. 2018;378:2171-81), increases in serum creatinine were modest and similar between groups (3% with bezafibrate and 5% with placebo). Myalgia and increases in serum alanine transaminase were observed in BEZURSO but not in FITCH. However, the short treatment duration provides "no judgment on long-term safety [of bezafibrate] in complex diseases such as primary sclerosing cholangitis or primary biliary cholangitis," the investigators wrote.

Four patients discontinued treatment – three stopped placebo because of "unbearable pruritus," and one stopped bezafibrate after developing acute bacterial cholangitis that required emergency treatment. Although FITCH excluded patients whose estimated glomerular filtration rate was less than 60 mL/min per 1.73 m^2, one such patient was accidentally enrolled. Her serum creatinine, measured in mmol/L, rose from 121 at baseline to 148 on day 21, and then dropped to 134 after 2 weeks off treatment.

The trial was supported by patient donations, the Netherlands Society of Gastroenterology, and Instituto de Salud Carlos III. The investigators reported having no conflicts of interest.

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SOURCE: de Vries E et al. Gastroenterology. 2020 Oct 5. doi: 10.1053/j.gastro.2020.10.001.

Itch really matters to patients with cholestatic liver diseases, and effective treatment can make a significant difference to life quality. Although therapies exist for cholestatic itch (such as cholestyramine, rifampin, and naltrexone) recent data from the United Kingdom and United States suggest that therapy in practice is poor. It is likely that this results, at least in part, from the limitations of the existing treatments which can be unpleasant to take (cholestyramine) or difficult to use because of monitoring needs and side effects (rifampin and naltrexone). Itch has therefore been identified as an area of real unmet need in cholestatic disease, and there are a number of trials in progress or in set-up. This is extremely positive for patients.


Dr. Jones

The FITCH trial is one of the first of these "new generation" cholestatic itch trials to report and explore the efficacy of the PPAR-agonist bezafibrate in a mixed cholestatic population. Clear benefit was seen with around 50% of all disease groups meeting the primary endpoint and good drug tolerance. Is bezafibrate therefore the answer to cholestatic itch? The cautious answer is ... possibly, but more experience is needed. The trial duration was only 21 days, which means that long-term safety and efficacy remain to be explored. Bezafibrate is now being used in practice to treat cholestatic itch with effects similar to those reported in the trial. It is therefore clearly an important new option. Where it ultimately ends up in the treatment pathway only time and experience will tell.

David Jones, BM, BCh, PhD, is a professor of liver immunology at Newcastle University, Newcastle Upon Tyne, England. He reported having no disclosures relevant to this commentary.

Lifestyle changes can have a big impact on NAFLD

Diet, exercise *from page 1*

Lifestyle modifications remain "the cornerstone for management" because, even though NAFLD affects approximately 25% of individuals worldwide according to one meta-analytic assessment (Hepatology. 2016 Jul;64[1]:73-84), interventions such as medications, bariatric endoscopy, and surgery are usually reserved for the subset of patients with severe obesity, comorbid diabetes, or nonalcoholic steatohepatitis (NASH) with at least stage 2 fibrosis, the experts wrote in Gastroenterology.

They note that achieving any sort of clinically significant weight loss typically requires a hypocaloric diet of 1,200-1,500 kilocalories/day or a decrease of 500-1,000 kilocalories/day from baseline. A Mediterranean diet of fresh vegetables, fruits, legumes, minimally processed whole grains, fish, olive oil, nuts, and seeds is recommended because its antioxidant, anti-inflammatory effects may slow NAFLD progression. This diet minimizes or eliminates sweets, refined grains, and red and processed meats. Fructose from fruit is not associated with NAFLD, but patients should consume little

Continued on following page

Continued from previous page

or no commercially prepared fructose, which has been linked to visceral adiposity, insulin resistance, hepatic inflammation, and fibrosis progression. Unfortunately other hypocaloric diets have not been studied enough to support their routine use in NAFLD treatment, according to the clinical practice update.

The recommndations also address patients with NASH, which is the more severe form of NAFLD and is associated with significant morbidity and mortality caused by complications from cirrhosis, hepatic decompensation, and hepatocellular carcinoma. It's been shown that different degrees of weight loss also has a big impact: Losing at least 5% of total body weight can decrease hepatic steatosis, losing at least 7% can resolve NASH, and losing at least 10% can lessen or stabilize hepatic fibrosis, according to level 1 evidence cited by the update. Weight loss "can significantly impact all aspects of NAFLD histology including fibrosis, but a goal of 10% total body weight loss should be considered for patients with overweight or obese NAFLD," the authors wrote. Fat loss also improves liver histology in patients with lean NAFLD (body mass index, 26 kg/m^2 in non-Asian patients or 24 in Asians), for whom a hypocaloric diet targeting a more modest 3%-5% total body weight loss is recommended.

Because aerobic exercise reduces hepatic fat levels independently of hypocaloric diet, patients with NAFLD should consider a weekly regimen of 150-300 minutes of moderate-intensity exercise or 75-150 minutes of vigorous activity. Resistance training can complement aerobic exercise "but [is] not a replacement," the authors noted. In addition, patients with NAFLD should restrict alcohol consumption to reduce the risk for liver-related events, and those with advanced hepatic fibrosis should "avoid alcohol entirely." These recommendations reflect the findings of a large prospective study in which the consumption of even low amounts of alcohol led to worse liver-related outcomes among patients with NAFLD (Hepatology. 2020 Mar;71[3]:835-48).

Clinicians should screen for and "aggressively" manage common NAFLD comorbidities, including diabetes mellitus, hypertension, and obstructive sleep apnea, according to the clinical practice update. Patients with coexisting metabolic conditions should be risk stratified for cardiovascular disease and treated based on guidelines from the American College of Cardiology and the American Heart Association (J Am Coll Cardiol. 2019 Sep 10;74[10]:1376-414).

It is believed that sarcopenia affects patients with NASH cirrhosis because their livers cannot effectively store, metabolize, or mobilize carbohydrates, which leads to a catabolic state in which protein and fat are used as energy sources, according to the update. To avoid exacerbations, these patients may need to optimize their protein intake – a minimum of 1.2-1.5 g/kg of body weight is recommended – from sources of branched-chain amino acids, such as chicken, fish, eggs, nuts, lentils, or soy. Patients with sarcopenic NAFLD also should consume small, frequent meals spaced no more than 4-6 hours apart. When possible, they should consult with a specialized nutritionist. Moderate-intensity exercise may also benefit patients experiencing sarcopenia.

The researchers disclosed ties to Gilead Sciences, Intercept, Bristol Myers Squibb, Novo Nordisk, and several other companies. The review was commissioned and approved by the AGA Institute's Clinical Practice Updates Committee and the AGA Governing Board.

ginews@gastro.org

SOURCE: Younossi ZM et al. Gastroenterology. 2020 Dec 8. doi: 10.1053/j.gastro.2020.11.051.

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Quick Quiz answers

Q1. Correct answer: E

Rationale

Transient lower esophageal sphincter relaxation (TLESR) is a physiologic phenomenon that allows venting of swallowed air from the stomach in response to distension of the proximal stomach. Patients with gastroesophageal reflux disease typically reflux gastric content through a compliant esophagogastric junction into the esophagus during a TLESR; the frequency of TLESRs may also be higher in patients with GERD. TLESRs are suppressed during deep sleep, and are less frequent when LES relaxation is abnormal (e.g., esophageal outflow obstruction). Baclofen, a $GABA_B$ receptor agonist, can reduce TLESR frequency, and can reduce reflux episodes in patients with reflux. Obese patients and those with obstructive sleep apnea can have increased frequency of TLESRs. The frequency of TLESR is not related to degree of gastric acid secretion in the stomach.

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Q2. Correct answer: E

Rationale

This patient has nausea and vomiting of pregnancy (NVP), and has tried conservative management. Doxylamine and vitamin B_6 have been found to be safe and effective for NVP and are considered first-line therapy. Further testing with gastric-emptying study is not necessary because NVP has a high prevalence at weeks 4-6 of gestation and peaks at week 9-16. A nuclear test such as gastric emptying is not appropriate during pregnancy, though decreased gastric emptying due to estrogen and progesterone is thought to be related to NVP. Upper endoscopy would be considered if the nausea and vomiting is refractory. Ondansetron can be considered, but there have been some questions raised regarding safety and it is not considered first line. Meals high in protein have been found to decrease nausea more that carbohydrate-rich meals.

Reference

ACOG Committee on Practice Bulletins-Obstetrics. Obstet Gynecol. 2018 Jan;131(1):e15-e30.

Normal FLIP findings usually ruled out esophageal motility disorders

BY AMY KARON
MDedge News

Most patients with normal findings on functional luminal imaging probe (FLIP) showed no clinical evidence of a major esophageal motor disorder, even when their high-resolution manometry (HRM) test results were abnormal, according to the results of a single-center retrospective cohort study.

Among 111 study participants with normal FLIP findings, 79% also showed no evidence of a major esophageal motor disorder on esophageal HRM, wrote Alexandra J. Baumann, DO, of Northwestern University, Chicago, and associates. "Among the remaining 21% with apparent disagreement with HRM, [those] with normal FLIP panometry carried overall clinical impressions of not having a major esophageal motor disorder and subsequently were treated conservatively without the need for surgical interventions," they reported. For patients with normal upper endoscopy and normal FLIP panometry, "the initial clinical management strategy could be directed toward addressing gastroesophageal reflux or a functional syndrome," they wrote in Clinical Gastroenterology and Hepatology.

Patients with normal FLIP panometry findings "did not have a clinical impression of a major esophageal motor disorder," the researchers reported.

FLIP uses high-resolution impedance planimetry to evaluate esophageal lumen parameters, distensibility, and contractility in response to distension. Although HRM is standard for evaluating esophageal motility, false negatives and positives can result from challenges with interpreting outflow obstructions and normal lower-esophageal sphincter relaxation pressures among patients with clinical achalasia.

Hence, the researchers evaluated correlations between FLIP and HRM in 111 patients with esophageal symptoms and nonobstructive endoscopy findings who were evaluated at the Esophageal Center of Northwestern University between 2012 and 2019. Gastroenterologists performed additional studies, such as barium esophagrams, at their discretion. By study design, all patients had normal FLIP results, defined as an esophagogastric junction distensibility index above 3.0 mm^2 per mm Hg and a normal contractile response (that is, normal repetitive retrograde contractions and a repetitive antegrade contraction pattern that met the Rule-of-6s). Three clinicians evaluated and reached consensus on each FLIP study. Esophageal HRM data were interpreted based on the Chicago classification system (version 3.0).

Patients with normal FLIP panometry findings "did not have a clinical impression of a major esophageal motor disorder," the researchers reported. In all, 23 (21%) patients with normal FLIP results had discrepant (abnormal) HRM findings, most of which were false positives or equivocal.

For example, among 20 patients whose HRM suggested an esophagogastric junction outflow obstruction, 17 showed normal bolus transit on supine swallows and 16 showed normalization of integrated relaxation pressure after adjunctive maneuvers. Similarly, among 10 patients who underwent a barium esophagram, 8 showed normal emptying, 1 showed a temporary delay but no retention, and 1 had an incomplete study. "The overall clinical impression was not of an achalasia variant in any of these 20 patients with [esophagogastric junction outflow obstruction] on HRM, and thus none underwent botulinum toxin injection, pneumatic dilation, or lower-esophageal sphincter myotomy at our center," the researchers wrote. Among 17 patients who were available for clinical follow-up, 4 underwent empiric dilation, of whom none had mucosal disruption. One patient was diagnosed with dysphagia lusoria based on cross-sectional imaging, while the rest were managed conservatively.

The strong correlation between HRM and esophagrams in this study indicates that "[n]ormal findings from FLIP panometry can be used to exclude esophageal motility disorders at the time of endoscopy, possibly reducing the need for high-resolution manometry evaluation of some patients."

Similarly, among 10 patients with at least 50% ineffective swallows on HRM, 5 showed normal barium emptying and 9 were managed conservatively (the remaining patient underwent cricopharyngeal dilation for concurrent oropharyngeal dysphagia). The strong correlation between HRM and esophagrams in this study indicates that"[n]ormal findings from FLIP panometry can be used to exclude esophageal motility disorders at the time of endoscopy, possibly reducing the need for high-resolution manometry evaluation of some patients," the investigators concluded. "However, further longitudinal studies are needed to support this approach."

The work was supported by the Public Health Service and the American College of Gastroenterology. Dr. Baumann reported having no conflicts of interest. Four coinvestigators disclosed relevant ties to Crospon, Given Imaging, Ironwood, Medtronic, Sandhill Scientific, Torax, and other companies..

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SOURCE: Baumann AJ et al. Clin Gastroenterol Hepatol. 2020 Mar 20. doi: 10.1016/j.cgh.2020.03.040.

Endoscopy is often the first step in the evaluation of dysphagia and other esophageal symptoms such as chest pain. When endoscopy is negative for a cause of these esophageal symptoms and biopsies rule out eosinophilic esophagitis, an esophageal motility disorder should be excluded, and high-resolution esophageal manometry is considered the standard method for this purpose. Functional lumen imaging probe (FLIP) panometry offers the opportunity to evaluate esophageal motor function during sedated endoscopy, and it can be easily added to the endoscopic procedure if there are no findings to explain esophageal symptoms. The prospect of establishing the presence of normal esophageal motility and ruling out a major motility disorder during endoscopy is very attractive because it would increase diagnostic efficiency while also obviating the need for an additional and potentially uncomfortable study for the patient. This study by Baumann and colleagues explores the yield of normal FLIP panometry to predict the presence of normal esophageal motility and rule out a major motility disorder. Their study showed that manometry was negative for a major motility disorder in 88 of 111 (79%) patients with normal FLIP panometry.

Dr. Vela

Manometry revealed a major motility disorder in 23 patients with normal FLIP topography, mainly because of esophagogastric junction outflow obstruction (EGJOO) seen in 20 patients, along with absent contractility in 2, and distal esophageal spasm in 1. The EGJOO was for the most part not confirmed by adjunctive swallows on manometry or by esophagram, and aggressive therapies were not needed, indicating likely falsely positive EGJOO diagnosed by manometry. These are very encouraging results. If the findings are confirmed in larger prospective studies, it would be reasonable to consider modifying our paradigm for the evaluation of esophageal symptoms, and FLIP panometry could be considered as a screening tool to rule out a clinically significant major motility disorders during the initial endoscopic evaluation for esophageal symptoms.

Marcelo F. Vela, MD, MSCR, AGAF, is professor of medicine, director of Esophageal Disorders, and program director of Esophageal Fellowship in the division of gastroenterology and hepatology at Mayo Clinic Arizona in Scottsdale. He reports being a consultant for Medtronic and receiving research support from Diversatek.

Estate plan: Misconceptions that can be costly

Should your estate plan cause you concern? Below are some common estate-planning misconceptions that can lead to problems down the road, plus ways to avoid them.

- **"I already have a will."** A will doesn't improve with age. The passage of time presents unanticipated circumstances, such as changes in marital status, new children or grandchildren, revised tax laws, a move, or fluctuations in assets. Revisit your will after major milestones or at least every couple of years.
- **"Everything is joint."** Joint ownership seems ideal because it avoids probate and expedites the survivor's access. But joint title may also inflict unnecessary tax burdens and upset your estate plan. To sidestep title traps, consult with an estate-planning attorney.
- **"My will covers everything."** Not necessarily. Jointly owned assets with rights of survivorship pass to the surviving owner regardless of what your will says. Plus, your retirement assets may never reach your intended loved ones if you've failed to update beneficiary designation forms. This could be true for assets such as 401(k)s, IRAs, and life insurance policies, which pass outside of your will or trust via beneficiary designations. Complete new forms so old ones won't leave these assets to a deceased parent or former spouse.
- **"I worry more about my heirs than myself."** A good estate plan should also reflect your current needs. Ask an attorney who specializes in estate planning about tools that can provide you income for life before supporting your family, friends, and favorite causes.

3D-Guru/Getty Images

Want to learn more about including a gift to the AGA Research Foundation in your future plans? Visit our website at https://gastro.planmylegacy.org.

New research fellowship supports undergraduate minority students

The new American Gastroenterological Association–Aman Armaan Ahmed Family Summer Undergraduate Research Fellowship (SURF) encourages promising students to pursue careers in science and medicine while expanding the pipeline of investigators from diverse backgrounds.

Six positions are available and support undergraduate students in performing 10 weeks of digestive disease–related research under the mentorship of an expert in gastroenterology and hepatology. Students may select their own mentor or choose from a roster of more than a dozen AGA members. The award provides a stipend, funding to offset travel and meal expenses, and opportunities to learn about future training and career options.

This is an incredible fellowship, and we need your help! Please share this opportunity with your networks and encourage any eligible undergraduate students you know to apply.

We encourage students from all traditionally underrepresented groups – members of racial and ethnic minorities, individuals from disadvantaged backgrounds, or individuals with disabilities – to apply. The application deadline is Feb. 24, 2021.

www.gastro.org/surf

What are the risks from surgery when removing colorectal polyps?

Romaset/Getty Images

Surgery to remove colorectal polyps is often unnecessary according to recent research, which has found it can lead to adverse postoperative events and increased rates of hospital readmissions.

To support GIs on how to best approach polyp removal, the American Gastroenterological Association has launched a new on-demand course, "Appropriate Referral for Endoscopic Polyp Removal." The program guides you with three interactive modules and a decision-support tool on the best course of action with education on how to differentiate between a simple and complex polyp and when or if to refer patients for surgery.

Endoscopic resection of polyps can eliminate the need for surgery more than 90% of the time. In fact, surgery almost doubles the risk of an adverse event. In the second module of the program, learn about risk factors related to surgery. Other modules focus on how to distinguish between lesions suitable for endoscopic mucosal resection, lesions that should be referred for surgery, and the benefits of endoscopic resection of tumors. Take the course and earn 0.75 American Medical Association PRA Category 1 credit™ on completion.

www.gastro.org/Polypectomy

AGA Community Updates

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

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

- COVID-19 vaccine and IBD patients (https://community.gastro.org/posts/23449)
- Simethicone use (https://community.gastro.org/posts/23448)
- COVID-19 vaccine – are you getting it or not? (https://community.gastro.org/posts/23442)
- Patient case: Unexplained jaundice in an established cirrhotic (https://community.gastro.org/posts/23244)
- Patient case: 76-year-old male with recurrent / persistent NET in proximal stomach (https://community.gastro.org/posts/23243)
- Patient case: Entyvio and chemotherapy (https://community.gastro.org/posts/23238)
- Discharge instructions for moderate sedation (https://community.gastro.org/posts/23193)

View all discussions in the AGA Community at https://community.gastro.org.

How to predict colonoscopy malpractice lawsuits

BY JIM KLING
MDedge News

Malpractice lawsuits related to colonoscopy continue to pose challenges for practitioners, and a new analysis reveals that errors related to sedation are more likely to be awarded to plaintiffs. Primary care physicians and surgeons are often codefendants, which emphasizes the importance of interdisciplinary care in colonoscopy.

Cases involving informed consent were more likely to be ruled for the defendant, while those tied to medication error favored the plaintiff, according to an analysis of cases from the Westlaw legal database. The study, led by Krishan S. Patel, MD, and Sushil Ahlawat, MD, MS, MBBS, AGAF, of Rutgers New Jersey Medical School, Newark, was published in the Journal of Clinical Gastroenterology .

According to the authors, 55% of physicians face a malpractice suit at some point in their careers, and gastroenterology ranks as the sixth most common specialty named in malpractice suits. Every year, about 13% of gastroenterologists confront malpractice allegations, and colonoscopy is the most common reason.

The researchers searched the Westlaw legal database for malpractice cases involving colonoscopy or sigmoidoscopy, identifying 305 cases between 1980 and 2017. The average patient age was 54.9 years, and 52.8% of cases were brought by female patients. The most cases were from New York (21.0%), followed by California (13.4%), Pennsylvania (13.1%), Massachusetts (12.5%), and New Jersey (7.9%). Gastroenterologists were named in 71.1% of cases, internists in 25.6%, and surgeons in 14.8%.

A little more than half (51.8%) of cases were ruled in favor of the defendant, and 25% for the plaintiff; 17% were settled, and 6% had a mixed outcome. Payouts ranged from $30,000 to $500,000,000, with a median of $995,000.

There were multiple causes

Continued on following page

Updated USPSTF HBV screening recommendation may be a 'lost opportunity'

BY JIM KLING
MDedge News

An update of the U.S. Preventive Services Task Force recommendation for hepatitis B screening shows little change from the 2014 version, but some wonder if it should have gone farther than a risk-based approach.

The recommendation, which was published in JAMA, reinforces that screening should be conducted among adolescents and adults who are at increased risk of hepatitis B virus (HBV) infection. The USPSTF named six categories of individuals at increased risk of infection: persons born in countries with a 2% or higher prevalence of hepatitis B, such as Asia, Africa, the Pacific Islands, and some areas of South America; unvaccinated individuals born in the United States to parents from regions with a very high prevalence of HBV (≥8%); HIV-positive individuals; those who use injected drugs; men who have sex with men; and people who live with people who have HBV or who have HBV-infected sexual partners. It also recommended that pregnant women be screened for HBV infection during their first prenatal visit.

"I view the updated recommendations as an important document because it validates the importance of HBV screening, and the Grade B recommendation supports mandated insurance coverage for the screening test," said Joseph Lim, MD, AGAF, who is a professor of medicine at Yale University and director of the Yale Viral Hepatitis Program, both in New Haven, Conn.

Still, the recommendation could have gone further. Notably absent from the USPSTF document, yet featured in recommendations from the Centers for Disease Control and Prevention and the American Association for the Study of Liver Disease (Hepatology. 2018 Apr;67[4]:1560-99), are patients who have diabetes, are on immunosuppressive therapy, or have elevated liver enzymes or liver disease. Furthermore, a single-center study found that, among physicians administering immunosuppressive therapy, a setting in which HBV reactivation is a concern, there were low rates of screening for HBV infection, and the physicians did not reliably identify high-risk patients (PLoS One. 2015. doi: 10.1371/journal.pone.0120749).

"This may also be viewed as a lost opportunity. Evidence suggests that risk factor–based screening is ineffective for the identification of chronic conditions such as hepatitis B. Risk factor–based screening is difficult to implement across health systems and exacerbates the burden on community-based organizations that are motivated to address viral hepatitis," said Dr. Lim.

"Risk factor–based screening is difficult to implement across health systems and exacerbates the burden on community-based organizations that are motivated to address viral hepatitis."

A similar view was expressed by Avegail Flores, MD, medical director of liver transplantation at the Michael E. DeBakey Veterans Affairs Medical Center and assistant professor of medicine at Baylor College of Medicine, both in Houston. "This is a good launching point, and with further evidence provided, hopefully it will also bring in a broader conversation about other persons who are at risk but not included in these criteria." Neither Dr. Lim nor Dr. Flores were involved in writing the guidelines.

She noted that resistance to universal screening may be caused by the relatively low prevalence of hepatitis B infection in the United States. However, the CDC estimates that only about 61% of people infected with HBV are aware of it. "I don't think we have done a good job screening those who are at risk," said Dr. Flores.

Universal screening could help, but would have a low yield, according to Dr. Flores, who suggested expansion into other at-risk groups, such as Baby Boomers. With respect to other risk groups that could be stigmatized or discriminated against, Dr. Flores recalled her medical school days when some students went directly into underserved communities. "We have to think of creative ways of how to reach out to people, not just relying on the usual physician-patient relationship."

The World Health Organization has declared a target to reduce new hepatitis B infections by 90% by 2030, and that will require addressing gaps in diagnosis. "We are at a critical juncture in terms of global hepatitis elimination efforts. There is a time-sensitive need to have multistakeholder engagement in ensuring that all aspects of the care cascade are addressed. Because of the central role of screening and diagnosis, it's of critical importance that organizations such as USPSTF are in alignment with other organizations that have already issued clear guidance on who should be screened. It is [my] hope that further examination of the evidence base will further support broadening USPSTF guidance to include a larger group of at-risk individuals, or ideally a universal screening strategy," said Dr. Lim.

The recommendation's authors received travel reimbursement for their involvement, and one author reported receiving grants and personal fees from Healthwise. Dr. Flores has no relevant financial disclosures. Dr. Lim is a member of the American Association for the Study of Liver Disease's Viral Hepatitis Elimination Task Force.

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SOURCE: U.S. Preventive Services Task Force. JAMA. 2020 Dec 15. doi: 10.1001/jama.2020.22980.

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of litigation listed in 83.6% of cases. Among these causes, the most frequent were delayed treatment (65.9%), delayed diagnosis (65.6%), procedural error/negligence (44.3%), and failure to refer/reorder tests (25.6%).

Of 135 cases alleging procedural negligence, 90 (67%) named perforation. Among 79 cases that cited a failure to refer and order appropriate tests, 97% claimed the defendant missed a cancerous lesion. In cases alleging missed cancers, 31% were in the cecum, and 23% in the anus.

Dr. Kosinski

A logistic regression analysis of factors associated with a verdict for the defendant found "lack of informed consent" to be an independent predictor of defendant verdict (odds ratio, 4.05; $P = .004$). "Medication error" was associated with reduced defendant success (OR, 0.17; $P=.023$). There were nonsignificant trends between reduced odds of a verdict for the defendant and lawsuits that named "delay in diagnosis" (OR, 0.35; $P = .060$) and "failure to refer" (OR, 0.51; $P = .074$).

The authors sound a dire note about the number of malpractice suits brought against gastroenterologists, but Lawrence Kosinski, MD, AGAF, is more sanguine. He notes that gastroenterologists have low insurance premiums, compared with other specialties, but recognizes that colonoscopies are a significant source of risk.

Dr. Kosinski, who is chief medical officer at SonarMD and formerly a managing partner at the Illinois Gastroenterology Group, said in an interview that the study is revealing. "It comes out in the article: Acts of omission are more dangerous to the physician than acts of commission. Not finding that cancer, not acting on that malignant polyp, not pursuing it, is much more likely to get you in trouble than taking it off and perforating a colon," said Dr. Kosinski, who was not involved in the study.

To gastroenterologists seeking to reduce their risks of litigation, he offered advice: You shouldn't assume that the patient has read the information provided. For example, risks of anesthesia and the procedure itself should be directly communicated. It's also important to document the procedure thoroughly, including pictures of the cecum and rectal retroflexion. Finally, don't rush.

"This isn't a race. Clean the colon; make sure you don't miss something. If that person pops up in 3 years with a cancer, someone may go after you."

"This isn't a race. Clean the colon; make sure you don't miss something. If that person pops up in 3 years with a cancer, someone may go after you," commented Dr. Kosinski.

No source of funding was disclosed. Dr. Kosinski has no relevant financial disclosures.

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Update on feeding tubes: Indications and troubleshooting of complications

BY GREGORY TOY, MD, AND JOHN C. FANG, MD

Dr. Toy (left) is with the department of internal medicine at the University of Utah, Salt Lake City. **Dr. Fang** is with the division of gastroenterology and hepatology at the University of Utah.

Introduction

Gastroenterologists are in a unique position to manage individuals with feeding tubes as their training underscores principles in digestion, absorption, nutrition support, and enteral tube placement. Adequate management of individuals with feeding tubes and, importantly, the complications that arise from feeding tube use and placement require a basic understanding of intestinal anatomy and physiology. Therefore, gastroenterologists are well suited to both place and manage individuals with feeding tubes in the long term.

Indications for tube feeding

When deciding on the appropriate route for artificial nutrition support, the first decision to be made is enteral access versus parenteral nutrition support. Enteral nutrition confers multiple benefits, including preservation of the mucosal lining, reductions in complicated infections, decreased costs, and improved patient compliance. All attempts at adequate enteral access should be made before deciding on the use of parenteral nutrition. Following the clinical decision to pursue artificial means of nutrition support and enteral access, the next common decision is the anticipated duration of nutrition support. Generally, the oral or nasal tubes are used for short durations (i.e., less than 4 weeks) with percutaneous placement into the stomach or small intestine for longer-term feeding (i.e., percutaneous endoscopic gastrostomy [PEG] or percutaneous endoscopic jejunostomy [PEJ]).

The most general indication for nutrition support is an inability to maintain adequate nutritional needs with oral intake alone. General categories of inadequate oral intake include neurologic disorders, malignancy, and gastrointestinal conditions affecting digestion and absorption (**Table 1**). Absolute and relative contraindications to PEG placement are listed in **Table 2**. If an endoscopic placement is not possible, alternative means of placement (i.e., surgery or interventional radiology) can be considered to avoid the consequences of prolonged malnutrition. In-hospital mortality following PEG placement has decreased 40% over the last 10 years, which can be attributed to improved patient selection, enhanced discharge practices, and exclusion of patients with the highest comorbidity and mortality rates, like those with advanced dementia or terminal cancer.[1]

When deciding on the appropriate route, the first decision to be made is enteral access versus parenteral nutrition support.

PEG placement in patients with dementia is controversial, with previous studies not demonstrating improved outcomes and association with high mortality rates,[2] so the practice is currently not recommended by the American Geriatrics Society in individuals with advanced dementia.[3] However, a large Japanese study showed that careful selection of patients with mild dementia to undergo gastrostomy increased independence fourfold; therefore, multidisciplinary involvement is often necessary in the decision to pursue artificial means of nutrition support in this population.[4]

The recent coronavirus disease 2019 (COVID-19) pandemic has placed additional strains on endoscopic placement and has highlighted the effect of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on GI symptoms. A recent meta-analysis showed an overall incidence of GI symptoms of 17.6% in the following conditions in decreasing order of prevalence: anorexia, diarrhea, nausea, vomiting, and abdominal discomfort.[5] In addition, the prolonged ventilatory requirements among a subset of individuals with the most severe COVID-19 results in extended periods of nutrition support via enteral tube placements. In individuals with ICU-acquired weakness and discharge to long-term care facilities, the placement of percutaneous endoscopic tubes may be required, although with the additional consideration of the need for an aerosolizing procedure. Delay of placement has been advocated, in addition to appropriate personal protective equipment, in order to ensure safe placement for the endoscopy staff.[6]

Types of feeding tubes

After the decision to feed a patient enterally and determination of the anticipated duration of enteral support, the next decision is to determine the most appropriate location of feeding delivery: into the stomach or the small bowel. Gastric feeding is advantageous most commonly because of its increased capacity, allowing for larger volumes

Dr. Rao

One of the most common consultations gastroenterologists receive is the request to place or manage an enteral tube. A thorough understanding of indications for placement, type of tubes available, and the ability to troubleshoot common associated complications is imperative in fielding these requests and managing these patients appropriately. For the early-career gastroenterologist, these calls can be daunting because experience with the placement and management of feeding tubes can be limited during training.

The In Focus article for this quarter, which is brought to you by *The New Gastroenterologist*, provides an in-depth review of feeding tubes written by Dr. John Fang and Dr. Gregory Toy (University of Utah). This piece details the indications for and contraindications to enteral tube placement, the variety of tubes available, the decision between gastric or small-bowel delivery of feeds, and how to identify and manage complications if they arise. This is an absolute must-read piece for any new gastroenterologist.

Vijaya L. Rao, MD
Editor in Chief
The New Gastroenterologist
Dr. Rao is assistant professor of medicine, University of Chicago, section of gastroenterology, hepatology & nutrition.

to be delivered over shorter durations. However, in the setting of postsurgical anatomy, gastroparesis, or obstructing tumors/pancreatic inflammation, distal delivery of tube feeds may be required into the jejunum. Additionally, percutaneous tubes placed into the stomach can have extenders into the small bowel (GJ tubes) to allow for feeding into the small bowel and decompression or delivery of medications into the stomach.

In general, gastric feeding is preferred over small-bowel feeding as PEG tubes are more stable and have fewer complications than either PEG-J or direct PEJ tubes. Gastrostomy tubes are generally shorter and larger in diameter making them less likely to clog. PEG-J tubes have separate lumens for gastric and small intestinal access, but the smaller-bore jejunal extension tubes are more likely to clog or become dislodged. While direct PEJ is shown to have higher rates of tube patency and decreased rates of endoscopic re-intervention, compared with PEG-J,[7] one limitation of a direct PEJ is difficulty in placement and site selection, which can be performed with a pediatric colonoscope or balloon enteroscopy

After deciding to feed a patient enterally, the next decision is to determine the most appropriate location of feeding delivery.

system. Most commonly, this procedure is performed under general anesthesia.

In the case of a critically ill patient in the ICU, it is recommended to start enteral nutrition within 48 hours of arrival to avoid complications of prolonged calorie deficits. Nasally inserted feeding tubes (e.g., Cortrak, Avanos Medical Devices, Alpharetta, Ga.) are most commonly used at the bedside and can be placed blindly using electromagnetic image guidance, radiographically, or endoscopy. However, the small caliber of nasoenteric tubes comes with the common complication of clogging, which can be overcome with slightly larger-bore gastric feeding tubes. If gastric feeding is not tolerated (e.g., in the case of vomiting, witnessed aspiration), small-bowel feeding should be initiated and can be a more durable form of enteral feeding with fewer interruptions as feedings do not need to be held for procedures or symptomatic gastric intolerance. In clinical areas of question, or if there is a concern for intolerance of enteral feeding, a short trial with nasogastric or nasojejunal tube placement should be performed before a more definitive percutaneous placement.

With respect to percutaneous tubes, important characteristics to choose are the size (diameter in French units), type of internal retention device, and external appearance of the tube (standard or low profile). All percutaneous tubes contain an external retention device (i.e., bumper) that fits against the skin and an internal retention device that is either a balloon or plastic dome or funnel that prevents the tube from becoming dislodged. Balloon retention tubes require replacement every 3-6 months, while nonballoon tubes generally require replacement annually in order to prevent the plastic from cracking, which can make removal complicated. Low-profile tubes have an external cap, which, when opened, allows for extension tubing to be securely attached while in use and detached while not in use. Low-profile tubes are often preferred among younger, active patients and those with adequate dexterity to allow for attachment of the external extension tubing. These tubes are most often inserted as a replacement for an initially endoscopically placed tube, although one-step systems for initial placement are available. The size of the low-profile tube is chosen based on the size of the existing PEG tube and by measuring the length of the stoma tract using specialized measuring devices.[8] Patients and caregivers can also be trained to replace balloon-type tubes on their own to limit complications of displaced or cracked tubes. Low-profile tubes are commercially available for both gastric placement and gastric placement with extension into the small bowel, which often requires fluoroscopy for secure placement.

All percutaneous enteral tubes are being transitioned to the ENfit connector system, which prevents connections from the enteral system to nonenteral systems (namely, intravenous lines, chest tubes) and vice versa. Tubing misconnections have been rarely reported, and the EnFIT system is designed to prevent such misadventures that have resulted in serious complications and even mortality.[9] Adapter devices are available that may be required for patients with feeding tubes who have not been transitioned yet. Most commonly with new tube placements and replacements, patients and providers will have to become familiar with the new syringes and feeding bags required with EnFIT connectors.

In the case of a critically ill patient in the ICU, it is recommended to start enteral nutrition within 48 hours of arrival to avoid complications.

Gastrostomy placement can be considered a higher-risk endoscopic procedure. One complicating factor is the increased use of antiplatelet and anticoagulant therapies in individuals with a history of neurologic insults. The American Society for Gastrointestinal Endoscopy guidelines recommend that coumadin be held 5 days before the procedure and bridged with heparin if the patient is at high risk of thromboembolic complications. For patients on dual-antiplatelet therapy, thienopyridines like clopidogrel are often stopped 5-7 days prior to procedure with continuation of aspirin,[10] but there are more recent data that PEG insertion is safe with continued use of DAPT.[11] Direct-acting anticoagulants are often stopped 24-48 hours prior to procedure and then restarted 48 hours after tube placement, but this is dependent on the half-life of the specific DOAC and the patient's renal function. Patients with decreased creatinine clearance may need to hold the DOAC up to 3-4 days prior to the procedure. In this situation, referring to ASGE guidelines and consultation with a hematologist or managing anticoagulation clinic is advised.[10]

Troubleshooting of complications

Nasoenteric tubes: One of the most common and irritating complications with nasoenteric feeding tubes is clogging. To prevent clogging, flush the tube frequently.[12] At least 30 mL of free water should be used to flush the tube every 4-8 hours for continuous feedings or before and after bolus feeding. Additionally, 15-30 mL of water should be given with each separate medication administration, and if possible, medication administration via small-bore small bowel feeding tubes should be avoided.[12] Water flushing is especially important with small-caliber tubes and pumps that deliver both feeding and water flushes. It is available for small-bowel feeding in order to allow for programmed water delivery.

Warm water flushes can also help unclog the tube,[12] and additional pharmacologic and mechanical devices have been promoted for clogged tubes. One common technique is mixing pancreatic enzymes (Viokase) with a crushed 325-mg tablet of nonenteric-coated sodi-

Continued on following page

Table 1. Indications for percutaneous feeding tube placement

Neurologic	Stroke, motor neuron disease (ALS), cerebral palsy, multiple sclerosis, Parkinson's disease, mild dementia
Oncologic	Head and neck cancer, obstructing esophageal cancer, malignant bowel obstruction requiring gastric decompression
Gastrointestinal	Motility disorders, chronic pancreatitis, short bowel syndrome
Miscellaneous	Polytrauma, coma, burns, cystic fibrosis, pulmonary/cardiac cachexia, prolonged critical illness

Source: Dr. Toy, Dr. Fang

Table 2. Contraindications to PEG placement

Absolute	Relative
Pharyngeal or esophageal obstruction	Abdominal wall abnormalities
Significant coagulopathy	Abdominal wall metastases
Inability to appose gastric and abdominal wall with transillumination and focal finger indention	Open abdominal wounds
	Hepatomegaly/splenomegaly
	Ascites
	Portal hypertension with gastric varices
	Prior gastric surgery

Source: Dr. Toy, Dr. Fang

Continued from previous page
um bicarbonate and 5 mL of water to create a solution that has the alkaline properties allowing for both pancreatic enzyme activation and clog dissolution. Additionally, an endoscopic retrograde cholangiopancreatography (ERCP) catheter can be placed into longer feeding tubes to directly infuse the activated agent to the site of the clog.[13] If water and enzymes are not successful in unclogging the tube, commercially available brushes can help remove clogs. The TubeClear® system (Actuated Medical, Bellefonte, Pa.) has a single-use stem that is connected to AC power to create a jackhammerlike movement to remove clogs in longer nasoenteral and gastrojejunal tubes.

More delayed complications of PEG insertion include wound infection, buried bumper syndrome, tumor seeding, peristomal leakage, and tube dislodgment.

PEG tubes (short-term complications): Procedural and immediate postprocedural complications include bleeding, aspiration, pneumoperitoneum, and perforation. Pneumoperitoneum occurs in approximately 50% of cases and is generally clinically insignificant. The risk of pneumoperitoneum can be reduced by using CO_2 insufflation.[14] If the patient develops systemic signs of infection or peritoneal signs, CT scan with oral contrast is warranted for further evaluation and to assess for inadvertent perforation of overlying bowel or dislodged tube. Aspiration during or following endoscopy is another common complication of PEG placement and risk factors include over-sedation, supine positioning, advanced age, and neurologic dysfunction. This risk can be mitigated by avoiding over-sedation, immediately aspirating gastric contents when the stomach is reached, and avoiding excessive insufflation.[15] In addition, elevating the head of the bed during the procedure and dedicating an assistant to perform oral suctioning during the entire procedure is recommended.

PEG tubes (long-term complications): More delayed complications of PEG insertion include wound infection, buried bumper syndrome, tumor seeding, peristomal leakage, and tube dislodgment. The prevalence of wound infection is 5%- 25%,[16] and randomized controlled trials have demonstrated the efficacy of a single dose of an IV antibiotic (i.e., cephalosporin) in those not already receiving a broad-spectrum antibiotic and administered prophylactically before tube placement.[17] The significance of this reduction is such that antibiotic administration before tube placement should be considered a quality measure for the procedure. A small amount of redness around the tube site (less than 5 mm) is typical, but extension of erythema, warmth, tenderness, purulent drainage, or systemic symptoms is consistent with infection and warrants additional antibiotic administration. Minor infections can be treated with local antiseptics and oral antibiotics, and early intervention is important to prevent need for hospital admission, systemic antibiotics, and even surgical debridement.

Peristomal leakage is reported in approximately 1%-2% of patients.[18] Photographs of the site can be very useful in evaluating and managing peristomal leakage and infections. Interventions include reducing gastric secretions with proton pump inhibitors and management of the skin with barrier creams, such as zinc oxide (Calmoseptine®) ointment. Placement of a larger-diameter tube enlarges the stoma track and only worsens the leakage. In such cases, thorough evaluations for delayed gastric emptying (gastroparesis), distal obstruction, or constipation should be performed and managed accordingly. Opiates are common contributors to constipation and delayed gastric emptying and often require reduction in use or directed antagonist therapy to reduce leaking.

Continuous feeding over bolus feedings and delivering nutrition distally into the small bowel (PEG-J placement) can improve leaking from gastrostomy tubes. Additional means of management include stabilizing the tube by replacing a traditional tube with a low-profile tube or using right-angle external bumpers. If all measures fail, removing the tube and allowing for stomal closure can be attempted,[16] although this option often requires parenteral nutrition support to prevent prolonged periods of inadequate nutrition.

Buried bumper syndrome (BBS) occurs in 1.5%-8.8% of PEG placements and is a common late complication of PEG placement, although early reports have been described.[18] The development of BBS occurs when the internal bumper migrates from the gastric lumen through and into the stomach or abdominal wall. It occurs more frequently with solid nonballoon retention tubes and is caused by excessive compression of the external bumper against the skin and abdominal wall. Patients with BBS usually present with an immobile catheter, resistance with feeds (because of a closure of the stomach wall around the internal portion of the gastrostomy tube), abdominal pain, or peristomal leakage. Physicians should be aware of and assess tubes for BBS, in particular when replacing an immobile tube (cannot be pushed into the free stomach lumen) or when there is difficulty in flushing water into the tube. This complication can be easily prevented by allowing a minimum of 0.5-1.0 cm (1 finger breadth) between the external bumper and the abdominal wall. In particular, patients and caregivers should be warned that if the patient gains significant amounts of weight, the outer bumper will need to be loosened. Once BBS is diagnosed, the PEG tube requires removal and replacement as it can cause bleeding, infection, or fasciitis. The general steps to replacement include endoscopic removal of the existing tube and replacement of new PEG in the existing tract as long as the BBS is not severe. In most cases a replacement tube can be pulled into place using the pull-PEG technique at the same gastrostomy site as long as the stoma tract can be cannulated with a wire after the existing tube is removed.

Gastroenterologists occupy a unique role in evaluation, diagnosis, and management of patients requiring enteral feeding.

Similar to nasoenteric tubes, PEG tubes can become clogged, although this complication is infrequent. The primary steps for prevention include adequately flushing with water before and after feeds and ensuring that all medications are liquid or well crushed and dissolved before instilling. Timely tube replacement also ensures that the internal portions of the gastrostomy tube remain free of debris. Management is similar to that of unclogging nasoenteral tubes, as discussed above, and specific commercial declogging devices for PEG tubes include the Bionix Declogger® (Bionix Development, Toledo, Ohio) and the Bard® PEG cleaning brush (Bard Peripheral Vascular Tempe, Ariz.). The Bionix system has a plastic stem with a screw and thread design that will remove clogs in 14-24 French PEG tubes, while the Bard brush has a flexible nylon stem with soft bristles at the end to prevent mucosal injury and can be used for prophylaxis against clogs, as well as removing clogs themselves.[12]

Lastly, a rare but important complication of PEG placement is tumor seeding of the PEG site in patients with active head and neck or upper gastrointestinal cancer.[19] The presumed mechanism is shearing of tumor cells as the PEG is pulled through the upper aerodigestive tract and through the wall of the stomach, as prior studies have demonstrated frequent seeding of tubes and incision sites as shown by brushing the tube for malignant cells after tube placement.[20] It is important to recognize this complication and not misdiagnose it as granulation tissue, infection, or bleeding as the spread of the cancer generally portends a poor prognosis. Therefore, it is best to use a PEG insertion technique that does not involve pulling or pushing the PEG through the upper aerodigestive tract in patients with active cancer and instead place tubes via an external approach by colleagues in interventional radiology or via direct surgical placement.

Conclusion

Gastroenterologists occupy a unique role in evaluation, diagnosis, and management of patients requiring enteral feeding. In addition, they are best equipped to place, prevent, and manage complications of tube feeding. For this reason, it is imperative that gastroenterologists familiarize themselves with indications for enteral tubes and types of enteral tubes available, as well as the identification and management of common complications. Comprehensive understanding of these concepts will augment the practicing gastroenterologist's ability to manage patients requiring enteral nutrition support with confidence.

See references at MDedge.com/gihepnews/new-gastroenterologist.

CRC in young adults: Lower than previously reported

Implications for screening recommendations

BY ROXANNE NELSON, RN, BSN

The risk for colorectal cancer (CRC) in young adults is actually lower than has been estimated, because previous studies did not differentiate between colorectal adenocarcinoma and the histologically different carcinoid tumors, which are incidental findings, say experts.

New estimates for the risk of CRC in young adults, which differentiate colorectal adenocarcinoma from other types, are reported in a study published Dec. 15, 2020, in Annals of Internal Medicine (doi: 10.7326/M20-0068).

They are important because this finding has implications for CRC screening, say a trio of experts in an accompanying editorial.

AGA Resource
Help your patients understand colorectal cancer prevention and screening options by sharing AGA's patient education from the GI Patient Center: www.gastro.org/CRC.

Reports of an increase in the incidence of CRC in younger adults have led to changes in screening for this cancer in the United States. The age for starting CRC screening has been lowered to 45 years (instead of 50 years) in recommendations issued in 2018 by the American Cancer Society, and also more recently in preliminary recommendations from the U.S. Preventive Services Task Force.

However, that 2018 ACS recommendation to lower the starting age to 45 years was based to a large extent on a report of a higher incidence of CRC in younger adults from a 2017 study that used the SEER (Surveillance, Epidemiology, and End Results) database (CA Cancer J Clin. 2017;67:177-93).

But that SEER-based study considered "colorectal cancer" as a homogeneous group defined by topology, the editorialists pointed out.

The new study, the editorialists said, uses that same SEER database but has "disentangled colorectal adenocarcinoma, the target for screening, from other histologic CRC types, including neuroendocrine (carcinoid) tumors, for which screening is not recommended."

The study authors explained that adenocarcinoma is a target for prevention through screening because it arises from precancerous polyps. Those growths can be detected and removed before cancer develops. That doesn't apply to carcinoid tumors, which are frequently incidental findings on flexible sigmoidoscopy or colonoscopy.

These carcinoid tumors typically are indolent, with a better prognosis than most other cancer types, the editorialists added. "Most likely, the majority of carcinoid tumors identified by screening represent incidental findings with little health benefit from detection. In fact, many may be characterized as overdiagnosed tumors, which by definition increase the burden and harms of screening without the balance of additional benefit."

This new analysis showed that 4%-20% of the lesions previously described as CRC were not adeno-

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carcinoma but carcinoid tumors, the editorialists pointed out.

This figure rose even higher in the subgroup of findings pertaining to the rectum, the colonic segment with the largest reported increase in early-onset CRC. Here, up to 34% of lesions (depending on patient age) were carcinoid tumors rather than adenocarcinoma, they noted.

The three editorialists – Michael Bretthauer, MD, PhD, and Mette Kalager, MD, PhD, both of the University of Oslo, and David Weinberg, MD, MSc, AGAF, of Fox Chase Cancer Center, Philadelphia – call for action based on the new findings.

"The ACS's 2018 estimate of about 7,000 new CRC cases among persons aged 45-49 years in the United States (the justification for screening) needs to be adjusted downward on the basis of the new evidence," the trio wrote.

They conclude that "caution is warranted when promoting the benefits of CRC screening for persons younger than 50 years."

However, the senior author of the new study, Jordan Karlitz, MD, of Tulane University, New Orleans, strongly disagreed.

DME Photography/Getty Images

Contrary to the editorialists, Dr. Karlitz said in an interview that he and his colleagues firmly believe that colorectal cancer screening for average-risk patients should begin at age 45 and that their new research, despite its clarification about carcinoid tumors, provides evidence for that.

"There are a number of other studies that support screening at age 45 as well," he said. "This [new] finding supports the presence of a large preclinical colorectal cancer case burden in patients in their 40s that is ultimately uncovered with screening initiation at age 45."

Adenocarcinomas also make up the "overwhelming majority" of colorectal cancers in patients under 50 overall and "are the main driving force behind the increased colorectal cancer burden we are seeing in young patients," Dr. Karlitz added.

Furthermore, "modeling studies on which the USPSTF screening recommendations were based [which recommended starting at age 45] were confined to adenocarcinoma, thus excluding carcinoids from their analysis," he said.

Steepest changes in adenocarcinomas in younger groups

In their study, Dr. Karlitz and colleagues assessed the incidence rates of early colorectal cancer, using SEER data from 2000 to 2016, and stratifying the data by histologic subtype (primarily adenocarcinoma and carcinoid tumors), age group (20-29, 30-39, 40-49, and 50-54 years), and subsite.

A total of 123,143 CRC cases were identified in 119,624 patients between the ages of 20 and 54 years during that time period.

The absolute incidence rates in the younger age groups (20-29 and 30-39 years) were very low vs. those aged 40-49 and 50-54 years.

The greatest 3-year average annual incident rate changes in adenocarcinoma (2000-2002 vs. 2014-2016) for any age group or subsite were for rectal-only cases in the 20-29 years group (+39%), as well as rectal-only cases in those aged 30-39 years (+39%), and colon-only cases in the age 30-39 group (+20%).

There was also significant increase in rectal-only adenocarcinoma in individuals aged 50-54 years (+10%). A statistically significant increase in the annual percentage change for adenocarcinomas was observed for all age groups, except for colon-only cases in the 20- to 29-years group (0.7%) and for both colorectal (0.2%) and colon-only cases (–0.1%) in those aged 50-54 years.

Even though the absolute carcinoid tumor incidence rates were lower than for adenocarcinoma in all age groups and subsites, a statistically significant increase was observed in the 3-year average annual incidence rate of combined-site colorectal carcinoid tumors in all age groups from 2000–2002 and 2014–2016. This increase was largely the result of increases in rectal carcinoid tumors, the authors note.

The authors also highlighted the results in the 40- to 49-year age group "because of differing opinions on whether to begin average-risk screening at age 45 or 50 years."

They reported that rates of rectal and colon adenocarcinoma are increasing "substantially," whether measured by changes in 3-year average annual incidence rate or by annual percentage changes. The change in average annual incidence rate of colon-only adenocarcinoma for persons aged 40-49 years was 13% (12.21-13.85 per 100,000), and that of rectal adenocarcinoma was 16% (7.50-8.72 per 100,000). Corresponding annual percentage changes were 0.8% and 1.2%, respectively. "These significant increases in adenocarcinoma incident rates add to the debate over earlier screening at age 45 years," they commented.

Calls for next steps

The editorialists emphasize restraint when promoting the benefits of colorectal screening for persons younger than 50 years.

They point out that the USPSTF released a provisional update of its CRC screening recommendations

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PDAC: Tumor reduction after neoadjuvant therapy may predict postsurgical survival

BY JIM KLING
MDedge News

In patients who undergo resection of pancreatic ductal adenocarcinoma (PDAC) after neoadjuvant therapy, reduction in tumor size between diagnosis and surgery is associated with improved survival, according to a new single-center, retrospective analysis. The researchers compared tumor size as measured by endoscopic ultrasound (EUS) and found that a threshold of 47% or greater reduction in tumor size at resection was associated with a doubling in the 3-year survival rate.

The study, led by Rohit Das, MD, of the University of Pittsburgh Medical Center, was published in Clinical Gastroenterology and Hepatology.

A threshold of 47% or greater reduction in tumor size at resection was associated with a doubling in the 3-year survival rate.

The research represents only a small percentage of patients since most diagnosed with PDAC have locally advanced or metastatic disease that rules out surgery. Still, the work puts more emphasis on measuring tumor size while performing EUS, according to Robert Jay Sealock, MD, who is an assistant professor of medicine at Baylor College of Medicine, Houston.

"This is some helpful information that you can relay to the patient, saying that you have a significant decrease in the size of the tumor based on your initial EUS, and your chance of 3- to 5-year survival is going to be a lot higher, compared to somebody that didn't have that tumor regression. Most of these patients will undergo an EUS anyway, and you'll commonly if not always measure the tumor size while you're in there. Now you can apply this information that you already have to give the patients some additional information if they do undergo surgery," said Dr. Sealock, who was not involved in the research.

Previous efforts to prognosticate postsurgical survival focused on overall tumor burden using multidetector CT (MDCT), carbohydrate antigen 19-9 (CA19-9) levels, and histologic examination following surgery, but all suffer from various limitations. MDCT is not always accurate in its measurement of tumor size, other conditions can also raise CA19-9 levels, and pathologic findings are subjective because sometimes the amount of tumor before neoadjuvant therapy is uncertain.

The researchers mapped survival statistics to EUS and pathologic findings for 340 treatment-naive and 365 neoadjuvant-treated PDAC patients at the University of Pittsburgh Medical Center. They used a 200-patient cohort from the same center who had been treated with neoadjuvant therapy for validation.

Pathology examination revealed that, in the treatment-naive group, 71% of tumors were larger than the size determined during EUS. In 9% of cases there was no change in size (EUS versus pathology T-staging Pearson correlation coefficient, 0.586; $P < .001$). A similar analysis of MDCT showed a weaker correlation. There was no correlation between preoperative EUS/MDCT findings and postoperative pathology among patients who received neoadjuvant therapy.

"This is some helpful information that you can relay to the patient, saying that you have a significant decrease in the size of the tumor based on your initial EUS."

In the neoadjuvant therapy group, tumor size was reduced in 31% of patients, was unchanged in 53%, and actually grew in 16%. Three-year overall survival was highest in the reduced group (50%), and lower in the unchanged (37%) and tumor-growth (34%) groups. At 5 years, overall survival was 31%, 19%, and 16%, respectively ($P = .003$). Compared with those whose tumor size remained the same or grew, those with reduced tumor size had higher 3-year overall survival (50% vs. 33%) and 5-year overall survival (31% vs. 18%; $P < .001$).

The researchers used recursive positioning to identify the optimal threshold for tumor reduction, and found that a 47% or greater reduction was associated with 67% overall survival at 3 years and 47% at 5 years, compared with 32% and 16% for those with smaller reduction or tumors that maintained or increased in size ($P < .001$).

The researchers noted that, although their study is large, it remains retrospective in design. Another limitation they cited was that not all patients received the same neoadjuvant therapy. Furthermore, both EUS and pathologic evaluation can be subjective, and it can be difficult to correct for that.

"While additional studies are required, incorporating preoperative EUS and postoperative pathologic tumor size measurements into the standard evaluation of neoadjuvant-treated PDAC patients may guide subsequent management in the adjuvant setting," the researchers concluded.

The study was funded in part by the National Pancreas Foundation, Sky Foundation, and the Pittsburgh Liver Research Center at the University of Pittsburgh. One author disclosed receiving an honorarium from Foundation Medicine, but the rest reported having nothing to disclose. Dr. Sealock has no relevant financial disclosures.

ginews@gastro.org

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about lowering the age to initiate screening to 45 years, as reported by this news organization.

"No new empirical evidence has been found since the USPSTF update in 2016 to inform the effectiveness of screening in persons younger than 50 years," they write, adding that similar to the American Cancer Society in 2018, the task force has relied exclusively on modeling studies.

These new data from Dr. Karlitz and colleagues "should prompt the modelers to recalculate their estimates of benefits and harms of screening," they suggested. "Revisiting the model would also allow competing forms of CRC screening to be compared in light of new risk assumptions.

"Previous assumptions that screening tests are equally effective in younger and older patients and that screening adherence will approach 100% may also be reconsidered," the editorialist commented.

The study authors concluded somewhat differently.

"In conclusion, adenocarcinoma rates increased in many early-onset subgroups but showed no significant increase in others, including colon-only cases in persons aged 20-29 and 50-54 years," the investigators wrote.

They also observed that "rectal carcinoid tumors are increasing in young patients and may have a substantial impact on overall CRC incident rates."

Those findings on rectal carcinoid tumors "underscore the importance of assessing histologic CRC subtypes independently," the researchers said.

This new approach, of which the current study is a first effort, "may lead to a better understanding of the drivers of temporal changes in overall CRC incidence and a more accurate measurement of the outcomes of adenocarcinoma risk reduction efforts, and can guide future research."

The study had no outside funding. Dr. Bretthauer reports grants from Norwegian Research Council, and grants from Norwegian Cancer Society for research in colorectal cancer screening. Dr. Weinberg and Dr. Kalager have disclosed no relevant financial relationships. Dr. Karlitz reported personal fees from Exact Sciences, personal fees from Myriad Genetics, and other fees from Gastro Girl and GI OnDEMAND, outside the submitted work.

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

During pandemic, many gastroenterologists report low resilience, insomnia

BY WILL PASS
MDedge News

Almost one-third of gastroenterologists may have low resilient coping skills, a finding linked with clinical insomnia, according to a national survey conducted between May and June of 2020.

The study, which was designed to characterize the psychological and emotional health of gastroenterologists during the COVID-19 pandemic, demonstrates how a complex array of factors drives poor psychological health, rather than specific challenges, such as coronavirus exposure risk, reported lead author Eric D. Shah, MD, MBA, of Dartmouth-Hitchcock Health in Lebanon, N.H., and colleagues.

"The COVID-19 pandemic poses unprecedented and unique challenges to gastroenterologists eager to maintain clinical practice, patients' health, and their own physical/mental well-being," the investigators wrote in Clinical Gastroenterology and Hepatology.

Dr. Shah

"[W]e found that singular personal challenges, practice-related challenges, and perceived COVID-19–related exposure risks (such as perception of PPE availability) had little association with important psychological health outcomes including depression or anxiety."

To learn more, Dr. Shah and colleagues conducted a national cross-sectional survey of gastroenterologists in the United States.

Primary outcomes included clinical insomnia (Insomnia Severity Index-7), general anxiety disorder (General Anxiety Disorder-7), and psychological distress (Patient Health Questionnaire-8). The investigators developed additional domains to characterize perceived coronavirus exposure risks, practice-related challenges, and personal challenges. Further assessment determined whether resilient coping skills (Brief Resilient Coping Scale) or well-being (Physician Well-Being Index) were associated with psychological health outcomes among surveyed gastroenterologists.

A total of 153 gastroenterologists from 32 states completed the questionnaire, among whom the mean age and years in practice were 46 years and 13 years, respectively. Almost one-quarter of respondents were female (22.7%).

The survey found that anxiety and depression were uncommon, with respective rates of 7.2% and 8.5%.

In contrast, 30.7% of gastroenterologists reported low resilient coping skills.

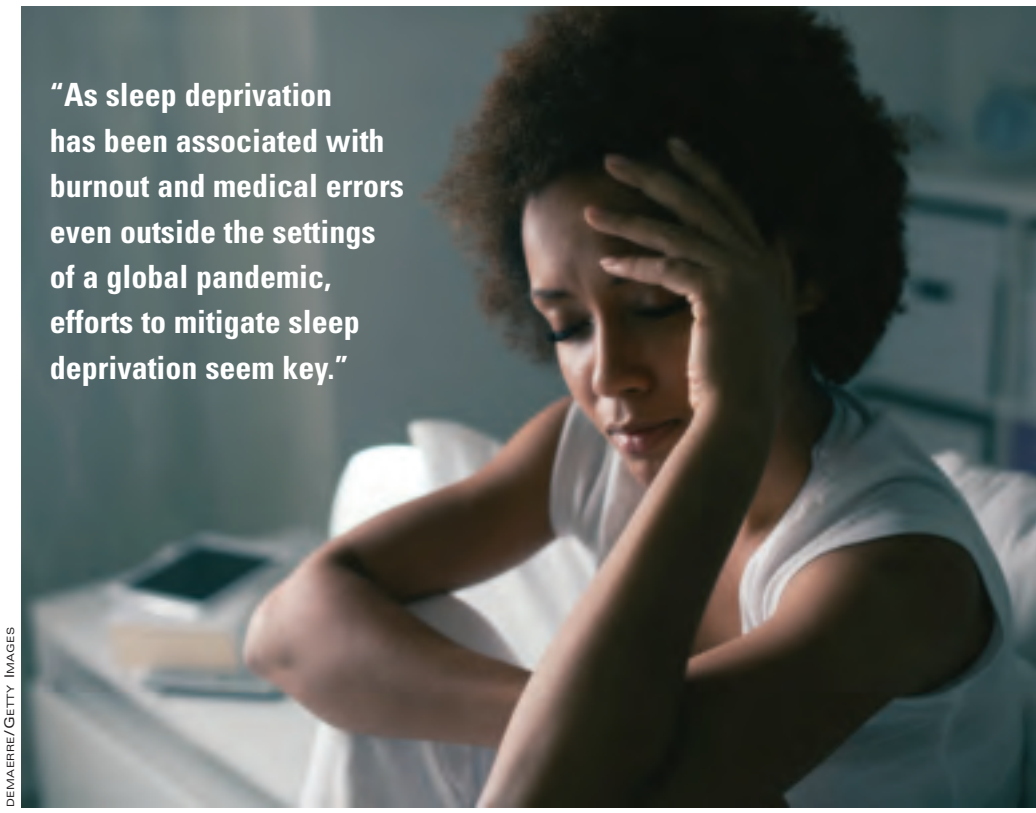
"Resilience is defined as the 'mental processes and behaviors that a person uses to protect themselves from the potential negative effects of stressors,'" the investigators wrote. "Resilient coping skills allow individuals in stressful situations to avoid negative psychological health consequences such as depression and anxiety."

The study showed that low resilience was associated with clinical insomnia (odds ratio, 3.80; 95% confidence interval, 1.16-12.46), which occurred in more than one-quarter of respondents (25.5%).

Insomnia was also associated with age greater than 60 years, isolation outside the home, and years in practice. After adjustment for sex, age, and resilient coping, univariate analysis showed that insomnia was associated with isolation, female sex, and smaller practice size (fewer than 15 attending physicians).

While most respondents (85%) reported moderate to high well-being, those who didn't were significantly more likely to report clinical anxiety, depression, and insomnia ($P < .001$ for all).

"[W]e found that singular personal challenges, practice-related challenges, and perceived COVID-19–related exposure risks (such as perception of PPE availability) had little association with important psychological health outcomes including depression or anxiety," wrote Dr. Shah and colleagues.



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Instead, the investigators pointed to resilience.

"Physician leaders and other administrators should consider strategies to maintain resilient coping skills among their colleagues such as dedicated resilience training and self-care," the investigators wrote.

They suggested that multiple stakeholders, including professional societies and policy makers, will be needed to implement such programs, and others. Additional interventions may include ensuring personal protective equipment availability, developing better technology for telemedicine, and supporting small practices that face financial obstacles in canceling elective procedures, the investigators wrote.

Edward L. Barnes, MD, MPH, of the University of North Carolina at Chapel Hill, said that the 30% prevalence rate for low resilient coping skills was the "most striking" finding.

Dr. Barnes went on to suggest that the survey results may actually underplay the current psychological landscape in gastroenterology.

"This study encompassed 2 of the early months of the COVID-19 pandemic (May-June 2020), which makes one wonder whether these same effects would be magnified over an even longer period of assessment," he said.

Dr. Barnes, who authored an article last year concerning interventions for burnout in young gastroenterologists, offered some practical insight (Dig Dis Sci. 2019 Feb;64[2]:302-6).

"As sleep deprivation has been associated with burnout and medical errors even outside the settings of a global pandemic [JAMA Netw Open. 2020. doi: 10.1001/jamanetworkopen.2020.28111], efforts to mitigate sleep deprivation seem key," he said. "Given that resilience is a skill that can be both learned and improved, focused interventions by health care systems to ensure the presence of resilient coping skills among gastroenterologists could be a critical way to reduce psychological stress, prevent burnout, and improve the overall well-being of health care providers."

Dr. Shah is supported by the AGA Research Foundation's 2019 AGA-Shire Research Scholar Award in Functional GI and Motility Disorders. He and his fellow investigators, as well as Dr. Barnes, reported no conflicts of interest.

ginews@gastro.org

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Experts discuss concerns

Vaccines *from page 1*

At a special session held during the 2020 annual meeting of the American Society of Hematology, Anthony S. Fauci, MD, the nation's leading infectious disease expert, said that individuals with compromised immune systems, whether because of chemotherapy or a bone marrow transplant, should plan to be vaccinated when the opportunity arises.


Dr. Fauci

In response to a question from ASH President Stephanie J. Lee, MD, of the Fred Hutchinson Cancer Center, Seattle, Dr. Fauci emphasized that, despite being excluded from clinical trials, this population should get vaccinated. "I think we should recommend that they get vaccinated," he said. "I mean, it is clear that, if you are on immunosuppressive agents, history tells us that you're not going to have as robust a response as if you had an intact immune system that was not being compromised. But some degree of immunity is better than no degree of immunity."


Dr. Lee

That does seem to be the consensus among experts who spoke in interviews: that as long as these are not live attenuated vaccines, they hold no specific risk to an immunocompromised patient, other than any factors specific to the individual that could be a contraindication.

"Patients, family members, friends, and work contacts should be encouraged to receive the vaccine," said William Stohl, MD, PhD, chief of the division of rheumatology at the University of Southern California, Los Angeles. "Clinicians should advise patients to obtain the vaccine sooner rather than later."

Kevin C. Wang, MD, PhD, of the department of dermatology at Stanford (Calif.) University, agreed. "I am 100% with Dr. Fauci. Everyone should get the vaccine, even if it may not be as effective," he said. "I would treat it exactly like the flu vaccines that we recommend folks get every year."

Dr. Wang noted that he couldn't think of any contraindications unless the immunosuppressed patients have a history of severe allergic reactions to prior vaccinations. "But I would even say patients with history of cancer, upon recommendation of their oncologists, are likely to be suitable candidates for the vaccine," he added. "I would say clinicians should approach counseling the same way they counsel patients for the flu vaccine, and as far as I know, there are no concerns for systemic drugs commonly used in dermatology patients."


Dr. Wang

However, guidance has not yet been issued from either the FDA or the Centers for Disease Control and Prevention regarding the use of the vaccine in immunocompromised individuals. Given the lack of data, the FDA has said that "it will be something that providers will need to consider on an individual basis," and that individuals should consult with physicians to weigh the potential benefits and potential risks.

The CDC's Advisory Committee on Immunization Practices has said that clinicians need more guidance on whether to use the vaccine in pregnant or breastfeeding women, the immunocompromised, or those who have a history of allergies. The CDC itself has not yet released its formal guidance on vaccine use.

COVID-19 vaccines

Vaccines typically require years of research and testing before reaching the clinic, but this year researchers embarked on a global effort to develop safe and effective coronavirus vaccines in record time. Both the Pfizer/BioNTech and Moderna vaccines have only a few months of phase 3 clinical trial data, so much remains unknown about them, including their duration of effect and any long-term safety signals. In addition to excluding immunocompromised individuals, the clinical trials did not include children or pregnant women, so data are lacking for several population subgroups.

But these will not be the only

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vaccines available, as the pipeline is already becoming crowded. U.S. clinical trial data from a vaccine jointly being developed by Oxford-AstraZeneca, could potentially be ready, along with a request for FDA emergency use authorization, soon.

In addition, China and Russia have released vaccines, and there are currently 61 vaccines being investigated in clinical trials and at least 85 preclinical products under active investigation.

The vaccine candidates are using both conventional and novel mechanisms of action to elicit an immune response in patients. Conventional methods include attenuated inactivated (killed) virus and recombinant viral protein vaccines to develop immunity. Novel approaches include replication-deficient, adenovirus vector–based vaccines that contain the viral protein, and mRNA-based vaccines, such as the Pfizer and Moderna vaccines, that encode for a SARS-CoV-2 spike protein.

"The special vaccine concern for immunocompromised individuals is introduction of a live virus," Dr. Stohl said. "Neither the Moderna nor Pfizer vaccines are live viruses, so there should be no special contraindication for such individuals."


Dr. Stohl

Live vaccine should be avoided in immunocompromised patients, and currently, live SARS-CoV-2 vaccines are being developed only in India and Turkey.

It is not unusual for vaccine trials to begin with cohorts that exclude participants with various health conditions, including those who are immunocompromised. These groups are generally then evaluated in phase 4 trials, or postmarketing surveillance. While the precise number of immunosuppressed adults in the United States is not known, the numbers are believed to be rising because of increased life expectancy among immunosuppressed adults as a result of advances in treatment and new and wider indications for therapies that can affect the immune system.

According to data from the 2013 National Health Interview Survey, an estimated 2.7% of U.S. adults are immunosuppressed (JAMA. 2016;316[23]:2547-8). This population covers a broad array of health conditions and medical specialties; people living with inflammatory or autoimmune conditions, such as inflammatory rheumatic diseases (rheumatoid arthritis, axial spondyloarthritis, lupus); inflammatory bowel disease (Crohn's disease and ulcerative colitis); psoriasis; multiple sclerosis; organ transplant recipients; patients undergoing chemotherapy; and life-long immunosuppression attributable to HIV infection.

AGA Resource

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

As the vaccines begin to roll out and become available, how should clinicians advise their patients, in the absence of any clinical trial data?

Risk vs. benefit

Gilaad Kaplan, MD, MPH, AGAF, a gastroenterologist and professor of medicine at the University of Calgary (Alta.), noted that the inflammatory bowel disease (IBD) community has dealt with tremendous anxiety during the pandemic because many are immunocompromised because of the medications they use to treat their disease.

"For example, many patients with IBD are on biologics like anti-TNF [tumor necrosis factor] therapies, which are also used in other immune-mediated inflammatory diseases such as rheumatoid arthritis," he said. "Understandably, individuals with IBD on immunosuppressive medications are concerned about the risk of severe complications due to COVID-19."

The entire IBD community, along with the world, celebrated the announcement that multiple vaccines are protective against SARS-CoV-2, he noted. "Vaccines offer the potential to reduce the spread of COVID-19, allowing society to revert back to normalcy," Dr. Kaplan said. "Moreover, for vulnerable populations, including those who are immunocompromised, vaccines offer the potential to directly protect them from the morbidity and mortality associated with COVID-19."

That said, even though the news of vaccines are extremely promising, some cautions must be raised regarding their use in immunocompromised populations, such as persons with IBD. "The current trials, to my knowledge, did not include immunocompromised individuals and thus, we can only extrapolate from what we know from other trials of different vaccines," he explained. "We know from prior vaccines studies that the immune response following vaccination is less robust in those who are immunocompromised as compared to a healthy control population."

Dr. Kaplan also pointed to recent reports of allergic reactions that have been reported in healthy individuals. "We don't know whether side effects, like allergic reactions, may be different in unstudied populations," he said. "Thus, the medical and scientific community should prioritize clinical studies of safety and effectiveness of COVID-19 vaccines in immunocompromised populations."

So, what does this mean for an individual with an immune-mediated inflammatory disease like Crohn's disease or ulcerative colitis who is immunocompromised? Dr. Kaplan explained that it is a balance between the potential harm of being infected with COVID-19 and the uncertainty of receiving a vaccine in an understudied population. For those who are highly susceptible to dying from COVID-19, such as an older adult with IBD, or someone who faces high exposure, such as a health care worker, the potential protection of the vaccine greatly outweighs the uncertainty.

"However, for individuals who are at otherwise lower risk – for example, young and able to work from home – then waiting a few extra months for postmarketing surveillance studies in immunocompromised populations may be a reasonable approach, as long as these individuals are taking great care to avoid infection," he said.

Lingering concerns

Steven R. Feldman, MD, PhD, of Wake Forest Baptist Health, in Winston-Salem, N.C., said that there are no contraindications for psoriasis patients to receive the vaccine, regardless of whether they are on immunosuppressive treatment, even though definitive data are lacking. "Fortunately, there's a lot of good data coming out of Italy that patients with psoriasis on biologics do not appear to be at increased risk of getting COVID or of having worse outcomes from COVID," he said.

Patients are going to ask about the vaccines, and when counseling them, clinicians should discuss the available data, the residual uncertainty, and patients' concerns should be considered, Dr. Feldman explained. "There may be some concern that steroids and cyclosporine would reduce the effectiveness of vaccines, but there is no concern that any of the drugs would cause increased risk from nonlive vaccines."


Dr. Feldman

He added that there is evidence that "patients on biologics who receive nonlive vaccines do develop antibody responses and are immunized."

Further advice

With other vaccines, biologic medicines are held for 2 weeks before and afterward, to get the best response. "But some patients don't want to stop the medication," said rheumatologist Brett Smith, DO, from Blount Memorial Physicians Group and East Tennessee Children's Hospital, Alcoa. "They are afraid that their symptoms will return."


Dr. Smith

As for counseling patients as to whether they should receive this vaccine, he explained that he typically doesn't try to sway patients one way or another until they are really high risk. "When I counsel, it really depends on the individual situation. And for this vaccine, we have to be open to the fact that many people have already made up their mind."

There are a lot of questions regarding the vaccine. One is the short time frame of development. "Vaccines typically take 6-10 years to come on the market, and this one is now available after a 3-month study," Dr. Smith said. "Some have already decided that it's too new for them."

The process is also new, and patients need to understand that it doesn't contain an active virus and "you can't catch coronavirus from it."

Dr. Smith also explained that, because the vaccine may be less effective in a person using biologic therapies, there is currently no information available on repeat vaccination. "These are all unanswered questions," he said. "If the antibodies wane in a short time, can we be revaccinated and in what time frame? We just don't know that yet."

ginews@gastro.org

IBD patients more likely to stick with vedolizumab

BY HEIDI SPLETE
MDedge News

Adults with inflammatory bowel disease were more likely to continue using vedolizumab, compared with anti–tumor necrosis factor (TNF) drugs over 3 years, based on data from a retrospective study of nearly 16,000 patients.

Patient persistence with prescribed therapy is essential to managing chronic inflammatory bowel disease (IBD), but data on the persistence of patients with treatments are limited, wrote Ulf Helwig, MD, of the Practice for Internal Medicine, Oldenburg, Germany, and colleagues. "With the advent of vedolizumab, physicians for the first time had the choice between biologicals with different modes of action," they wrote.

In a study published in the Journal of Clinical Gastroenterology, the researchers used a national prescription database to identify 15,984 adults aged 18 years and older who were treatment naive to biologics and received prescriptions between July 2014 and March 2017. Treatment persistence was defined as continuous treatment time of at least 90 days without prescription.

A total of 2,076 vedolizumab patients were matched with 2,076 adalimumab patients; 716 vedolizumab patients were matched with 716 golimumab patients; and 2,055 vedolizumab patients were matched with 2,055 infliximab patients. Within 3 years after the first prescription, the overall persistence rates were 35.9% for vedolizumab, 27.8% for adalimumab, 20.7% for golimumab, and 29.8% for infliximab.

In matched-pair analysis, 35.2% of vedolizumab patients were persistent, compared with 28.9% of adalimumab patients over a 3-year period; the difference was statistically significant. In addition, 30.5% of vedolizumab patients persisted, compared with 25.4% of golimumab patients, also statistically significant. A matched-pair comparison between vedolizumab and infliximab (35.7% vs. 30.2%) was not statistically significant ($P = 0.119$).

In addition, vedolizumab patients were significantly less likely to discontinue therapy, compared with both adalimumab and golimumab patients, with hazard ratios of 0.86 and 0.60, respectively, in the matched pair analysis; discontinuation, compared with infliximab, was not statistically significant.

"Several reasons may account for significant rates of discontinuation reported for all biological treatments in IBD," the researchers noted. "These comprise differences in health care systems in the concerned countries, including differences in availability of biologicals, access to reimbursed drugs, or different patient care settings," they wrote.

The study findings were limited by several factors including the lack of data on specific IBD diagnoses, IBD severity, disease course, and dose escalation, they noted.

However, the study was strengthened by the large sample size and use of a real-world setting, they said.

Comparisons inform choices

"There are multiple biologic options for therapy of inflammatory bowel disease, and response to therapy tends to drop off over time in many patients for a variety of reasons including development of antibodies and escape from the mechanism of the action of the drug," said Kim L. Isaacs, MD, AGAF, of the University of North Carolina at Chapel Hill, in an interview.

"Intolerance or side effects of medication also may lead to discontinuation of therapy," said Dr. Isaacs. "This trial looks at therapy discontinuation among four biologics used for inflammatory bowel disease over a 3-year period after initiation of therapy in patients who were previous biologically naive. Reasons for discontinuation cannot be assessed with this data set," she noted. "There are very few comparative trials with the different biologic therapies in IBD. This trial is important because it compares the two distinct biologic mechanisms of action and continuation of therapy in biologically naive patients," she said.

Dr. Isaacs said she was not surprised by the study findings. "Discontinuation of anti-TNF therapy was more common, compared to vedolizumab and golimumab. There was no statistical difference in terms of therapy discontinuation with infliximab," she said. "In general, vedolizumab is felt to be less systemically immunosuppressant with targeting of white blood cell trafficking to the gut, whereas anti-TNF therapy is more systemically immunosuppressant and may be associated with more systemic side effects," she explained.

The study design does not allow for comment on comparative efficacy, "although the findings are intriguing," said Dr. Isaacs. "If the discontinuations were caused by lack of efficacy, the findings in this study may help in positioning biologic therapy in the biologic-naive patients," she said.

The study is "a 'real-world' experiment that suggests there is a difference between different biologic therapies for inflammatory bowel disease," said Dr. Isaacs. "More controlled comparative efficacy trials are needed that can look at reasons for drug discontinuation between different populations. To date, the VARSITY trial comparing vedolizumab to adalimumab in ulcerative colitis is the only published trial to do this," she added.

The study received no outside funding. Lead author Dr. Helwig disclosed lecture and consulting fees from AbbVie, Amgen, Biogen, Celltrion, Hexal, MSD, Ferring, Falk Foundation, Takeda, Mundipharma, Pfizer, Hospira, and Vifor Pharma. Dr. Isaacs disclosed serving on the Data and Safety Monitoring Board for Janssen.

ginews@gastro.org

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AGA Resource
Help your patients better understand their IBD treatment options by sharing AGA's patient education, "Living with IBD," in the AGA GI Patient Center at www.gastro.org/IBD.

DOACs look safe in elective endoscopic procedures

BY JIM KLING
MDedge News

Among patients taking direct oral anticoagulants (DOACs), elective endoscopy procedures carry a risk of bleeding and thromboembolic events similar to that seen in those receiving vitamin K antagonists (VKAs), according to a multicenter, prospective observational study conducted at 12 Spanish academic and community centers.

DOACs have several advantages over VKAs, including more predictable pharmacokinetic profiles and fewer food and drug interactions, but they have not been well studied in the elective endoscopy setting. Some previous studies suggested a lower risk with DOACs, but they were retrospective or based on administrative databases.

The new study, which was led by Enrique Rodríguez de Santiago of Universidad de Alcalá (Spain) and was published in Clinical Gastroenterology and Hepatology.

"It certainly showed there was an acceptable rate of clinically significant rate of bleeding for patients on anticoagulants, and the thing I appreciated the most was that there was no statistically significant difference in terms of bleeding depending on when you resumed the anticoagulant," said Robert Jay Sealock, MD, assistant professor of medicine at Baylor College of Medicine in Houston. Dr. Sealock was not involved in the study.

The researchers examined data from 1,623 patients who underwent 1,874 endoscopic procedures. Among these patients, 62.7% were taking VKAs, and 37.3% were taking DOACs; 58.9% were men, and the mean age was 74.2 years. Overall, 75.5% were on anticoagulant therapy for atrial fibrillation. The most common procedures were colonoscopy (68.3%) and esophagogastroduodenoscopy (27.3%).

Within 30 days, the risk of bleeding was similar between patients taking VKAs (6.2%; 95% confidence interval, 4.8%-7.8%) and DOACs (6.7%; 95% CI, 4.9%-9%). This was true regardless of intervention and site.

Clinically significant gastrointestinal bleeding occurred in 6.4% of subjects (95% CI, 5.3-7.7%); 2.7% of clinically significant gastrointestinal bleeding events were intraprocedural, and 4.1% were delayed. The risk of bleeding for high-risk procedures was 11.5% (95% CI, 9.4-14%). The overall mortality was 1.4%, with two deaths related to thromboembolic events, both in the DOAC group.

The researchers also examined the timing of anticoagulant resumption. Overall, 59.2% of subjects received bridging therapy, including 85% of the VKA group and 16% of the DOAC group ($P < .001$). This was not associated with increased endoscopy-related bleeding in either the VKA (3.3% with bridging therapy vs. 6.4% without; $P = .14$) or the DOAC group (8.3% vs. 6.4%; $P = .48$).

DOACs have several advantages over VKAs, including more predictable pharmacokinetic profiles and fewer food and drug interactions, but they have not been well studied in the elective endoscopy setting.

A total of 747 patients underwent a high-risk procedure, 46.3% of patients resumed anticoagulant therapy within 24 hours of the procedure, and 46.2% between 24 and 48 hours. After inverse probability of treatment weighting adjustment, a delay in anticoagulant resumption was not associated with a reduction in the frequency of postprocedural clinically significant gastrointestinal bleeding.

Still, the research left some questions unanswered. Most of the high-risk procedures were hot (41.8%) or cold snare polypectomies (39.8%). There weren't enough data in the study to evaluate risk in patients undergoing other high-risk procedures such as balloon dilation for strictures, endoscopic ultrasound with fine-needle aspiration, and sphincterotomy. "That's one group that we still don't really have enough data about, particularly those patients who are on DOACs," said Dr. Sealock.

The study also found a high number of patients on bridging therapy. "It highlighted the fact that we probably use bridging therapy too much in patients undergoing endoscopy," said Dr. Sealock. He recommended using tools that generate recommendations.

The study was funded by the Spanish Society of Gastrointestinal Endoscopy. The investigators reported having no conflicts of interest. Dr. Sealock reported having nothing to disclose.

ginews@gastro.org

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FDA clears device to remove dead pancreatic tissue

BY MEGAN BROOKS

The Food and Drug Administration has approved the EndoRotor System (Interscope) for removal of necrotic tissue in patients with walled-off pancreatic necrosis (WOPN).

"This device has shown its potential to provide a minimally invasive way to remove harmful necrotic pancreatic tissue in patients with walled-off pancreatic necrosis," Charles Viviano, MD, PhD, acting director, Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors Office, FDA Center for Devices and Radiological Health, said in a statement.

"Currently, in order to remove dead tissue from a patient's necrotic pancreatic cavity, health care providers need to perform an invasive surgery or use other endoscopic tools not specifically indicated to treat this condition. With [this] marketing authorization, patients with walled-off pancreatic necrosis now have a new treatment option," said Dr. Viviano.

WOPN is a potentially deadly condition that occurs in about 15% of patients with severe pancreatitis. Often, the dead tissue must be removed.

The EndoRotor System is made up of a power console, foot control, specimen trap, and single-use catheter.

The device is used to perform endoscopic necrosectomy. In this procedure, a stent is used to create a portal between the stomach and the necrotic cavity in the pancreas to accommodate a standard endoscope through which the EndoRotor cuts and removes necrotized tissue.

The FDA approved the EndoRotor System on the basis of a clinical trial involving 30 patients with WOPN who underwent a total of 63 direct endoscopic necrosectomies with the EndoRotor System. The effectiveness of the EndoRotor System was determined by how well it cleared pancreatic necrotic tissue measured during CT with contrast before and after the procedure, endoscopy, or MRI 14-28 days after the last procedure. Results showed an average 85% reduction in the amount of necrotic tissue, with half of the patients having 98.5% clearance of necrotic tissue, the FDA said.

Three patients suffered procedure-related serious adverse events (10% complication rate). Two patients experienced gastrointestinal bleeding. One patient had a pneumoperitoneum and later died after suffering from sepsis and multiorgan system failure caused by massive collections of infected pancreatic necrotic tissue.

The EndoRotor System should not be used for patients with known or suspected pancreatic cancer, and the device will carry a boxed warning stating this. The FDA said it knows of one patient who died from pancreatic cancer 3 months after having necrotic pancreatic tissue removed with the EndoRotor System.

"This patient did not have a diagnosis of pancreatic cancer prior to treatment, although the patient's outcome is believed to be unrelated to the device or procedure," the FDA said. The EndoRotor System should be used only after patients have undergone other procedures to drain the WOPN. It is also not appropriate for patients with walled-off necrosis who have a documented pseudoaneurysm greater than 1 cm within the cavity or with intervening gastric varices or unavoidable blood vessels within the access tract.

The EndoRotor System was approved under the de novo premarket review pathway for new low- to moderate-risk devices.

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

AGA white paper highlights interventional endoscopic ultrasound

BY WILL PASS
MDedge News

Despite the surgery-sparing potential demonstrated by interventional endoscopic ultrasound (I-EUS), widespread clinical adoption will require more prospective trials, formalized training programs, and greater support from key stakeholders, according to an American Gastroenterological Association white paper.

The publication, which was conceived during a session at the 2019 AGA Tech Summit, addresses the current status and future directions of I-EUS, included EUS-guided access, EUS-guided tumor ablation, and endohepatology.

"We hope this white paper guides those interested in adoption of these technologies into clinical practice and serves as a foundation for future research and innovation in the field," the investigators wrote in Clinical Gastroenterology and Hepatology.

According to senior author Joo Ha Hwang, MD, PhD, of Stanford (Calif.) University, and colleagues, some of the described techniques are not new, but they have yet to be fully realized.

"Some of these techniques initially were reported more than a decade ago," the investigators wrote. "However, with further device development and refinement in technique there is potential for expanding the application of these techniques and new technologies to a broader group of interventional gastroenterologists."

EUS-guided access

"There has been exponential growth in EUS-guided biliary (including gallbladder) access and drainage procedures, as well as entero-enteric anastomotic procedures in recent years," the investigators wrote. "This change can be attributed to the availability of lumen-apposing metal stents (LAMS)."

Previous studies have reported promising success rates with LAMS across a variety of EUS-guided procedures, including biliary drainage (equal to or greater than 85%), gallbladder drainage (90%-98%), and gastrojejunostomy (greater than 90%). Success with other techniques, however, has been mixed.

While LAMS "have gained popularity in the management of pseudocysts and walled-off necrotic collections," data regarding superiority over plastic stents have been conflicting, and LAMS may increase risk of bleeding in necrotic cavities, wrote Dr. Hwang and colleagues.

"Placement of coaxial plastic stents through the lumen of LAMS has been advocated to try to minimize the risk of complications related to LAMS," they added.

EUS-guided pancreatic interventions remain most challenging; Both pancreaticogastrostomy and EUS-guided pancreatic rendezvous are associated with technical failure rates up to 40%, and adverse event rates may be as high as 35%.

"Unlike other EUS-guided drainage and access procedures, there has been limited improvement in technology to make EUS-guided pancreatic access easier or safer."

Dr. Hwang and colleagues concluded this discussion of LAMS by calling for randomized prospective trials. They also noted the expense of LAMS, which may cost $4,000-$6,000.

EUS-guided tumor ablation

"Because of the close proximity of the gastrointestinal tract to organs such as the esophagus, liver, and pancreas, EUS would appear to be an ideal tool to provide imaging and potentially ablation of benign and malignant lesions in these locations," wrote Dr. Hwang and colleagues.

But several challenges may stand in the way, including insufficient endoscope length and working channel caliber, "the tortuosity of the gastrointestinal lumen" and its location relative to some parts of the liver and pancreas, prohibitive tumor characteristics, and cost. In addition, concerns remain for collateral damage to surrounding organs.

"Further studies evaluating the safety and treatment response to ablation of solid neoplasms is required," the investigators wrote.

EUS-guided liver applications

According to Dr. Hwang and colleagues, a growing body of evidence supports EUS-guided liver biopsy, including a high rate of histologic diagnoses (93.9%), Doppler-based detection of blood flow within the needle track prior to needle removal, ability to perform several needle actuations through a single puncture in the liver capsule, rapid patient recovery, ability to sample both liver lobes, potential for simultaneous endoscopy, and lower overall cost (accounting for complications, recovery time, and nondiagnostic yield). And biopsies may be the first of many EUS-guided liver procedures to come, the investigators suggested.

"[EUS-guided liver biopsy] likely will be followed by EUS-guided portal pressure gradient measurement and EUS-guided shear wave elastography," the investigators wrote. "There now is potential for a one-stop-shop diagnosis and staging of liver disease."

Still, work is needed to facilitate greater clinical adoption of interventional EUS.

"[W]idespread implementation of interventional EUS is likely to require support from gastrointestinal societies and buy-in from other key stakeholders including payors," wrote Dr. Hwang and colleagues.

The white paper resulted from a session focused on interventional EUS at the 2019 AGA Tech Summit, organized by the AGA Center for GI Innovation and Technology. The investigators disclosed additional relationships with Boston Scientific, Vyaire Medical, Cook Medical, and others.

ginews@gastro.org

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