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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

University of Virginia Health System

Dr. Patrick G. Northup recommended that multiple risk-stratification systems be used to determine operative risk in patients with cirrhosis.

AGA CPU: Surgical risk and periop management in cirrhosis

BY AMY KARON
MDedge News

Patients with cirrhosis should be risk stratified and counseled accordingly before all but the most urgent surgeries, cautions a clinical practice update from the American Gastroenterological Association.

These risks, which include mortality and reflect "the profound effects of hepatic synthetic dysfunction and portal hypertension," require presurgical evaluation based on CTP score (Child-Pugh class), Model for End-Stage Liver Disease (MELD) score, Mayo Postoperative Mortality Risk Score, or another proven risk-stratification system, writes Patrick G. Northup, MD, of the University of Virginia, Charlottesville, together with his associates. "There is no single definitive risk-stratification system to determine operative risk in all patients with cirrhosis, and we recommend using multiple methods," they elaborated in Clinical Gastroenterology and Hepatology.

The prevalence of cirrhosis is rising, affected patients are living longer, and liver disease is more

See **Cirrhosis** · *page 19*

Positive FIT test should prompt new colonoscopy

BY JIM KLING
MDedge News

Patients who test positive on a fecal immunochemical test (FIT), even after a recent colonoscopy, should be offered a repeat colonoscopy. That is the conclusion following a review of 2,228 subjects who were FIT positive, which revealed a greater risk of colorectal cancer (CRC) and advanced colorectal neoplasia (ACRN) the longer the gap since the last colonoscopy. The findings support the recommendations of the U.S. Multi-Society Task Force on CRC Screening to offer repeat colonoscopies to FIT-positive patients, even if they recently underwent a colonoscopy.

That recommendation was based on low-quality supporting evidence, and there is currently little agreement about whether annual FIT should be performed along with colonoscopy.

The researchers set out to detect the frequency of CRC and ACRN among patients with a positive FIT test. They analyzed data from the National Cancer Screening Program in Korea, which offers an annual FIT for adults aged 50 years and older as an initial screening, followed by a colonoscopy in case of a positive result.

The researchers analyzed data from 52,376 individuals who underwent FIT at a single center in Korea during January 2013–July 2017. They

See **Positive FIT** · *page 27*

INSIDE

Perceptions of liver transplantation for ALD are evolving

BY CALEB RANS
MDedge News

In recent years, the proportion of patients undergoing liver transplantation for alcohol-associated liver disease (ALD) has doubled, suggesting a major shift in attitudes related to transplant indication, according to an analysis of registry data.

"The findings suggest that early liver transplant for alcoholic hepatitis may be leading to broader acceptance of ALD for liver transplant," Brian P. Lee, MD, of the University of

See **ALD Transplant** · *page 26*

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LETTER FROM THE EDITOR: The Poison Squad


DR. ALLEN

This month I am reading *The Poison Squad*, by Deborah Blum. It's a fascinating book about Harvey Wiley, the first commissioner of the FDA and head chemist for 29 years (until 1912). He spearheaded passage of the Pure Food and Drug Act of 1906, the first legislation to regulate what could be put into our food and drink. Before (and even after) passage, hundreds of deaths, mostly children, were linked to toxic additives or adulteration of food. Formaldehyde, for example, was routinely added to milk as a preservative and was linked to dozens of children's deaths. This single, dedicated scientist fought governmental corruption and big business to protect the public. The book describes dark money corrupting senators, fake news, suppression of FDA scientific studies that ran counter to administration goals, solicitation of "scientists" who would publicly denounce test results, advocates of states' rights who fought federal overreach, those that predicted regulation would "ruin American business," and other themes that parallel what we encounter in current news. There are even examples of policy by Executive Order (related to purity of whiskey of all things). One could easily be reading about tobacco, climate change, or vaccines and encounter the same themes. "Those who fail to learn from history are doomed to repeat it" (Santayana 1905 and Churchill 1948).

We are covering a number of important articles this issue. Our cover stories concern surgery in patients with cirrhosis, postcolonoscopy FIT testing, and liver transplant in patients with alcoholic liver disease. Another important story reminds us to help our IBD patients with reproductive counseling.

Just a few months to go before Digestive Disease Week® (DDW) in San Diego. Registration is open and hotels are filling; visit www.DDW/registration for information. This year's scientific lineup is stellar.

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

DDSEPeight Quick Quiz

Q1. A 63-year-old woman undergoes a right upper quadrant ultrasound for intermittent epigastric pain. A 5-mm fixed hyperechoic protrusion in the gallbladder is identified, but there are no gallstones or wall thickening. Upper endoscopy shows moderate gastritis. Biopsies reveal active *H. pylori* gastritis. She is treated with triple therapy and reports complete resolution of her symptoms.

What is the best next step in management?
A. Refer for cholecystectomy
B. Gallbladder ultrasound in 6-12 months
C. Start ursodiol therapy
D. Reassurance and no further therapy
E. Continue proton pump inhibitor therapy

Q2. A 66-year-old woman presents for an evaluation of a 3-year history of constipation. She reports some mild abdominal pain, which is related to constipation. She denies GI bleeding and any relevant family history of colorectal neoplasia or IBD. A previous trial of fiber and polyethylene glycol was unsuccessful. Physical examination is normal, including the rectal examination. Evaluation including routine blood work and thyroid evaluation is normal. Her last colonoscopy was 1 year ago and was normal. She undergoes anorectal manometry, balloon expulsion testing, and defecography, which do not reveal any significant abnormalities. Sitz marker test reveals 14 markers remaining in the colon on day 5. She is started on intestinal secretagogue therapy with no significant improvement in symptoms.

What is the next best step in the evaluation of this patient?
A. Gastric emptying scan
B. Repeat anorectal manometry
C. Repeat balloon expulsion testing
D. Trial of biofeedback therapy
E. Colon transit testing on medications

The answers are on page 13.

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FROM THE AGA JOURNALS

Meta-analysis generally supports LI-RADS classification accuracy

BY AMY KARON
MDedge News

Higher (more severe) Liver Imaging Reporting and Data System (LI-RADS) categories contained increasing proportions of hepatocellular carcinomas and overall malignancies, supporting the general reliability of the system, according to a systematic review and meta-analysis of 17 retrospective studies.

But 13% of LR-2 ("probably benign") observations were actually hepatocellular carcinomas, as were 38% of LR-3 ("intermediate probability of malignancy") observations, reported Christian B. van der Pol, MD, of McMaster University, Hamilton, Ont., and Christopher S. Lim, BBS, of Harvard Medical School, Boston, and their associates. Thus, clinicians should consider biopsy of many LR-3s, and LR-2s might need "more active management" than the currently recommended "return to surveillance," including consideration for biopsy of solid LR-2 nodules measuring 1 cm or more, they wrote in Gastroenterology.

Histopathology confirmed that 93% of CT and MRI observations designated as LR-M ("definite or probable malignancy") were indeed malignancies and that 36% were hepatocellular carcinomas,

The LI-RADS system, like its counterparts in breast and prostate imaging (BI-RADS and PI-RADS), classifies CT and MRI findings based on level of suspicion for malignancy. These categories include LR-M, LR-3, LR-2, LR-1 ("definitely benign"), LR-TIV ("definitely tumor in vein"), and LR-4 and LR-5 ("probably" and "definitely" hepatocellular carcinoma). However, CT and MRI interpretation is only as useful as it is accurate. To calculate actual percentages of hepatocellular carcinomas and overall malignancies within each LI-RADS category, the investigators analyzed aggregate data from studies found by searching MEDLINE, Embase, Cochrane CENTRAL, and Scopus during 2014-2018.

These 17 studies included 2,760 patients and 3,556 imaging observations. Pathology was the reference standard for LR-M, but for other LI-RADS categories, the researchers accepted strong clinical indicators of hepatocellular carcinoma, such as a 50% increase in lesion size within 6 months, or posttreatment recurrence of a previously confirmed malignancy. They classified observations as negative if they stayed stable in size for at least 12 months, spontaneously diminished in size, or disappeared without treatment.

In all, 94% and 97% of LR-5 observations were (respectively) hepatocellular carcinomas and other malignancies, as were 79% and 92% of LR-TIVs, 36% and 93% of LR-Ms, 74% and 80% of LR-4s, 38% and 40% of LR-3s, and 13% and 14% of LR-2s. No LR-1s were confirmed as malignant.

"Our data suggest biopsy of LI-RADS 3 observations should be considered in many patients, as a risk of 38% of HCC would usually provoke biopsy of a lesion elsewhere in the body," the researchers wrote. They suggested consideration for biopsy of certain LR-2 lesions, but added that many "are small, perfusional alterations caused by arterioportal shunts, which are often not reported" and would be difficult or impossible to biopsy.

The study did not cover the most recent (2018) LI-RADS system, which featured several changes to simplify and better align it with American Association for the Study of Liver Diseases criteria, the researchers noted. They called for prospective studies to help confirm the accuracy of the LI-RADS system, particularly with regard to intermediate categories, such as LR-2.

The researchers disclosed no funding sources. Dr. van der Pol, Dr. Lim, and three other investigators reported having no conflicts of interest. Five researchers reported that they are members of the LI-RADS Steering Committee and four disclosed ties to pharmaceutical companies.

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SOURCE: van der Pol CB et al. Gastroenterology. 2018 Nov 13. doi: 10.1053/j.gastro.2018.11.020.

Maltodextrin may increase colitis risk

BY WILL PASS
MDedge News

The food additive maltodextrin may increase risk of inflammatory bowel disease, according to a recent study.

Compared with control subjects, mice given drinking water that contained 5% maltodextrin were significantly more likely to develop colitis and lose weight when challenged with dextran sodium sulfate (DSS), reported lead author Federica Laudisi, PhD, of the department of systems medicine at the University of Rome Tor Vergata in Rome, and her colleagues.

Further experiments with murine intestinal crypts and a human cell line echoed these results and offered mechanistic insight. Treatment with maltodextrin stressed the endoplasmic reticulum of goblet cells, predisposing the intestinal epithelium to mucus depletion and inflammation. With these results,

Continued on following page

Maltodextrin is a polysaccharide derived from starch hydrolysis and broadly used as a thickener and filler in processed food. While it is regarded as inert and considered "generally regarded as safe" by the U.S. Food and Drug Administration, multiple recent studies have demonstrated detrimental roles played by maltodextrin in the intestinal environment, suggesting that this broadly used food additive may play a role in chronic inflammatory diseases.

This study by Laudisi et al. added a new line to this list of evidence. Using two different models of colitis, the authors found that consumption of maltodextrin exacerbated intestinal inflammation. Mechanistically, such detrimental effects of maltodextrin were linked to activation of endoplasmic reticulum stress and subsequent alterations of the protective mucus layer.

Importantly, in addition to the use of a murine model of colitis, Laudisi and colleagues also investigated the impact that maltodextrin may have on a "normal" host; i.e., without genetic susceptibility nor induced colitis. While maltodextrin did not induce visible levels of intestinal inflammation, it led to the development of low-grade intestinal inflammation, characterized by subtle but nonetheless consistent elevation in intestinal inflammatory markers, ultimately leading to metabolic abnormalities.

DR. CHASSAING

Altogether, these recent results, together with previous reports, suggest that consumption of the food additive maltodextrin may be a risk factor for the IBD-prone population, as well as a factor promoting chronic low-grade intestinal inflammation leading to metabolic abnormalities in the general population. These findings further support the concept that FDA testing of food additives should be performed in disease-prone and resistant host models, designed to detect chronic and low-grade inflammation, as well as consider impacts on the gut microbiota.

Benoit Chassaing, PhD, is an assistant professor in the Neuroscience Institute and Institute for Biomedical Sciences, Georgia State University, Atlanta. He has no conflicts. These remarks include excerpts from an editorial accompanying Dr. Laudisi's article (CMGH. 2019 Jan 18. doi.org/10.1016/j.jcmgh.2018.09.014).

FROM THE AGA JOURNALS

NASH: Fastest-growing cause of liver cancer in transplant candidates

BY AMY KARON
MDedge News

Nonalcoholic steatohepatitis may soon supplant chronic hepatitis C as the leading cause of hepatocellular carcinoma (HCC) among patients awaiting liver transplantation, according to the findings of a national longitudinal registry study.

The proportion of affected patients with nonalcoholic steatohepatitis (NASH) rose nearly 700% between 2002 and 2017 (*P* less than .0001), making NASH the only etiology to significantly rise in prevalence, reported Zobair Younossi, MD, MPH, of Inova Health System in Falls Church, Va., and his associates. Chronic hepatitis C remained the most common cause of liver cancer during the study period, but its prevalence fell by more than 10% in the last 3 years (2014-2017). These trends reflect the advent of "new, highly effective antiviral regimens" for hepatitis C, the global epidemic of obesity, and the urgent need for treatments for NASH, they wrote in Clinical Gastroenterology and Hepatology.

Historically, HCC is usually caused by chronic hepatitis C or B infection, but the global rise of obesity and type 2 diabetes mellitus has led to epidemic levels of NASH, a progressive form of nonalcoholic fatty liver disease that lacks useful predictive noninvasive biomarkers or treatments. This phenomenon, coupled with the advent of new curative treatments for viral hepatitis, is making NASH a leading driver of both fibrosis and liver transplantation in the United States. To compare trends in liver cancer etiologies among transplant candidates, Dr. Younossi and his associates analyzed data on 158,347 adults who were wait-listed between 2002 and 2017 and captured by the national Scientific Registry of Transplant Recipients.

A total of 26,121 (16.5%) patients awaiting liver transplant had HCC. This proportion nearly quadrupled over the study period, from 6% to 23% (*P* less than .0001) and rose significantly (*P* less than .0001) for all liver cancer etiologies (hepatitis C and B, alcoholic liver disease, and NASH). However, the absolute rise in prevalence was far greater for NASH (1,050%) than for chronic hepatitis C (more than 500%) or any other etiology.

Furthermore, while most (65%) liver cancers involved chronic hepatitis C, the proportion of cases involving NASH rose from 2% in 2002 to 18% in 2017 (*P* less than .0001). By 2017, NASH topped alcoholic liver disease, comorbid hepatitis C with alcoholic liver disease, and chronic hepatitis B as an etiology of HCC among patients listed for transplant. Conversely, by 2017, less than 50% of liver cancers were caused by hepatitis C – a more than 10% drop from 2014. Over the study period, NASH was the only etiology whose prevalence significantly increased among transplant-listed patients with HCC.

In this study, etiology of liver cancer did not seem to affect the likelihood of either death or transplantation. However, serious cardiovascular disease or late-stage cancer diagnosis might exclude many NASH

Continued on following page

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maltodextrin joins polysorbate 80 and carboxymethylcellulose on a growing list of food additives in the Western diet with proinflammatory potential.

"Although the U.S. Food and Drug Administration recognizes these dietary elements as safe," the investigators wrote in Cellular and Molecular Gastroenterology and Hepatology, "their use has been linked to the development of intestinal pathologies in both animals and human beings.

"It also has been shown that the polysaccharide maltodextrin, which is commonly used as a filler and thickener during food processing, can alter microbial phenotype and host antibacterial defenses. Maltodextrin expands the *Escherichia coli* population in the ileum and induces necrotizing enterocolitis in preterm piglets (Am J Physiol Gastrointest Liver Physiol. 2009 Dec;297:G1115-25)."

The present study began by administering three compounds dissolved in drinking water to wild-type Balb/c mice for 45 days: 5% maltodextrin, 0.5% propylene glycol, or 5 g/L animal gelatin. Control mice drank plain water. None of the treatments triggered clinical or histologic signs of colitis, and stool levels of lipocalin-2 (Lcn-2), a biomarker of intestinal inflammation, remained comparable with that of control mice. However, outcomes changed when mice were challenged with DSS (1.75% in drinking water) on days 35-45 or injected subcutaneously with indomethacin (5 mg/kg) on day 35 and sacrificed 24 hours later. When challenged with DSS, mice in the maltodextrin group developed severe colitis and lost 10%-15% of body weight, compared with minimal colitis and negligible weight loss in the other groups. In addition, compared with other mice, maltodextrin-fed mice had increased colon tissue expression of Lcn-2 and inflammatory cytokine interleukin (IL)-1beta. These initial findings suggested that dietary maltodextrin could increase susceptibility to clinical colitis.

To determine the pathophysiology of this phenomenon, the investigators performed microarray analysis of colonic samples. Multiple genes associated with carbohydrate and lipid metabolism were upregulated in maltodextrin-fed mice, including genes that controlled the unfolded protein response (UPR), a process in which unfolded proteins accumulate in the endoplasmic reticulum (ER) during ER stress. The most prominently expressed among the UPR-related genes was Ern-2, which regulates inositol-requiring enzyme 1beta, found exclusively in the ER of goblet cells in the small intestine and colon. When maltodextrin causes ER stress in goblet cells, it leads to misfolding of mucin glycoprotein Mucin-2 (Muc-2), a major component of gut mucus, causing gut mucus levels to drop. A diminished mucus barrier exposes the intestine to infection and damage, as demonstrated by higher rates of pathogenic bacteria in Muc-2–deficient mice than in control mice, and more severe intestinal damage than in controls when Muc-2 mice are deliberately infected with pathogens.

The investigators found that humans likely have similar responses to dietary maltodextrin. Treating the mucus-secreting HT29-methotrexate treated (HT29-MTX) cell line with 5% maltodextrin resulted in upregulation of Ern-2, which is the same mechanism observed in mice. Additional testing showed that this process was mediated by p38 mitogen-activated protein kinase, and pharmacologic inhibition or knockdown of p38 suppressed RNA expression of Ern-2. The investigators found that p38 was similarly involved in maltodextrin-fed mice.

To show that maltodextrin enhances susceptibility to inflammation via ER stress, the investigators used tauroursodeoxycholic acid (TUDCA) to inhibit ER stress. Indeed, inhibition led to reduced Ern-2 expression in HT29-MTX cells and in mice treated with maltodextrin. Giving TUDCA to maltodextrin-fed mice resulted in less weight loss, improved histology, and lower expression of Lcn-2 and IL-1beta.

The study concluded with three final experiments: The first showed that maltodextrin did not alter mucosa-associated microbiota; the second showed that mice fed 5% maltodextrin long term (for 10 weeks) had low-grade intestinal inflammation on histology, albeit without clinical colitis or weight loss; and the third showed that mice consuming maltodextrin long term had higher 15-hour fasting blood glycemic levels than control mice, supporting recent research suggesting that food additives can disrupt metabolism in a nonsusceptible host.

"In conclusion," the investigators wrote, "this study shows that a maltodextrin-enriched diet reduces the intestinal content of Muc-2, thus making the host more sensitive to colitogenic stimuli. These data, together with the demonstration that maltodextrin can promote epithelial intestinal adhesion of pathogenic bacteria, supports the hypothesis that Western diets rich in maltodextrin can contribute to gut disease susceptibility."

The study was funded by the Italian Ministry of Education, Universities, and Research. The authors reported no conflicts of interest.

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SOURCE: Laudisi F et al. CMGH. 2019 Jan 18. doi: 10.1016/j.jcmgh.2018.09.002.

FROM THE AGA JOURNALS

Long-term budesonide oral suspension well tolerated in EoE

BY AMY KARON
MDedge News

Treatment with budesonide oral suspension (BOS) was generally well tolerated and maintained a histologic response in some patients with eosinophilic esophagitis (EoE), according to the results of the 24-week, open-label extension phase of a multicenter, randomized, placebo-controlled, industry-sponsored trial.

Rates of histologic response (up to 6 eosinophils per high-power field) were "modest" – 23% among patients who stayed on BOS throughout the study and 48.5% among patients who initiated BOS after 12 weeks on placebo, reported Evan S. Dellon, MD, MPH, AGAF, of the University of North Carolina in Chapel Hill and his associates. However, these rates "need to be viewed in the context of a highly symptomatic and histologically severe population with eosinophilic esophagitis," they contended. A total of 11% of budesonide initiators developed esophageal candidiasis, they reported in Clinical Gastroenterology and Hepatology.

Budesonide oral suspension is a mucoadherent formulation of topical corticosteroid that has recently been developed to treat EoE. Previously, during the randomized, double-blind component of this phase 2 trial, 93 patients aged 11-40 years with active EoE and dysphagia received either BOS (2 mg) or placebo twice daily (Gastroenterology. 2017 Mar;157[4]:776-86). After 12 weeks, rates of histologic response were 39% for BOS versus 3% for placebo, and BOS significantly improved patients' mean peak eosinophil count and scores on the Dysphagia Symptom Questionnaire, compared with baseline and compared with the response in the placebo group. During the open-label extension phase, 45 BOS continuers and 37 BOS initiators received 2 mg once daily for 12 weeks and then had the option to increase the BOS dose to 1.5-2.0 mg twice daily.

The rate of drug-related adverse events was 19% among BOS initiators and 4% among BOS continuers. One patient in each group developed oral candidiasis, while four BOS initiators (11%) developed esophageal candidiasis. Three BOS continuers had subnormal morning cortisol levels; while these were subclinical cases, they merit attention since long-term corticosteroids for EoE have been linked with possible hypothalamic–pituitary–adrenal axis suppression, the researchers noted.

In addition, while BOS initiators tended to maintain their endoscopic response, only 42% of those with an initial histologic response maintained a histologic response after 36 weeks of treatment or when leaving the study. Post hoc analyses confirmed that prolonged BOS treatment does not increase the chances of histologic or endoscopic response. Prior studies have suggested that EoE can become steroid refractory over time and that certain molecular and histologic markers might predict resistance, the investigators noted.

Meritage Pharma (now part of Shire) was involved in the study design and conduct, data collection and management, and manuscript review. Dr. Dellon disclosed research funding from Meritage and Shire and a consulting relationship with Shire, along with ties to several other pharmaceutical companies. All six coinvestigators also disclosed ties to Meritage, Shire, or both, and two are Shire employees and stockholders.

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SOURCE: Dellon ES et al. Clin Gastroenterol Hepatol. 2018 Jun 11. doi: 10.1016/j.cgh.2018.05.051.

Guidelines regarding the management of eosinophilic esophagitis (EoE) with topical steroids are still unclear with regard to dosing and duration. Here, Dellon et al. present evidence that long-term budesonide oral suspension (BOS) therapy is safe and efficacious. Both the BOS and placebo cohorts of the initial, 12-week trial demonstrated clinical improvement on BOS over this 24-week period, with few adverse events. Maintenance of histologic response was seen in only 42% of initial BOS responders, suggesting steroid tolerance or resistance may develop. Another important observation was that peak eosinophil count increased with decreased steroid dosing.

DR. CHOKSHI

Controversy remains regarding appropriate endpoints for therapy and the role of steroid de-escalation. Histologic improvement is generally seen as important, but whether minor variations affect long-term outcomes is unclear. In addition, finding the right balance between consistent improvement of the clinicopathologic parameters of EoE and avoidance of side effects remains a challenge. Serious adverse events were minimal in this study, though, and even potential HPA axis effects were subclinical.

Finally, these data support the notion that initial nonresponders are unlikely to gain response with continued therapy and may be better served with early transition to alternatives. Further research is needed to clarify which patients may be predisposed to nonresponse or loss of response.

Reena V. Chokshi, MD, is assistant professor of medicine in the department of gastroenterology at Baylor College of Medicine, Houston. She has no conflicts of interest.

Continued from previous page

patients from transplantation, the researchers wrote. "Thus, the population reported here actually may underestimate the true proportion of [HCC] cases related to nonalcoholic fatty liver disease and NASH in the United States. Because NASH is on a trajectory to become the most common cause of HCC in the United States, effective prevention strategies and treatment options are urgently needed for this currently underserved patient population."

Minneapolis Medical Research Foundation is the contractor for the registry and supplied the data. Dr. Younossi reported ties to Bristol-Myers Squibb, Gilead Sciences, AbbVie, Intercept Pharmaceuticals, and GlaxoSmithKline.

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SOURCE: Younossi Z et al. Clin Gastroenterol Hepatol. 2018 Jun 14. doi: 10.1016/j.cgh.2018.05.057.

Acceptance and commitment therapy reduced IBD stress, depression

BY AMY KARON
MDedge News

Eight weeks of a mindfulness intervention known as acceptance and commitment therapy (ACT) significantly improved stress and depression among patients with inflammatory bowel disease, and these improvements persisted for at least 12 weeks after therapy ended, according to the results of a randomized, controlled trial.

In the intention-to-treat analysis, stress symptoms, as measured by the Depression Anxiety and Stress Scales (DASS-21), improved by 39% at week 8 and by 45% at week 20, reported Brona Wynne, PhD, of University College Dublin together with her associates. These improvements were highly significant compared with baseline and treatment as usual ($P = .001$ for both comparisons). "Post hoc analyses indicated that baseline stress levels were similar in control and treatment groups," the researchers wrote in Gastroenterology. "The results of

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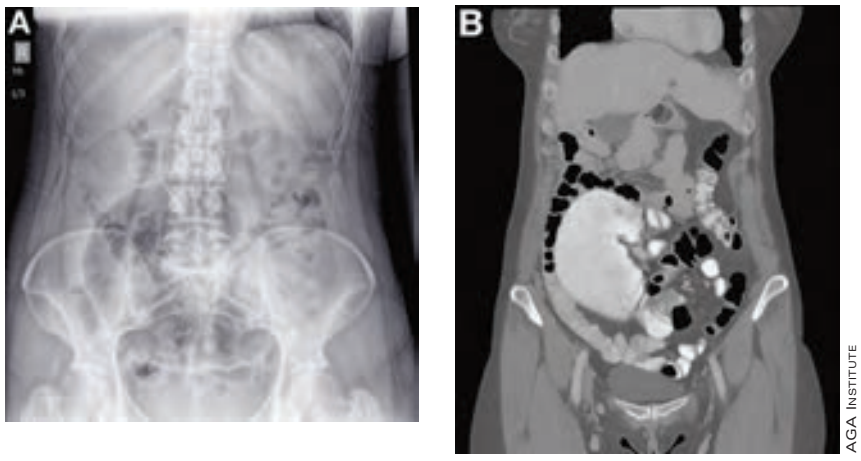
CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Derek J. Erstad, MD, Leandra S. Krowsoski, MD, and Haytham M.A. Kaafarani, MD, MPH. Published previously in Gastroenterology (2017;152[3]:486-7).

A 56-year-old woman with no prior medical history presented to the emergency department with abdominal pain 12 hours after a screening colonoscopy. The procedure was uneventful with no suspicious masses or lesions detected and no biopsies performed. The patient was discharged to home after recovery from anesthesia, where she slept for several hours. She was awoken with right-sided abdominal pain, nausea, vomiting, and abdominal distension. Her nausea, distension, and abdominal pain worsened as the evening progressed, prompting the patient to seek evaluation at the emergency department.

On examination, she was afebrile with normal vital signs. Her abdomen was mildly distended with right-sided tenderness but no peritoneal signs. Her white blood cell count was 8.5 × 10^9/L and all of her other laboratory values were normal. An upright abdominal radiograph showed no evidence of free air under the diaphragm, although a markedly dilated colon on the right side was noted (Figure A). An abdominal computed tomography scan was obtained (Figure B).



AGA Institute

See the diagnosis on page 37.

Continued from page 8

the per protocol analysis were comparable, with a 43% and 49% reduction in stress in the treatment group from baseline to 8 and 20 weeks."

Multiple studies have documented high levels of stress and psychological dysfunction among patients with Crohn's disease and ulcerative colitis. Studies of various mindfulness therapy, relaxation, stress management, cognitive-behavioral therapy, and hypnotherapy interventions often failed to collect key clinical data or were underpowered, uncontrolled, and unrandomized. Acceptance and commitment therapy uses mindfulness to identify adverse thoughts and experiences, accept these as part of life, and recommit to "move towards values that have been identified and adopted by the individual," the investigators wrote. "This can be defined as the ability to contact the present moment more fully as a conscious human being and to change, or persist in, behavior when doing so serves valued ends."

Acceptance and commitment therapy uses mindfulness to identify adverse thoughts and experiences, accept these as part of life, and recommit to "move towards values that have been identified and adopted by the individual."

Their single-center study, which they said was the first to evaluate ACT in IBD patients, included 79 individuals with stable or mildly active Crohn's disease (38 patients) or ulcerative colitis (41 patients) who were randomly assigned to ACT (37 patients) or control treatment as usual (42 patients). The two comparison groups were demographically and clinically similar. The ACT program involved eight 90-minute, weekly sessions of groups of 14-16 individuals, led by a single psychologist who tailored the course material toward IBD with a focus on lowering stress. An independent psychologist observed each session to assess adherence to protocol.

Not only did ACT meet the primary study endpoint, it also produced a 25% decrease in perceived stress (on a 1-10 scale) by week 8 and a 27% decrease in perceived stress by week 20 (*P* less than .001 versus treatment as usual). Depression scores in the ACT group also fell by 47% by week 8 and by 45% at week 20 (*P* = .01 versus treatment as usual). Anxiety levels decreased by 29% at week 8 and by 31% at week 20, but these improvements did not significantly differ from those in the control group (*P* = .39).

Interestingly, ACT did not significantly improve symptom burden, activities of daily living, disease-related worry, general well-being, C-reactive protein (CRP) levels, fecal calprotectin levels, or scores on the version used of the Clinical Assessment of Depression (CAD) or the short Mayo assessment. Hair cortisol levels showed an association with baseline stress and anxiety, but not with treatment response.

Care programs for IBD increasingly emphasize mental health services despite a lack of robust trials to support these interventions, the investigators noted. Thus, their findings highlight "the need for researchers and clinicians to further develop and optimize the content and delivery of psychological programs for IBD patients."

Tillotts Pharma and Boston Scientific provided partial funding, but had no other role in the study. The researchers reported having no relevant conflicts of interest.

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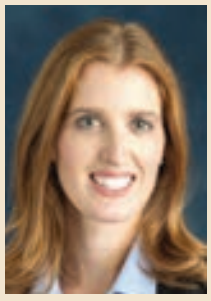
SOURCE: Wynne B et al. Gastroenterology. 2018 Nov 16. doi: 10.1053/j.gastro.2018.11.030.

Factors that affect stress level and mood symptoms are vast when it comes to living with inflammatory bowel disease (IBD). Comorbid mood symptoms are common in patients with IBD, and psychological interventions are increasingly recommended as part of holistic, multidisciplinary treatment planning. Additionally, patients are open to GI-focused psychology treatments given the recognition that the complexities of living with IBD strongly influence emotional factors.



DR. RIEHL

DR. KINNUCAN

While access to trained mental health professionals who can offer these types of treatment options is a current barrier, randomized controlled trials such as this one are much needed in the area of psychogastroenterology. An advantage of this protocolized acceptance and commitment therapy (ACT) intervention is the reproducibility, which leads to easier dissemination and increasing availability of these interventions for IBD patients.

What must be acknowledged is the importance of long-term adherence to skills learned during the 8 weeks of ACT. Stress and mood symptoms tend to be more prevalent during times of flare. Given the relapsing and remitting nature of IBD, it must be conveyed that patients will need to continue the practice of this mindfulness-based intervention in the long term. Future studies are encouraged to look at longitudinal data assessing the manner in which these patients used their skill set during periods of flare or disease-related stress.

Megan E. Riehl, PsyD, and Jami A. Kinnucan, MD, are both assistant professors of medicine in the division of gastroenterology and hepatology at the University of Michigan, Ann Arbor. Dr. Riehl disclosed no conflicts. Dr. Kinnucan is a consultant for AbbVie, Janssen, and Pfizer.

AGA Legacy Society members bolster research

The AGA Research Foundation has provided more than $50 million in research funding since its inception in 1984. Gifts from AGA members have helped fuel discoveries in the GI field. The most generous of AGA members are our Legacy Society members.

Members of the AGA Legacy Society provide tax-deductible gifts to the AGA Research Foundation of $5,000 or more per year for 5 years ($25,000 total) or $50,000 or more in a planned gift, such as a bequest. Legacy Society member donations directly support young GI investigators as they establish independent research careers.

"The support of the AGA Research Foundation indicates that our peers share in our enthusiasm for research and gives me and my group added confidence to pursue questions about the pathology of IBD. Our overall plan is to translate this work into key components of larger federally funded grants in the near future," states David L. Boone, PhD, Indiana University School of Medicine, Indianapolis, 2017 AGA Research Foundation Pilot Research Award grant recipient.

Donors who make gifts at the Legacy Society level before Digestive Disease Week® (DDW) will receive an invitation to the annual Benefactors' Dinner, which will be held at the San Diego Wine and Culinary Center this year. Individuals interested in learning more about Legacy Society membership may contact Stacey Hinton Tuneski, Senior Director of Development at stuneski@gastro.org or via phone (301) 222-4005. More information on the AGA Legacy Society including the current roster and acceptance form is available on the foundation's web site at https://www.gastro.org/foundation/our-donors/aga-legacy-society.

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A celebration of research support

Beginning with a memorable gathering at the United States Library of Congress in 2007, the AGA Benefactors' Dinner has welcomed members of the AGA Legacy Society and other AGA dignitaries to special locations nationwide. The San Diego Wine and Culinary Center will be the location of the 2019 AGA Research Foundation Benefactors' Dinner during DDW in San Diego. Located near the convention center, the San Diego Wine and Culinary Center feels worlds away and will allow guests to relax and enjoy time with friends. Members of the AGA Legacy Society will be among the distinguished honorees at the annual event.

Photos courtesy San Diego Wine and Culinary Center

Top AGA Community patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community (https://community.gastro.org/discussions) to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses.

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

1. Ileocolonic Crohn's in VA patient (http://ow.ly/THz130nw90P)
A 77-year-old patient with chronic kidney disease, dementia, and congestive heart failure was seen to evaluate chronic diarrhea. His colonoscopy revealed active inflammation and a stricture at the anastomosis, which prevented the physician from bypassing it with a pediatric colonoscope. The patient's diarrhea improved once he was started on budesonide. The discussion in the AGA Community forum outlined next steps and the best course of treatment for this complicated patient.

2. *H. pylori* in a penicillin allergic patient (http://ow.ly/NDYv30nw95Z)
A patient diagnosed with *H. pylori* during an endoscopy has a history of a severe penicillin allergy and has used clarithromycin in the past year. Antibiotic resistance testing revealed genetic pattern suggesting resistance to clarithromycin, fluoroquinolones, and metronidazole. Recommendations from GIs included combination therapy with proton pump inhibitors (PPIs), antacids, and antibiotics.

3. Reintroduction of azathioprine after moderate leukopenia (http://ow.ly/H09330nw990)
This 48-year-old patient has a history of ulcerative colitis pancolitis and developed antibodies to Humira monotherapy. Her GI is adjusting her azathioprine dose and repeating lab work to recover her white blood cell counts and is soliciting advice from the practice community on using methotrexate for combination therapy.

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

DDSEP eight

Answers

Q1: Correct Answer: B

Rationale
The ultrasound finding of a hyperechoic protrusion is suggestive of a gallbladder polyp. These polyps can have malignant potential and should be monitored or referred for surgical management depending on their size. There is consensus that polyps larger than 10 mm should be referred for cholecystectomy. There is some debate about whether polyps greater than 6 mm should also be referred for surgery or whether they can be surveyed. For gallbladder polyps less than 6 mm, surveillance with ultrasound in 6-12 months is the recommended surveillance strategy.

Reference
1. Gallahan WC, Conway JD. Diagnosis and management of gallbladder polyps. Gastroenterol Clin North Am. 2010;39(2):359-67.

Q2: Correct Answer: E

Rationale
This patient has slow-transit constipation without concomitant defecatory disorder, which is unresponsive to newer pharmacologic agents. According to the recently published AGA medical position paper on constipation, the next step in this patient's evaluation should be to repeat colon transit testing on medications. If abnormal, the next step would be evaluation for possible upper GI motility disorder including a gastric-emptying scan. There is no role for repeat anorectal manometry, balloon expulsion testing, or a trial of biofeedback therapy in this patient.

References
1. Wald A, Bharucha AE, Cosman BC, Whitehead WE. ACG clinical guideline: management of benign anorectal disorders. Am J Gastroenterol. 2014;109(8):1141-57.
2. Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. Gastroenterology. 2013;144:218.

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GI leaders recognized by AGA's prestigious recognition awards

AGA has announced the 2019 recipients of the annual recognition awards, given in honor of outstanding contributions and achievements in gastroenterology.

"AGA members honor their colleagues and peers for outstanding contributions to the field of gastroenterology by nominating them for the AGA Recognition Awards," said David A. Lieberman, MD, AGAF, president of the AGA Institute. "We are proud to announce the 2019 AGA Recognition Prize winners, who are just a few of the distinguished and talented members who help make AGA such an accomplished organization. We are honored that such esteemed individuals are representative of AGA."

The AGA Recognition Awards will be presented during Digestive Disease Week® 2019, May 18-21, 2019, in San Diego.

Julius Friedenwald Medal

AGA bequeaths its highest honor, the Julius Friedenwald Medal, to John I. Allen, MD, MBA, AGAF, for his incredible contributions to the field of gastroenterology and AGA over several decades. The Julius Friedenwald Medal, presented annually since 1941, recognizes a physician for lifelong contributions to the field of gastroenterology.

Dr. Allen is internationally renowned for bringing unique and critical knowledge about health care delivery and health care economics to the field of gastroenterology, as well as for his decades of AGA leadership. His experience is unique within the national gastroenterology community, encompassing private practice, nonacademic health systems, and leadership within two academic medical centers. As AGA Institute President, he led the development of AGA's 5-year strategic plan and made AGA a national player at the federal, state, and local levels during a time of massive health care delivery transformation. Dr. Allen is a clinical professor of medicine in the division of gastroenterology and hepatology and chief clinical officer of the University of Michigan Medical Group at the University of Michigan School of Medicine, Ann Arbor.

Distinguished Achievement Award in Basic Science

AGA honors Harry B. Greenberg, MD, with the AGA Distinguished Achievement Award in Basic Science, for his major accomplishments in basic science research, which have significantly advanced the science and practice of gastroenterology. Throughout his career, Dr. Greenberg's incredible contributions over several decades contributed to the development of rotavirus vaccines and increased physicians' understanding of viral pathogenesis, particularly rotavirus, norovirus, and hepatitis. Dr. Greenberg is an associate dean for research at Stanford University School of Medicine, Palo Alto, California.

William Beaumont Prize

AGA honors Timothy C. Wang, MD, AGAF, with the William Beaumont Prize in gastroenterology, which recognizes an individual who has made a unique, outstanding contribution of major importance to the field of gastroenterology. Dr. Wang's extraordinary contribution to the understanding and practice of modern gastroenterology and digestive science are exemplified through his work, which includes defining the mechanisms and cellular origins of Barrett's esophagus and gastroesophageal cancer. Dr. Wang, who has served AGA in numerous positions, including as president of the AGA Institute, is currently chief of the division of digestive and liver diseases at Columbia University Medical Center and as the Dorothy L. and Daniel H. Silberberg Professor of Medicine at Columbia University Vagelos College of Physicians and Surgeons, New York, New York.

Distinguished Educator Award

AGA recognizes and honors Deborah D. Proctor, MD, AGAF, with the Distinguished Educator Award, which recognizes an individual who has made outstanding contributions as an educator in gastroenterology on both local and national levels, over a lifelong career. Dr. Proctor is a national expert in gastroenterology training and education who has taught and inspired generations of future gastroenterologists, nurses and physician assistants. Currently serving as the AGA Institute Education & Training Councillor, Dr. Proctor is a professor of medicine, and the medical director of the inflammatory bowel disease program, at Yale School of Medicine, New Haven, Connecticut.

Distinguished Clinician Awards

The AGA Distinguished Clinician Award recognizes members of the practicing community who, by example, combine the art of medicine with the skills demanded by the scientific body of knowledge in service to their patients.

AGA presents the Distinguished Clinician Award, Private Practice, to Naresh T. Gunaratnam, MD, AGAF. Dr. Gunaratnam has made a huge impact on patient care in his community and improved gastroenterology-oncology care by starting the endoscopic ultrasound & interventional GI program at St. Joseph Mercy Ann Arbor hospital in Ypsilanti, Michigan. Dr. Gunaratnam is a director of research and obesity management at Huron Gastro.

AGA is honored to present the Distinguished Clinician Award, Clinical Academic Practice, to Edward V. Loftus Jr., MD, AGAF. Dr. Loftus is an outstanding role model in practice, an effective researcher and a recognized leader who is devoted to treating patients with ulcerative colitis and Crohn's disease with quality clinical care, including understanding the predictors of treatment response. Dr. Loftus is a practicing gastroenterologist at the Mayo Clinic and a professor of medicine at the Mayo Clinic College of Medicine and Science, Rochester, Minnesota.

Distinguished Mentor Award

AGA bestows the Distinguished Mentor Award, which recognizes an individual who has made a lifelong effort dedicated to the mentoring of trainees in the field of gastroenterology and for achievements as outstanding mentors throughout their careers, to Fred S. Gorelick, MD. Dr. Gorelick has been an inspiration to generations of trainees, many of whom have gone on to successful academic careers as faculty members, section chiefs, program directors, department chairs, and institute directors. Dr. Gorelick is a professor of medicine and cell biology at Yale School of Medicine, and deputy director of the Yale MD-PhD Program, New Haven, Connecticut.

Research Service Award

AGA honors Ann G. Zauber, PhD, with the Research Service Award, which recognizes individuals whose work has significantly advanced gastroenterogical science and research. Dr. Zauber's accomplishments have changed and advanced the practice of gastroenterology. Her work involving colorectal cancer screening and surveillance studies has had far-reaching effects on public policy. She is well-known for her leadership role in the development of colorectal cancer screening guidelines in the U.S., which has significantly reduced mortality and incidence rates. Dr. Zauber is an attending biostatistician in the department of epidemiology & biostatistics at the Memorial Sloan Kettering Cancer Center, New York, New York.

Young Investigator Awards

The AGA Young Investigator Award recognizes two young investigators, one in basic science and one in clinical science, for outstanding research achievements.

AGA honors Sonia S. Kupfer, MD, with the Young Investigator Award in Clinical Science. Dr. Kupfer is nationally and internationally recognized as an expert in colorectal cancer in high-risk populations including individuals with hereditary cancer syndromes and African Americans. During her clinical and translational research to better understand factors that increase the risk of colorectal cancer, Dr. Kupfer identified distinctions in the African-American population compared with the white population. Dr. Kupfer is an associate professor of medicine at the University of Chicago, and director of the Gastrointestinal Cancer Risk and Prevention Clinic.

AGA honors Costas A. Lyssiotis, PhD, with the Young Investigator Award in Basic Science. His research, work ethic, and innovative approaches have made Dr. Lyssiotis a distinguished leader in pancreatic cancer. His work has broad implications for harnessing the power of the immune system to treat the disease and his laboratory is working to develop new drug therapies that target a pancreatic cancer metabolism-specific enzyme. Dr. Lyssiotis is an assistant professor in the department of molecular and integrative physiology in the division of gastroenterology at University of Michigan Medical School, Ann Arbor.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

What's next for the AGA Center for Gut Microbiome Research and Education?

BY GAIL A. HECHT, MD, MS, AGAF

AGA established its Center for Gut Microbiome Research and Education in 2012 as the microbiome was just beginning to explode in the scientific literature. I have been privileged to chair the center's scientific advisory board over the last 3 years. As I enter my final few months in this role, I wanted to look ahead to the issues we've prioritized for 2019 – many of which build on our accomplishments in 2018.

Diet and nutrition

More than ever before, clinicians and patients appreciate that what we eat can have an important impact on our digestive health and our gut microbes. Recognizing the need for a stronger evidence base, the NIH developed a nutrition research strategic plan, which AGA wrote in support of late last year. We will continue providing updates on the latest advances in the new year. In March, AGA will host the eighth annual Gut Microbiota for Health World Summit in Miami, Florida. This continues our long-standing collaboration with the European Society of Neurogastroenterology and Motility and the 2019 edition will focus on the interplay between what we eat and the microbes that live on and in us. Materials from the meeting will be made available through AGA's educational platform, AGA University, later in the year.

Pro-, pre-, and synbiotics

Last fall, the center published its first two scientific statements on several important clinical studies on the gut microbiome. We collaborated with AGA's GI Patient Center to issue patient-friendly resources on probiotics. Probiotics will continue to be a key topic for AGA guidance in 2019. In the spring issue of this newsletter, look for the first of a four-part educational series on prebiotics and digestive health. AGA also continues to develop a technical review and clinical guideline on the role of probiotics in the management of GI disease. A "first look" can be found on AGA's clinical guidelines page under "Upcoming Guidelines."

Inspired by discussions among clinicians within the AGA Community, scientific advisory board member Alexander Khoruts, MD, wrote a primer for clinicians on microbiome-based tests which was published recently.

Microbiome-based diagnostics

As clinicians, we've experienced the growing popularity of direct-to-consumer genetic tests and questions from patients wanting to know what their results mean for existing or potential medical conditions. Inspired by discussions among clinicians within the AGA Community, scientific advisory board member Alexander Khoruts, MD, wrote a primer for clinicians on microbiome-based tests which was published recently; it was also disseminated through this newsletter and MedPage Today's KevinMD.com. This issue will continue to be a challenge for researchers and clinicians as the research moves beyond correlation to causative relationships between our gut microbiome and human health and disease. The center will continue to provide guidance on this issue as the field evolves.

Microbiome-based therapeutics

The FMT National Registry announced the enrollment of its first patient this time last year. As it continues to recruit new sites, the registry's steering committee (under the leadership of AGA members Colleen Kelly, MD, Loren Laine, MD, AGAF, and Gary Wu, MD, AGAF) will begin looking at data to develop an interim publication on lessons learned from the earliest-enrolled patients. FMT, of course, is the just the beginning of a revolution in microbiome-based therapeutics. As new pharmaceuticals targeting the gut microbiome advance in clinical trials, the center will help prepare health care professionals for what this will mean for their patients and their practices.

2019 promises to be another banner year in gut microbiome research. AGA and its Center for Gut Microbiome Research and Education will continue to provide evidence-based information and guidance on one of the most exciting emerging areas of science and medicine.

Dr. Hecht is professor of medicine and microbiology/immunology and chief, gastroenterology and nutrition, Loyola University Medical Center, Maywood, Ill. and chair of the AGA Center for Gut Microbiome Research and Education scientific advisory board.

AGA releases guide to care for women with IBD throughout family planning

AGA launched the IBD Parenthood Project to address misperceptions and fears women with inflammatory bowel disease and their health care providers (HCPs) experience throughout all phases of family planning. This patient-directed initiative, which was created by gastroenterologists, maternal-fetal medicine subspecialists, and patients, is led by AGA with support from the Society for Maternal-Fetal Medicine, the Crohn's & Colitis Foundation, and patient support network, Girls With Guts.

HCPs are encouraged to visit the program's new website, www.IBDParenthoodProject.org, which houses medical facts about IBD and pregnancy, and share it with their patients. The website provides answers to common questions and provides a downloadable patient toolkit that features visual and patient-friendly information. Resources include easy-to-digest lists of key questions to ask a provider as women are thinking of becoming pregnant, a flow diagram outlining the various HCPs potentially involved in a woman's care, a guide to postnatal care and provider locator tools. These tools are a direct response to AGA survey findings that reported women with IBD want more and better information about managing their disease (BabyCenter. 2018. IBD and Preconception, Pregnancy, Early Motherhood).

AGA on MOC: 3 key points

Reforming MOC is a priority for AGA so our comments were extensive. Here are three key points we made.

Recertification shouldn't burden physicians

In an era of epidemic physician burnout threatening access to care from reductions in the physician workforce, we seek a recertification pathway that is not unnecessarily burdensome, while maintaining relevance to the practice of a matured, experienced clinician.

Requirements should be relevant to practice

Requirements need to be relevant to practice and able to be adopted by our physicians with minimal additional investment in an already overburdened practice environment. Physicians have a narrowly defined practice, and assessments and certification should be "tailored to a diplomate's area of practice." However, it is necessary that physicians have knowledge outside of a narrow subspecialty, and thus the specialty societies should help the Boards identify what constitutes the key "core knowledge, judgment and skills" for the specialty. It is AGA's view that this knowledge should be much less detailed than the expectations for initial board certification.

Certification ≠ credential

The issue of continuous certification being misappropriated as an employment credential is not acceptable. AGA calls on the commission to make it unequivocally clear that board certification should not be used in any way as a requirement for hospital credentialing.

AGA CLINICAL PRACTICE UPDATE

Always dangerous

Cirrhosis *from page 1*

advanced and may involve comorbidities that merit consideration of surgery, noted Dr. Northup and his associates. However, cirrhosis increases the risk for serious postoperative complications, including hepatic decompensation, worsening of liver synthetic function, exacerbated portal hypertension, wound dehiscence, pleural effusions, pneumonia, bacterial peritonitis, bleeding, and multiple organ failure. Because clinical trials of surgery in cirrhotic patients are lacking, the experts stress the need for case-by-case management.

There is no definite threshold that precludes all surgeries in cases of cirrhosis, but a Child-Pugh class C (CTP score over 10) or MELD score over 20 greatly increases the risk of postoperative decompensation and death. For these patients, "all but the most urgent and life-saving procedures" should be canceled or postponed until after liver transplantation, the experts wrote. For less severe cirrhosis, it is key to consider the type and anatomic site of the proposed surgery. Hepatobiliary surgeries, other intra-abdominal surgeries, cardiovascular surgeries, and thoracic procedures are most likely to lead to serious complications.

Preoperative care should emphasize control of ascites, variceal bleeding risk, and hepatic encephalopathy. Bleeding and clotting safety thresholds in cirrhosis are unknown, and individualized management, ideally with viscoelastic testing–directed therapy, is warranted instead of protocol transfusions to a target international normalized ratio (INR). Bleeding events are more common in critically ill patients with plasma fibrinogen ratios under 100 mg/dL.

Segmental hepatic resection (usually for malignancy), the most studied procedure in cirrhosis, is generally safe in the absence of clinically significant portal hypertension. For patients who do have portal hypertension, transjugular intrahepatic portosystemic shunt (TIPS) has not clearly been shown to outperform conservative management, although small case series have found that TIPS during deep pelvic or colonic resection decompresses abdominal collaterals.

Because of the risk of poor outcomes, patients with cirrhosis and incompletely controlled ascites should not undergo abdominal hernia repair unless they have an incarceration that is not manually reducible or suspected strangulation. Bariatric surgery is contraindicated in cases of clinically significant portal hypertension but otherwise can be performed at a center with cirrhosis expertise. Sleeve gastrectomy at the same time as liver transplantation is also an option for select patients with obesity.

Elective cholecystectomy should be avoided, and required cases should be performed in experienced centers. "The gallbladder wall may appear thickened on imaging, which may lead to the erroneous diagnosis of acute cholecystitis," the experts noted. Hence, the diagnosis "should be made only in the appropriate clinical setting, usually in the presence of biliary pain."

Hepatic decompensation after surgery can be severe enough to merit liver transplantation. There is no agreed-on MELD score that mandates liver transplant evaluation before elective surgery, but the experts recommend doing so if the MELD score is 15 or greater or if risk of mortality within 3 months after surgery exceeds 15%.

GORODENKOFF/ISTOCK/GETTY IMAGES

Postoperative management of patients with cirrhosis should include aggressive measures to prevent portal hypertension. Monitor renal function closely and avoid volume depletion or overload, the experts advised. Patients should receive only short-acting benzodiazepines and lower opiate doses, administered less often, than in the general population. Avoiding constipation is vital to minimize hepatic encephalopathy, which makes oral rifaximin a better choice than lactulose. Patients should not receive NSAIDs, which can impair renal blood flow. To prevent liver toxicity, they should not be discharged on opiate/acetaminophen combinations, which they might unknowingly take along with another drug that contains acetaminophen.

The experts disclosed no external funding sources and reported having no conflicts of interest.

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SOURCE: Northup PG et al. Clin Gastroenterol Hepatol. 2018 Sep 28. doi: 10.1016/j.cgh.2018.09.043.

Diet low in free sugars shows promise for adolescent NAFLD

BY HEIDI SPLETE
MDedge News

Teenage boys with nonalcoholic fatty liver disease (NAFLD) who followed a diet low in free sugars demonstrated significantly improved hepatic steatosis after 8 weeks, compared with boys on a usual diet.

"Because of growing evidence implicating dietary sugars in NAFLD, well-controlled studies in children with NAFLD are needed to inform clinical practice and public policy," wrote Jeffrey B. Schwimmer, MD, of the University of California, San Diego, La Jolla, and colleagues in JAMA.

The researchers randomized 40 boys aged 11-16 years with active NAFLD to a diet low in free sugars or their usual diet. The intervention diet involved personalized menu planning and provision of meals for the boys' entire households that were designed to restrict free-sugar intake to less than 3% of daily calories. Adherence to the diet was assessed by twice-weekly phone calls.

In the intervention group, hepatic steatosis decreased from an average of 25% at baseline to 17% after 8 weeks, compared with a change from 21% to 20% in the control group. The adjusted mean difference at 8 weeks was −6.23%, which was statistically significant (*P* less than .001).

The average age of the participants was 13 years, 95% were Hispanic. All 40 completed the study, and 18 of the 20 boys in the intervention group reported less than 3% of calories from free sugar during the study period. No adverse events were reported related to study participation.

The results were limited by several factors, including the small sample size and homogeneous population. In addition, neither hepatic steatosis or serum alanine aminotransferase levels decreased enough to enter the normal range, the researchers noted. The findings, though preliminary, support the value of reducing free sugars, including glucose, fructose, and sucrose, to help manage NAFLD in adolescents, and "further research is required to assess long-term and clinical outcomes," they said.

The study was supported by grants from multiple foundations and organizations, including the Nutrition Science Initiative, the University of California, San Diego, the National Institutes of Health, Children's Healthcare of Atlanta and Emory University Pediatric Biostatistics Core, and the Georgia Clinical and Translational Science Alliance. Dr. Schwimmer reported receiving research support from Galmed and Intercept.

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SOURCE: Schwimmer JB et al. JAMA. 2019;321(3):256-65.

Residential HCV program improves veterans' diagnosis and care

BY MARK S. LESNEY
MDedge News

Integrating comprehensive and collaborative hepatitis C virus (HCV) care within a Veterans Affairs residential treatment program can substantially increase diagnosis and treatment of HCV-infected veterans with substance use disorder (SUD), according to the results of an evaluation study for the period from December 2014 to April 2018.

A total of 97.5% (582/597) of patient admissions to the program were screened for HCV infection, and 12.7% (74/582) of the cases were confirmed to be HCV positive. All of the positive cases were sent to an infectious disease (ID) clinic for further evaluation and, if appropriate, to begin HCV pharmacotherapy, according to the report, published in the Journal of Substance Abuse Treatment.

Of the HCV-positive cases, 78.4% (58/74) received pharmacotherapy, with a sustained virologic response rate of 82.8% (48/58), wrote Mary Jane Burton, MD, of the G.V. (Sonny) Montgomery VA Medical Center, Jackson, Miss., and her colleagues.

As part of the program, all veterans admitted to the SUD residential program were offered screening for HCV. Veterans with negative screening results received education about how to remain HCV negative via handouts and veterans who screened positive received brief supportive counseling and were referred to the ID clinic via a consult. Veterans confirmed to have chronic HCV infection receive education and evaluation in the HCV clinic while they attend the residential SUD program. Treatment for HCV is instituted as early as feasible and prescribing is in accordance with VA guidelines (Department of Veterans Affairs, 2018), with the goal of initiating pharmacotherapy treatment for HCV while the veteran is still in the residential program, according to the researchers.

Following discharge from the program, veterans on HCV treatment are scheduled for follow-up every 2 weeks in the HCV treatment clinic for the remainder of their pharmacotherapy, the researchers added.

Patient-level barriers to HCV treatment among the SUD population include reduced health literacy, low health care utilization, comorbid mental health conditions, and poor social support, according to the literature. Because multidisciplinary approaches to HCV treatment that mitigate these barriers have been shown to increase treatment uptake among these patients, the VA program was initiated, the researchers stated. Dr. Burton and her colleagues reported that 18.9% (14/74) of the HCV-positive cases were newly diagnosed and would have likely gone undetected without this program (J Substance Abuse Treatment. 2019;98:9-14).

"We have demonstrated that integrating a comprehensive HCV screening, education, referral, and treatment program within residential SUD treatment is feasible and effective in diagnosing previously unrecognized HCV infections, transitioning veterans into HCV care, and promoting treatment initiation," the researchers concluded.

The Department of Veterans Affairs and the VA Center for Innovation supported the study. Dr. Burton reported research support from Merck Sharpe & Dohme.

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AGA Resource
The AGA GI Patient Center provides hepatitis C education by specialists, for patients at https://www.gastro.org/practice-guidance/gi-patient-center/topic/hepatitis-c-hcv. Want to learn more? Visit AGA University for live and on demand education at agau.gastro.org.

Vary by region

ALD Transplant *from page 1*

California, San Francisco, and his colleagues wrote in JAMA Internal Medicine.

The researchers conducted a prospective cohort study of 9,438 patients with ALD who received a liver transplant from 2002 to 2016. Data were obtained from the United Network for Organ Sharing national database.

Study participants were evaluated for patterns, both nationally and regionally, related to liver transplant for the treatment of ALD. In addition, Dr. Lee and his colleagues completed a sensitivity analysis, which evaluated specific clinical parameters, including patient and graft survival, hepatocellular carcinoma, and hepatitis C viral (HCV) infection.

"Because there is no national policy regarding early liver transplant, we hypothesized that changes may vary regionally as liver transplant programs shifted their attitudes toward increased acceptance of early liver transplant for alcoholic hepatitis and ALD," the researchers wrote.

After analysis, the researchers found that liver transplantation for patients with ALD increased proportionally from 24.2% to 36.7% from 2002 to 2016, respectively. With HCV-infected recipients included, the proportion of liver transplants rose from 15.3% to 30.6% over the same period, representing a twofold increase of transplants received for this indication.

The degree of increase was reported to vary based on geographic region and was linked with differences in patient-specific factors.

"There may be regional disparities in access to liver transplant for ALD; whether this is related to different attitudes toward ALD and requirements for sobriety is unknown," they added.

The researchers acknowledged that a key limitation of the study was the use of registry data. As a result, Dr. Lee and his colleagues reported that all conclusions are not causal, but rather only by association.

The study was supported by the National Institute of Diabetes and Digestive and Kidney Diseases UCSF Liver Center. The authors reported no conflicts of interests.

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SOURCE: Lee BP et al. JAMA Intern Med. 2019 Jan 22. doi: 10.1001/jamainternmed.2018.6536.

PERSPECTIVE

Attitudes are changing, report commentators

One of the most significant findings of the study by Brian P. Lee, MD, and his colleagues is the major shift in attitudes surrounding the eligibility criteria for patients with ALD to undergo liver transplantation.

More than 3 decades ago, a group of surgical experts gathered together to discuss evaluation criteria for candidacy of individuals to undergo liver transplantation. They recommended that patients with ALD be required to restrict alcohol consumption for 6 months prior to being listed eligible for surgery. The group presumed that a period of complete avoidance may induce some degree of disease remission, circumventing the need for transplant altogether.

However, these suggestions were given without the use of evidence, formed largely on the basis of opinion, and recent data dispute these recommendations. On the contrary, relapse rates for alcohol use disorder has been shown to be due to factors other than length of abstinence. While these findings have lessened bias surrounding ALD and liver transplantation, the assumption still remains prevalent in clinical practice today.

These results highlight the unanswered question of how to best approach treatment of individuals with ALD, and whether the recent rise of patients undergoing liver transplantation for ALD, without a continued duration of abstinence, should be a concern of clinicians.

Mack C. Mitchell, MD, is affiliated with the department of internal medicine at the University of Texas in Dallas. Dr. Mitchell reported having financial affiliations with the National Institute of Alcohol and Alcohol Abuse. These comments are adapted from his accompanying editorial (JAMA Intern Med. 2019 Jan 22. doi: 10.1001/jamainternmed.2018.6532).

Time from colonoscopy matters

Positive FIT *from page 1*

excluded patients with a history of CRC or colorectal surgery, inflammatory bowel disease, or poor bowel preparation.

FIT-positive and FIT-negative patients were divided into three groups based on the length of time since their last colonoscopy: less than 3 years, 3-10 years, or more than 10 years or no colonoscopy.

Compared with FIT-negative subjects, FIT-positive individuals were more likely to be diagnosed with any colorectal neoplasia (61.3% vs. 51.8%; *P* less than .001), ACRN (20.0% vs. 10.3%; *P* less than .001), and CRC (5.0% vs. 1.9%; *P* less than .001).

A total of 6% of subjects had a positive FIT result, and data from 2,228 were analyzed after exclusions. They were compared with 6,135 participants who had negative FIT results but underwent a colonoscopy.

Of patients with a positive FIT result, 23.1% had a colonoscopy less than 3 years before, 19.2% had one 3-10 years prior, and 57.8% had a colonoscopy more than 10 years earlier or had never had one.

The more-than-10-year group had a higher frequency of colorectal neoplasia, ACRN, or CRC (26.0%) than did the 3 to 10-year group (12.6%), and the less-than-3-year group (10.9%; *P* less than .001 for all). A similar trend was seen for CRC: 7.2%, 1.6%, and 2.1%, respectively (*P* less than .001).

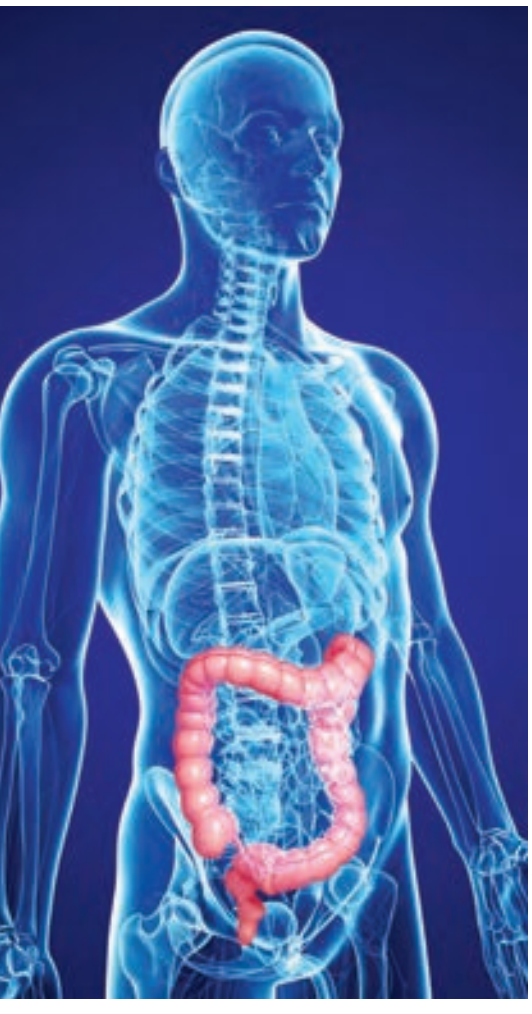
Of the 6,135 FIT-negative participants, 22.2% were in the less-than-3-years group, 28.9%, 3-10 years; and 48.8%, more-than-10 years-or-never group. The more-than-10-years group had a higher frequency of ACRN (14.7%) than did the 3 to 10-year group (0.4%) and the 0 to 3-year group (0.7%, *P* less than .001).

Among FIT-positive patients, the more-than-10-year group was at higher risk of ACRN diagnosis during follow-up colonoscopy than was the less-than-3-year group (adjusted OR, 3.63; 95% confidence interval, 2.48-5.31), but not compared with the 3-10-year group (aOR, 1.17; 95% CI, 0.71-1.93). The more-than-10-year group also was at greater risk of a CRC diagnosis than was the

Continued on following page

AGA Resource

March is Colorectal Cancer Awareness Month. AGA is here to help with patient education materials and a new video series. Visit http://crcawareness.gastro.org/ to access all the resources and share on your practice website and social media channels.



PIXOLOGICSTUDIO/THINKSTOCK

Cancer vaccine fails in CRC but trial yields lessons

BY SUSAN LONDON
MDedge News

SAN FRANCISCO – The cancer vaccine tecemotide (L-BLP25) does not improve outcomes when given after resection of isolated liver metastases of colorectal cancer, according to final results of the German and Austrian phase 2 randomized LICC trial. However, information gleaned from the results, which were reported at the 2019 GI Cancers Symposium, will help inform future research.

"Hepatic metastectomy ... is deemed the only potential curative treatment for stage IV colorectal cancer with limited liver disease. However, high recurrence rates after resection remain a major challenge: They range up to 50%-75% within the first 2 years," said lead investigator Carl C. Schimanski, MD, PhD, of the Klinikum Darmstadt GmbH in Darmstadt, Germany.

Tecemotide is a liposome carrying mucin 1 (MUC1) antigen and an adjuvant that is taken up by antigen-presenting cells, ultimately leading to production of MUC1-specific cytotoxic T lymphocytes that target tumors. "MUC1 has been described to be expressed in up to 100% of colorectal cancer metastasis, so we thought this might be a good target," Dr. Schimanski explained.

All 121 patients in the LICC trial had recently undergone primary or secondary resection, with either R0 or R1 outcome, for liver-only metastases of colorectal cancer. They were treated on a double-blind basis with a single dose of cyclophosphamide to reduce regulatory T cells, followed by tecemotide (weekly for 8 weeks, then every 6 weeks for up to 2 years) or with placebo.

Results showed that recurrence-free survival was actually shorter, by more than 5 months, with the vaccine versus placebo. In addition, the 3-year rate of overall survival was lower by an absolute 10%. Interestingly, tumor expression of MUC1 did not influence benefit from the vaccine.

But Dr. Schimanski noted that survival was better than expected at the trial's outset. For example, the 65-month median overall survival among all patients in LICC undergoing secondary resection was about a year longer than that of similar patients in the CELIM trial (54 months) and the FIRE-3 trial (56 months).


DR. CARL C. SCHIMANSKI


DR. MICHAEL J. OVERMAN

"The LICC trial failed to meet its primary endpoint of significantly improving recurrence-free survival or overall survival with tecemotide. We had unexpectedly high overall survival in both arms, highlighting the critical importance of accurate staging and intensive surveillance, in our eyes," he concluded. "We have further analysis of a very large translational program, and we hope to learn a lot about recurrence independent of tecemotide."

A good space for testing immune therapies

In 2009, a consensus panel of immunologists ranked MUC1 as the second-best cancer antigen for translational research, "so there was clearly a feeling that this was a good target at that time for going forward," noted invited discussant Michael J. Overman, MD, a professor in the department of gastrointestinal medical oncology, division of cancer medicine, University of Texas MD Anderson Cancer Center, Houston.

He agreed with the LICC investigators' conclusions that the trial was negative and that MUC1 expression does not appear to predict outcome. "Whether that's the wrong target, or whether it was the wrong formulation in regards to cancer vaccine, I think we do not know. I do think that survival was encouraging," he said.

"There's many unanswered questions in regards to the LICC study and in regards to cancer vaccines in general," Dr. Overman noted. Among them, what are the optimal antigens to target, what are the optimal vaccine formulations and adjuvant agents, what is the best way to address the immunosuppressive tumor microenvironment, and what is the correct disease setting for vaccine testing?

"The LICC study is very impressive in demonstrating that we can enroll in this posthepatectomy space, postmetastectomy space. It's a very increasingly interesting space for, potentially, drug development and immunologic exploration," he maintained. "One of the benefits of this space when we talk about a minimal residual disease setting is that you potentially do not have the suppressive effects from the tumor microenvironment that potentially are hindering success in regards to having immune therapy response. So I would say that this is a space we should consider for drug development going forward."

Study details

In the LICC trial, tecemotide and placebo yielded a respective median recurrence-free survival of 6.1 months and 11.4 months (P = .1754) and a respective overall survival of 62.8 months and not reached (P = .2141), Dr. Schimanski reported at the symposium, sponsored by the American Gastroenterological Association, the American Society for Clinical Oncology, the American Society for Radiation Oncology, and the Society of Surgical Oncology. The 3-year overall survival rate was 69.1% with tecemotide and 79.1% with placebo.

That survival "was astonishing for us," Dr. Schimanski said. "We think – but we cannot prove it – that has resulted from careful staging due to the retrospective radiological review and the initial staging, and a very tight surveillance program."

Findings were similar regardless of whether patients had low, medium, or high tumor MUC1 expression; therefore, "we have to conclude that the target is not really validated."

Patients in the tecemotide arm had higher rates of any-grade nausea, fatigue, diarrhea, and viral upper respiratory tract infections, at least some of which was likely attributable to the single dose of cyclophosphamide, according to Dr. Schimanski. They also had higher (but still low) rates of grade 3 or 4 back pain, anemia, ileus, cholestatic jaundice, and increased blood uric acid levels (2.5% for each). There was a single death in that arm from Merkel cell carcinoma that was deemed potentially related to the vaccine.

Dr. Schimanski disclosed that an immediate family member is employed by Merck and that he receives research funding from Merck KGaA (institutional). The trial was funded by Merck KGaA.

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SOURCE: Schimanski CC et al. GI Cancers Symposium, Abstract 480.

Continued from previous page

less-than-3-year group (aOR, 3.66; 95% CI, 1.74-7.73). There was no significant difference in CRC risk between the less-than-3-year group and the 3 to 10-year group (aOR, 0.58; 95% CI, 0.17-1.93).

The authors suggest that CRC and ACRN found in patients who had a colonoscopy in the past 3 years are likely to be lesions that were missed in the previous exam, rather than new, fast-growing lesions. That suggests that FIT may help catch lesions that were missed during earlier screenings, though just 2.1% of the less-than-3-year group and 1.6% of the 3 to 10-year group were diagnosed with CRC, and 10.9% and 12.6% with ACRN, respectively.

The authors conclude that it may not be appropriate to offer interval FIT to all patients, since it can lead to unnecessary colonoscopies. They call for more research to determine which categories of patients are most likely to benefit from interval FIT.

The study received no funding. The authors reported no conflicts of interest.

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SOURCE: Kim NH et al. Gastrointest Endosc. 2019 Jan 23. doi: 10.1016/j.gie.2019.01.012.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Obesity-related cancers increasing in younger adults

BY BIANCA NOGRADY
MDedge News

The incidence of obesity-related cancers such as kidney and gallbladder cancer has increased significantly in young adults over the past two decades in the United States, according to an analysis of data from 25 population-based state registries.

The incidence of 6 of the 12 obesity-related cancers increased among individuals aged 25-49 years, Hyuna Sung, PhD, of the American Cancer Society, Atlanta, and her colleagues reported Feb. 4 in the Lancet Public Health.

Among more than 14.6 million incident cases of cancer diagnosed in adults aged 25-84 years between 1995 and 2014, the greatest increase in incidence, 6.23% annually, was seen with kidney cancer among the 25- to 29-year age group.

The incidence rate for kidney cancer among individuals born around 1985 was nearly fivefold higher than in individuals born in 1950, the investigators said (Lancet Public Health. 2019 Feb 4. doi: 10.1016/S2468-2667[18]30267-6).

The analysis also showed significant increases from 1995 to 2014 in the incidence of cancer of the gallbladder among younger adults: 3.71% per year among those aged 25-29 years and 2.58% per year in those aged 30-34 years.

Similarly, the incidence of uterine corpus cancer increased in the 25- to 29-year age group by 3.34% per year and by 3.22% in the 30- to 34-year age group. The incidence of colorectal cancer increased by 2.41% among those aged 25-29 years and by 2.38% in those aged 30-34 years, Dr. Sung and her associates said.

For pancreatic cancer, significant annual increases in incidence were seen among individuals aged 25-29 years (4.34%) and 30-34 years (2.47%).

The study also showed increases in the same obesity-related cancers – except for colorectal cancer – among adults aged 50 years and older. The incidence of colorectal cancer actually decreased annually in older adults, while the incidence of uterine corpus cancer increased among women aged 50-69 years but decreased in those over 75 years.

Dr. Sung and her coauthors suggested that these trends may be related to the rise of obesity and overweight in the United States, noting that excess body weight could be responsible for up to 60% of all endometrial cancers, 36% of gallbladder cancers, and 33% of kidney cancers in adults aged over 30 years.

"Because most epidemiological studies have primarily focused on older populations, the effect of excess bodyweight in early life or of weight change from young adulthood on cancer risk in different stages of the life course is not well characterized," they wrote. "In concert with excess bodyweight, obesity-related health conditions and lifestyle factors can contribute to the increasing burden of obesity-related cancers in young adults, which include diabetes, gallstones, inflammatory bowel disease, and poor diet."

World Obesity Federation

The incidences of breast cancer and gastric cardia cancer were relatively stable in all age groups over the study period, and the incidence of ovarian cancer decreased in all age groups.

Researchers looked at the incidence of 30 cancers in total, including 18 cancers not related to obesity. Here they saw increases among younger adults only in the incidence of gastric noncardiac cancer – which showed a 2.16% annual increase in incidence among those aged 30-34 years – and leukemia, where there was a 1.33% annual increase in incidence in the same age group.

But the incidence of eight cancers, including those related to smoking and infection, decreased each year among younger adults.

"Our findings expose a recent change that could serve as a warning of an increased burden of obesity-related cancers to come in older adults," study senior author Ahmedin Jemal, PhD, of the American Cancer Society, said in a statement. "Most cancers occur in older adults, which means that as the young people in our study age, the burden of obesity-related cancer cases and deaths are likely to increase even more. On the eve of World Cancer Day, it's timely to consider what can be done to avert the impending rise."

The future burden of these cancers could halt or even reverse the reductions in cancer mortality achieved over the past several decades, the investigators warned.

The study was funded by the American Cancer Society and the National Cancer Institute. No conflicts of interest were declared.

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SOURCE: Sung H et al. Lancet Public Health. 2019 Feb 4 doi: 10.1016/ S2468-2667(18)30267-6.

FDA approves cabozantinib for previously treated HCC

BY LAURA NIKOLAIDES
MDedge News

The Food and Drug Administration has approved cabozantinib tablets (Cabometyx) for patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Approval was based on an improvement in overall survival over placebo seen in the phase 3 CELESTIAL trial for patients with advanced HCC who received prior sorafenib.

Median overall survival was 10.2 months with cabozantinib versus 8.0 months with placebo (hazard ratio, 0.76; 95% confidence interval, 0.63-0.92; *P* = .0049). Median progression-free survival was 5.2 months with cabozantinib and 1.9 months with placebo (HR, 0.44; 95% CI, 0.36-0.52; *P* less than .0001). Objective response rates were 4% with cabozantinib and 0.4% with placebo (*P* = .0086), Exelixis, makers of the drug, said in a press release.

The most common grade 3 or 4 adverse events in the patients who received cabozantinib, compared with those who received placebo, were palmar-plantar erythrodysesthesia (17% vs. 0%), hypertension (16% vs. 2%), increased aspartate aminotransferase (12% vs. 7%), fatigue (10% vs. 4%), and diarrhea (10% vs. 2%). Treatment-related grade 5 adverse events occurred in six patients in the cabozantinib group (hepatic failure, esophagobronchial fistula, portal vein thrombosis, upper gastrointestinal hemorrhage, pulmonary embolism, and hepatorenal syndrome) and in one patient in the placebo group (hepatic failure).

Cabozantinib is also approved to treat renal cell carcinoma and medullary thyroid cancer.

Checkpoint inhibitor pembrolizumab was granted accelerated approval for the same HCC indication – to treat patients who have been previously treated with sorafenib – in late 2018.

Exelixis and its partner Ipsen have launched a phase 3 trial of cabozantinib in combination with the checkpoint inhibitor atezolizumab versus sorafenib in previously untreated advanced HCC. The trial will also explore single-agent activity of cabozantinib in the first-line setting, the company said in the press release.

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Delays of 1-2+ years in IBD diagnosis are common, patients say

BY RANDY DOTINGA
MDedge News

LAS VEGAS – Delays in diagnosis of inflammatory bowel disease (IBD) appear to be very common and often extensive, a new survey of U.S. patients suggests. Nearly two-thirds said their diagnosis was delayed past symptom onset for more than a year, and almost half reported a delay of more than 2 years.

On average, patients who experienced diagnosis delays said they'd seen an average of 3.5 physicians. "Most patients reported that they received an uncertain or wrong diagnosis by their primary care physician or gastroenterologist," said study coauthor Ryan C. Ungaro, MD, of Icahn School of Medicine at Mount Sinai, New York, in an interview prior to the presentation of the study findings at the Crohn's & Colitis Congress – a partnership of the Crohn's and Colitis Foundation and the American Gastroenterological Association.

"Working at a tertiary care IBD center, we noticed that many patients tell us it took them a long time to get diagnosed with Crohn's disease [CD] or ulcerative colitis [UC]," said Dr. Ungaro. "There are some studies on delay in diagnosis in Europe but none in the U.S. We hypothesized that diagnostic delay is a major issue for IBD patients in the U.S."


DR. UNGARO

The study authors offered a survey to 2,341 patients with IBD; 1,121 responded to the questions. Of those, 68% reported their diagnosis was delayed, with 64% reporting a delay of over 1 year and 48% reporting a delay over 2 years.

Compared with those with UC, patients with CD were more likely to report more than 1-year delays (70% vs. 48%; *P* less than .0001) and more than 2-year delays (52% vs. 37%; *P* = .0008).

Patients who reported delays said they saw an average of 3.5 physicians before getting an IBD diagnosis. The patients most commonly blamed their incorrect diagnosis on primary care providers (58%) and gastroenterologists (28%).

"Most likely, CD may be misdiagnosed because the common presenting symptoms – abdominal pain, diarrhea – are also seen in other common gastrointestinal conditions such as irritable bowel syndrome," Dr. Ungaro said. "In contrast, most patients with UC present with rectal bleeding which is a 'red flag' symptom that is more likely to get worked up."

In some cases, patients blamed themselves, reporting "that they personally did not feel their symptoms warranted work-up or were too embarrassed by their symptoms to tell anyone," Dr. Ungaro said. "The other theme that was noted was access – delay or difficulty seeing a gastroenterologist."

"Diagnostic delay may be improved through patient education regarding awareness of alarm symptoms for IBD," said gastroenterologist and study lead author Zane Gallinger, MD, FRCPC, of the University of Toronto at Mount Sinai Hospital, in an interview. According to him, these symptoms include diarrhea, abdominal pain, weight loss, family history of CD, perianal abscess, and fistula and fever.

At the primary care level, Dr. Gallinger said that noninvasive tests such as fecal calprotectin can help identify patients with inflammatory conditions and that "more rapid access to gastroenterologists for earlier diagnosis of IBD can improve patient outcomes."

The Crohn's & Colitis Foundation funded the study. Dr. Gallinger reported relationships with Takeda and AbbVie.

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SOURCE: Gallinger Z et al. Crohn's & Colitis Congress, Abstract P030.

AGA CLINICAL PRACTICE UPDATE

Changing utility of serology and histologic measures in celiac disease

BY AMY KARON
MDedge News

For children and adolescents with strong clinical suspicion for celiac disease, repeated transglutaminase-2-IgA (TG2-IgA) levels that are more than 10 times higher than the upper limit of normal often suffice for diagnosis, according to an American Gastroenterological Association clinical practice update.

This approach precludes the need for esophagogastroduodenoscopy in about 30%-50% of cases, wrote Steffen Husby, MD, PhD, of Odense University Hospital (Denmark), together with his associates in Gastroenterology. "When such a strongly positive TG2-IgA is combined with a positive endomysial antibody in a second blood sample, the positive predictive value for celiac disease is virtually 100%." But for adults, they recommend confirmatory histologic analysis of duodenal biopsies with Marsh classification, counting of lymphocytes per high-power field, and morphometry.

Transglutaminase-2 is the major autoantigen present in celiac disease and can now be assessed with accurate, convenient, high-throughput tests, such as ELISAs. To maximize test TG2-IgA accuracy, Dr. Husby and his associates recommend testing patients who have compatible signs and symptoms of celiac disease or are asymptomatic but have other risk factors, such as confirmed autoimmune diseases (type 1 diabetes, autoimmune thyroid, or liver diseases), chromosome abnormalities (Down or Turner syndrome), or first-degree relatives with celiac disease.

Several other serologic tests are available but have a more limited role in diagnosing celiac disease, according to the practice update. Perhaps most useful is the endomysial antibody (EMA) test, which evaluates tissue-bound TG2-IgA. This test is highly specific but labor intensive and user sensitive and thus is best used to confirm a positive TG2-IgA result. Deamidated gliadin peptide antibody assays are less accurate than TG2-IgA, while HLA-DQ2/DQ8 testing is best reserved for cases where the diagnosis is complicated by a prior gluten-free diet or inconclusive antibody titers or histology.

For adults from populations with less than a 5% prevalence of celiac disease, all guidelines recommend following serology with confirmatory biopsy, and the experts concur. If biopsy was part of the initial work-up, they recommend performing confirmatory serology before starting a gluten-free diet. If the biopsy was negative but celiac disease is strongly suspected, they recommend TG2-IgA testing followed by repeat biopsies, when possible.

For children with suspected celiac disease, the North American Society for Pediatric Gastroenterology Hepatology and Nutrition recommends starting with biopsy, while the European Society for Paediatric Gastroenterology Hepatology and Nutrition suggests starting with quantitative TG2-IgA testing, followed by TG2-IgA, EMA, or HLA-DQ2/DQ8 assays if TG2-IgA is 10 times higher than the upper limit of normal. However, EGD with biopsies and even a gluten challenge may be needed if serology results are unclear, the experts state. They recommend against gluten-free or low-gluten diets prior to diagnosis, since these can lower the sensitivity of both histology and serology. If a patient has unclear test results and is already on a gluten-free diet, they suggest resuming eating three slices of wheat bread daily for 1-3 months, followed by TG2-IgA testing.

A small but important subgroup of patients have strong suspicion for celiac disease but are negative on IgA isotype tests because of IgA deficiency. In such suspected cases, the experts recommend measuring total IgA, IgG deamidated gliadin antibodies, and TG2-IgG levels. They note that IgG isotype testing for TG2 antibodies is not celiac specific outside the setting of IgA deficiency.

Serology has a useful but more limited role in managing celiac disease, according to the practice update. Negative TG2-IgA and other serology does not guarantee that the intestinal mucosa has healed, so patients with ongoing or relapsing symptoms without another obvious cause should have repeat biopsies. However, serology that stays positive over time usually indicates ongoing mucosal damage and gluten exposure, so these follow-up tests are appropriate 6 and 12 months after diagnosing celiac disease and yearly thereafter.

Dr. Husby reported receiving grant support from the University of Southern Denmark, the Region of Southern Denmark, and the Novo Nordisk Research Fund. He reported receiving payments from Thermo Fisher Scientific and an advisory relationship with Inova. Two coauthors reported ties to Alba Therapeutics, Celimmune, GlaxoSmithKline, Intrexon, and several other pharmaceutical companies.

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SOURCE: Husby S et al. Gastroenterology. 2018 Dec 19. doi: 10.1053/j.gastro.2018.12.010.

Survey: Reproductive counseling is often MIA in IBD

BY RANDY DOTINGA
MDedge News

LAS VEGAS – Inflammatory bowel disease (IBD) can disrupt both fertility and pregnancy, especially if it's not fully controlled, and there's a risk that the condition can be passed onto an unborn child. Still a new study suggests many patients with IBD don't receive appropriate reproductive counseling.

Nearly two-thirds of 100 patients surveyed at a single center reported that no physician had talked to them about reproductive topics, coauthor and gastroenterologist Sarah Streett, MD, AGAF, of Stanford (Calif.) University, said in an interview before the study was presented at the Crohn's & Colitis Congress – a partnership of the Crohn's & Colitis Foundation and the American Gastroenterological Association.

IBD can lower fertility in both sexes and boost complications in pregnancy. "The good news is that almost all the medications used for IBD appear safe," Dr. Streett said. "In fact, the safety risks for the baby and the pregnancy revolve around not having IBD under good control."

AGA Resource
With proper planning, care, and coordination among treating health care providers via a multidisciplinary approach, women with IBD can have healthy pregnancies and healthy babies. Learn more at www.IBDParenthoodProject.org.

Unfortunately, she said, misinformation is common. "Patients who become pregnant or are trying to become pregnant, and are worried about potential harm to the baby, will stop the medications due to incorrect information.. "

Dr. Streett and study lead author Aarti Rao, MD, a GI fellow at Stanford, launched their study of IBD clinic patients to gain more understanding about patient knowledge. "We wanted to evaluate that in our population and see how much people knew and what the need was," Dr. Streett said.

In 2018 and 2019, Dr. Streett and Dr. Rao gave an anonymous, validated 17-question survey to patients aged 18-45 with IBD. One hundred patients responded (median age = 30, 54% female, 59% white, 66% with incomes over $100,000, 52% with ulcerative colitis, 21% with prior IBD surgery, 71% with prior IBD hospitalization).

Just over a third – 35% – of the patients said they'd been counseled about reproductive health by a physician. This outcome reflects findings in previous research, said Dr. Rao, who spoke in an interview.

Just 15% of those who'd undergone IBD surgery reported getting guidance about the effects of surgery on fertility.

More than a third (35%) of women and 15% of men said they'd considered not having children because of their IBD.

The study was funded by a philanthropic grant. The authors report no relevant disclosures.

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SOURCE: Rao A et al. Crohn's & Colitis Congress, Abstract P009.

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GI & HEPATOLOGY NEWS

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Risk models fail to predict lower GI bleeding outcomes

BY WILL PASS
MDedge News

In cases of lower gastrointestinal bleeding (LGIB), albumin and hemoglobin levels are the best independent predictors of severe bleeding, according to investigators.

These findings came from a sobering look at LGIB risk-prediction models. While some models could predict specific outcomes with reasonable accuracy, none of the models demonstrated broad predictive power, reported Natalie Tapaskar, MD, of the department of medicine at the University of Chicago, and her colleagues.

LGIB requires intensive resource utilization and proves fatal in 5%-15% of patients, which means timely and appropriate interventions are essential, especially for those with severe bleeding.

"There are limited data on accurately predicting the risk of adverse outcomes for hospitalized patients with LGIB," the investigators wrote in Gastrointestinal Endoscopy, "especially in comparison to patients with upper gastrointestinal bleeding (UGIB), where tools such as the Glasgow-Blatchford Bleeding Score have been validated to accurately predict important clinical outcomes."

To assess existing risk models for LGIB, the investigators performed a prospective observational study involving 170 patients with LGIB who underwent colonoscopy during April 2016–September 2017 at the University of Chicago Medical Center. Data were collected through comprehensive medical record review.

The primary outcome was severe bleeding. This was defined by acute bleeding during the first 24 hours of admission that required a transfusion of 2 or more units of packed red blood cells, and/or caused a 20% or greater decrease in hematocrit; and/or recurrent bleeding 24 hours after clinical stability, involving rectal bleeding with an additional drop in hematocrit of 20% or more, and/or readmission for LGIB within 1 week of discharge. Secondary outcomes included blood transfusion requirements, in-hospital recurrent bleeding, length of stay, ICU admission, intervention (surgery, interventional radiology, endoscopy), and the comparative predictive ability of seven clinical risk-stratification models: AIMS65, Charlson Comorbidity Index, Glasgow-Blatchford, NOBLADS, Oakland, Sengupta, and Strate. Area under the receiver operating characteristic curve (AUC) was used to compare model predictive power. Risk of adverse outcomes was calculated by univariable and multivariable logistic regression.

LGIB requires intensive resource utilization and proves fatal in 5%-15% of patients, which means timely and appropriate interventions are essential, especially for those with severe bleeding.

Results showed that median patient age was 70 years. Most of the patients (80%) were African American and slightly more than half were female (58%). These demographic factors were not predictive of severe bleeding, which occurred in about half of the cases (52%). Upon admission, patients with severe bleeding were more likely to have chronic renal failure (30% vs. 17%; *P* = .05), lower albumin (3.6 g/dL vs. 3.95 g/dL; *P* less than .0001), lower hemoglobin (8.6 g/dL vs. 11.1 g/dL; *P* = .0001), lower systolic blood pressure (118 mm Hg vs. 132 mm Hg; *P* = .01), and higher creatinine (1.3 mg/dL vs. 1 mg/dL; *P* = .04). After adjustment for confounding variables, the strongest independent predictors of severe bleeding were low albumin (odds ratio, 2.56 per 1-g/dL decrease; *P* = .02) and low hemoglobin (OR, 1.28 per 1-g/dL decrease; *P* = .0015).

On average, time between admission and colonoscopy was between 2 and 3 days (median, 62.2 hours). In three out of four patients (77%), etiology of LGIB was confirmed; diverticular bleeding was most common (39%), followed distantly by hemorrhoidal bleeding (15%).

Compared with milder cases, patients with severe bleeding were more likely to stay in the ICU (49% vs. 19%; *P* less than .0001), have a blood transfusion (85% vs 36%; *P* less than .0001), and need to remain in the hospital for a longer period of time (6 days vs. 4 days; *P* = .0009). These findings exemplify the high level of resource utilization required for LGIB and show how severe bleeding dramatically compounds intensity of care.

Further analysis showed that none of the seven risk models were predictive across all outcomes; however, some predicted specific outcomes better than others. Leaders were the Glasgow-Blatchford score for blood transfusion (AUC, 0.87; *P* less than .0001), the Oakland score for severe bleeding (AUC, 0.74; *P* less than .0001), the Sengupta score for ICU stay (AUC, 0.74; *P* less than .0001), and the Strate score for both recurrent bleeding during hospital stay (AUC, 0.66; *P* = .0008) and endoscopic intervention (AUC, 0.62; *P* = .01).

The investigators noted that the Glasgow-Blatchford score, which also is used in cases of UGIB, has previously demonstrated accuracy in predicting blood transfusion, as it did in the present study, suggesting that, "[i]n instances where there may be uncertainty of the origin of the bleeding, the Blatchford score may be a preferential choice of risk score."

"Overall, we found that no singular score performed best across all the outcomes studied nor did any score have an extremely strong discriminatory power for any individual variable," the investigators wrote, concluding that "... simpler and more powerful prediction tools are required for better risk stratification in LGIB."

The investigators reported no financial support or conflicts of interest.

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SOURCE: Tapaskar N et al. Gastrointest Endosc. 2018 Dec 18. doi: 10.1016/j.gie.2018.12.011.

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What is your diagnosis? on page 11: Partial malrotation and cecal volvulus after colonoscopy

The patient presented with partial malrotation and cecal volvulus after colonoscopy, which was confirmed by abdominal computed tomography scan. The patient gave consent and taken urgently to the operating room where she underwent an exploratory laparotomy and right hemicolectomy. A mesenteroaxial cecal volvulus was noted immediately upon entering the abdomen. The involved colon segment was dusky without frank necrosis. The distal ascending and proximal transverse colon were tethered to the left abdominal wall, and the ascending colon lacked its usual retroperitoneal attachments, consistent with partial malrotation. The adhesions were lysed, and a right hemicolectomy with primary side-to-side ileocolonic anastomosis was performed. The patient recovered well and was discharged to home on postoperative day 4.

Screening colonoscopy for colorectal cancer is a commonly performed procedure with an established survival benefit. Up to one-third of patients experience abdominal pain, nausea, or bloating afterward, which may last hours to several days. Fortunately, severe complications including hemorrhage, perforation, and death are rare, with a total incidence of 0.28%.[1] Although abdominal pain is common after colonoscopy, severe pain that persists or worsens warrants investigation. Perforation is the most frequently encountered complication in this context, although splenic injury/rupture and intestinal obstruction do occur. Cecal volvulus is a very rare complication with few reports in the literature.[2,3] Colonic malrotation, which occurs in up to 0.5% of the population, increases the risk of volvulus owing to a lack of retroperitoneal attachments. This diagnosis should be considered for patients with known risk factors for volvulus.

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Culture change needed to improve gender inequalities in science and medicine

BY SARA FREEMAN
MDedge News

LONDON – A concerted effort is needed by everyone to address gender inequality in science and medicine, a group of prominent female physicians and thought-leaders said at a recent event hosted by The Lancet.

"Gender equality is everyone's business," Sarah Hawkes, MBBS, PhD, a professor of global public health at University College London, said at the event.

"We're not talking about women taking over the shop, but women being given an equal opportunity to run the shop. It doesn't matter where we place ourselves on the gender spectrum as far as advancing equality in science is concerned. What matters is that we all, irrespective of gender, call ourselves feminists."

For years, women have been "underrepresented in positions of power and leadership, undervalued, and experience discrimination and gender-based violence in scientific and health disciplines across the world," according to an editorial in the British-based journal (Lancet. 2019;393:493). Such inequalities are compounded and hard to separate from other inequalities, including ethnicity, disability, class, geography, and sexuality.

Despite efforts to readdress the predominantly male culture of medicine, the problem of gender inequality remains "stubbornly persistent," the editorial said.

"We have spent years being told that the problem lies with us as individuals and that we just need to be better, stronger, more vocal, as women," Dr. Hawkes observed. "But what really needs to happen is for change to happen in places that hold power." She further argued: "We don't need any more individual change; we need organizational and institutional norm change."

Gender inequality has a long history, and not just in medicine, said British journalist Caroline Criado-Perez OBE, who gave a keynote speech. Ms. Criado-Perez, who is a well-respected feminist campaigner, noted that the world was largely "modeled to fit men." From architecture to transport, and even crash-test dummies, everything was largely modeled on, or to accommodate, the male rather than the female body.

"I don't need to tell you that women are 50% more likely to be misdiagnosed following a heart attack" than men. There is no more urgent need to challenge gender inequality than in medicine, Women are dying because of the gender data gap in medicine," she asserted. "In medical research, in medical education, in medical practice, it needs to be closed as a matter of urgency."


DR. OSLER

Original data published in the Advancing Women in Science, Medicine and Global Health special edition of The Lancet found that only 31% of biomedical research papers published in 2016 reported outcomes for both men and women (Lancet. 2019;393:550-9). Reporting of sex differences was somewhat better in clinical or public health–related research papers, at 67% and 69%, respectively. Sex-differences were more likely to be reported if a woman was one of the key authors, Cassidy R. Sugimoto, PhD, associate professor of informatics at Indiana University in Bloomington, and associates, observed in their paper.

That said, women often have to fight to be included as an author on a paper, even when they have done the majority of the work, the event participants highlighted. Women were still less likely than men to be named as the first or last author on a paper, as well as be less likely to receive research funding to enable them to do the work in the first place (Lancet. 2018;393:531-40).

"Was it really you?" was a question sometimes asked of a woman named as a lead or first author, noted Sonia Gandhi, MD, PhD, group leader of the Neurodegeneration Biology Laboratory at the Francis Crick Institute in Cambridge (England). Women network differently to men, Dr. Gandhi observed, and not necessarily in networks that forward careers. Women were also often questioned about their productivity, and regardless of any training on unconscious bias, women were still at a disadvantage if they took a career break to have children.

Women's credentials and capabilities were often felt to be less respected by male colleagues, and there was talk of being met with microaggressions in the workplace, as in one example given by Nana Odom, MSc, a clinical engineer at the Royal United Hospital Bath (England). She was told "you're not an engineer, because I have not got a set of screwdrivers and sit at a computer and program." Such comments can deeply affect a person, Dr. Odom said. "Sometimes I feel that if I don't go into the workshop and open up a bit of kit that I am not an engineer, but it's so unconscious, it carries on with you." These types of stories need to be told so then they can be properly addressed when they do happen, she said.


DR. HAWKES

Female representation is so important, said F. Gigi Osler, MD, head of otolaryngology-head and neck surgery at St. Boniface Hospital in Winnipeg. Dr. Osler is the 2018-2019 president of the Canadian Medical Association, the eighth woman to hold this prestigious position in the organization's 151 years of operation. She also happens to be the first female surgeon and the first woman of color in the role. "When I stepped into the presidency last August, I thought very long and very hard about how I was going to use my voice and this platform," Dr. Osler said. "It became very clear to me after I started how important representation was. I can't tell you how many women, young women, and women of color ... have come up to me to say, 'I'm so excited to have you in this position. I've never seen someone who looks like me in that type of leadership position,' " she observed.

"As leaders, I think we can advocate for structures and processes," Dr. Osler added, "I think we set the culture." Leaders have the responsibility for creating and nurturing and fostering a professional, respectful, and inclusive environment, she said.

"We need more strong leaders; we need more diversity in leadership." Dr. Osler was keen to point out that greater diversity does not mean only women, but other groups as well. "Look around the room. Who is not here? How can I make it easier for them to get here?"

Another strong female role model at the event was Dame Sally Davies, the Chief Medical Officer for England, a hematologist by training. Not only is she the first female in that role, she will also become the first female Master of Trinity College Cambridge starting in October 2019, a role dominated by men for more than 500 years.

"If the system isn't right, or we are treated badly, we need to call it out," Dame Sally said. "I do think that we often let things pass that we shouldn't." A classic situation is where a woman may suggest something at a meeting and it is ignored, but when a man says the same thing it is taken on board. That kind of behavior needs to stop and be addressed when it happens, by everyone at the table, she said.

Dr. Hawkes observed in her summing up of the day: "Throughout the history of health, change comes about not just through action at the top, but also from action from the bottom up." She added: "The question is how do we make that change happen?" That's where the next phase of research needs to take place, she suggested, "we need to actually see, in a very evidence-informed way, what actually works to make and sustain change."

AGA is committed to fostering and promoting the involvement and advancement of women within the organization and the field and addressing women's health issues. AGA offers several leadership development programs for women members throughout the year including the AGA Women's Leadership Conference, the AGA Women's Talent Bank and the annual Women in GI luncheon during Digestive Disease Week.® Learn more about these and other programs at www.gastro.org.

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HHS to target step therapy, Stark Law in 2019

BY GREGORY TWACHTMAN
MDedge News

WASHINGTON – Addressing issues related to step therapy and adapting the Stark Law for a value-based care environment are on the Department of Health & Human Service's agenda this year, according to agency Secretary Alex M. Azar II.

Speaking Feb. 12 at the American Medical Association's National Advocacy Conference, Secretary Azar said the agency will be looking into ensuring that patients on medical plans who have found a working drug after going through a step-therapy protocol will not have to restart on a drug that has already failed for them if they switch insurance providers.

"I was very disturbed to hear that stable patients switching among insurance plans, like switching among Medicare Advantage plans, can often be required to start over again on a step-therapy regimen," he said.

"This is not just potentially injurious to their health, it's also penny-wise and pound-foolish," Secretary Azar continued. "We know that getting a patient on the right drug, at the right time, is one of the best investments we can make in their health, and we do not want to impede physicians from making that happen. We're looking at how we can address that issue now."

The other area Secretary Azar highlighted that the agency is working on is making changes to the Stark Law.

"The Stark Law was written with noble purposes in mind, but it was designed for a fee-for-service system, not the kind of system we are moving toward today," he said. "We've heard from many, many stakeholders, including the AMA, about the need to update the enumerated exceptions in the Stark Law to include value-based approaches to care."

He added that how care coordination interacts with the antikickback statutes and HIPAA are also going to be examined.

He used most of his speech to discuss recent regulatory actions around drug pricing and pushed for support for the Part B drug pricing model that the agency is preparing for a formal proposed rule, despite having received a critical reception from medical societies.

"If you have a small practice that uses infusions, and you don't want to bear the risk of buy and bill, now you're off the hook," he said. "We'll allow you to work with private vendors who can take the risk for buying the drugs in a way that isn't possible today. But if you're part of a much larger practice that's able to drive a better deal than you could on your own, or want to band together with other practices to do the purchasing, then you can do that, too."

He continued: "Next is the launch of the actual proposed rule, followed by the rule itself, which, I'll remind you, is just a model."

However, despite its being a model under test from the Center for Medicare & Medicaid Innovation, the advanced notice of proposed rule making that was issued in October 2018 suggested that participation in the so-called International Pricing Index model would be mandatory.

AGA is pleased about Secretary Azar's commitment to ensuring Medicare beneficiaries will continue to have access to and coverage of medications that work for them. Patients should not be forced to switch to a therapy that they have already failed if they change insurance plans. Read more about AGA's advocacy for similar federal legislation at http://ow.ly/2t3030nLbcB.

AGA, in conjunction with other physician specialty organizations, continues to advocate for changes in the Stark Law to allow physician practices to participate in advanced payment models in the Medicare program that will improve care coordination and patient outcomes.

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PRACTICE MANAGEMENT TOOLBOX: Training the endo-athlete – an update in ergonomics in endoscopy

BY MANISH SINGLA, MD, RYAN M. KWOK, MD, GJORGI DERIBAN, MD, AND PATRICK E. YOUNG, MD


DR. SINGLA


DR. KWOK


DR. DERIBAN


DR. YOUNG

As physicians, we work hard to take excellent care of our patients. We often take poor care of ourselves, which can lead to burnout and physical injuries. As gastroenterologists, we spend substantial time performing endoscopic procedures that require repetitive motions such as flexion and extension of the wrist and fingers and torsional movements of the right hand, which may lead to overuse injuries. The volume of endoscopic procedures performed by a typical gastroenterologist has increased significantly in the past 20 years. Moreover, experts predict that by 2020 we will have too few endoscopists to meet clinical demands.[1] It is imperative that we do whatever possible to ensure overuse injuries do not prematurely prevent us from providing much-needed care. One way to achieve this goal is to focus on ergonomics. The study of ergonomics, derived from the Greek words ergo (work) and nomos (law), seeks to optimize the interface between the worker, the equipment, and the work environment. This article reviews basic ergonomic principles that endoscopists can apply today and possible innovations that may improve endoscopic ergonomics in the future.

Breadth of the problem

Examinations of injuries related to endoscopy are limited to survey-based and small controlled studies with a 39%-89% overall prevalence of pain or musculoskeletal injuries reported.[2] In a survey of 684 American Society for Gastrointestinal Endoscopy members examining injury prevalence and risk factors,[3] 53% experienced an injury believed to be definitely or probably related to endoscopy. Risk factors included higher procedure volume (more than 20 cases/wk), greater number of hours spent performing endoscopy (more than 16 h/wk), and total number of years spent performing endoscopy.[2,4] Community practitioners reported injuries at higher rates than those in an academic center. Other suggested but unproven risk factors include age,[5] sex, hand size, room design, and level of training in ergonomics and endoscopy.[2] Injuries can be severe and may lead to workload reduction, missed days of work,[3-5] reduction of activities outside of work, and long-term disability.[2]

Most surveys reflect symptoms localized to the back, neck, shoulder, elbow, hands/fingers, and thumbs likely from overuse causing strain and soft-tissue microtrauma.[6] Without time to heal, these injuries may lead to connective tissue weakening and permanent damage. Repetitive hand movements in endoscopy include left thumb abduction, flexion, and extension while manipulating dials and right wrist flexion, extension, and deviation from torqueing the insertion tube. The use of torque is a necessary part of successful colonoscopy; during scope reduction and maneuvering through the sigmoid colon, torque forces and forces applied against the wall of the colon are highest. When of sufficient magnitude and duration, these forces are associated with an increased risk of thumb and wrist injuries. These movements may result in "endoscopist's thumb" (i.e., de Quervain's tenosynovitis) and carpal tunnel syndrome.[2] Prolonged standing and lead aprons are implicated in back and neck injuries[2,7-9]; two-piece aprons[7,10] and antifatigue mats[7] are recommended to decrease pressure on the lumbar and cervical disks as well as delay muscle fatigue.

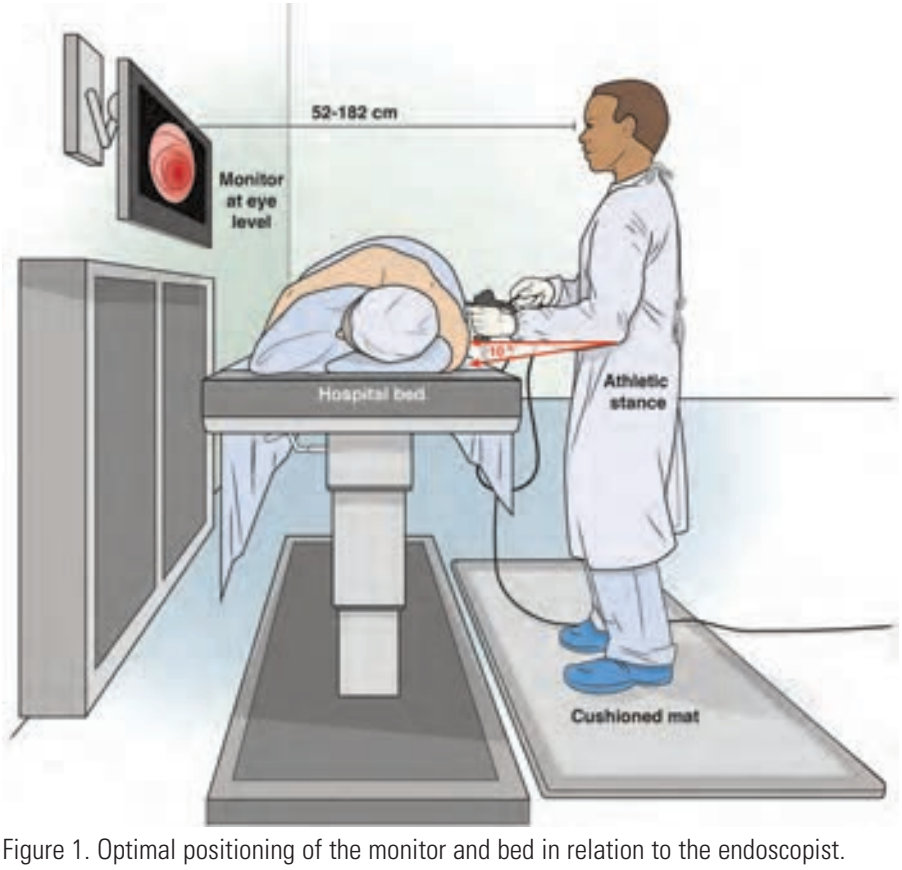

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Figure 1. Optimal positioning of the monitor and bed in relation to the endoscopist.

Position of equipment

Endoscopist and patient positioning can be optimized. In the absence of direct data about ergonomics in endoscopy, we rely on surgical laparoscopy data.[11,12]These studies show that monitors placed directly in front of surgeons at eye level (rather than off to the side or at the head of the bed) reduced neck and shoulder muscle activity. Monitors should be placed with a height 20 cm lower than the height of the surgeon (endoscopist), suggesting that optimized monitor height should be at eye level or lower to prevent neck strain. Estimates based on computer simulation and laparoscopy practitioners show that the optimal distance between the endoscopist/surgeon and a 14" monitor is between 52 and 182 cm, which allows for the least amount of image degradation. Many modern monitors are larger (19"-26"), which allows for placement farther from the endoscopist without losing image quality. Bed height affects both spine and arm position; surgical data again suggest that optimal bed height is between elbow height and 10 cm below elbow height.

Immediate practice points

Since poor monitor placement was identified as a major risk factor for musculoskeletal injuries, the first steps in our endoscopy unit were to improve our sightlines. Our adjustable monitors previously were locked into a specific height, and those same monitors now easily are adjusted to heights appropriate to the endoscopist. Our practice has endoscopists from 61" to 77" tall, meaning we needed monitors that could adjust over a 16" height. When designing new endoscopy suites, monitors that adjust from 93 to 162 cm would accommodate the 5th percentile of female height to the 95th percentile of male height. We use adjustable-height beds; a bed that adjusts between 85 and 120 cm would accommodate the 5th percentile of female height to the 95th percentile of male height.

We also moved our monitors to be closer to the opposite side of the bed to accommodate the 3' to 6' appropriate to our 16" screens. Our endoscopy suites have cushioned washable mats placed where endoscopists stand that allow for slight instability of the legs, leading to subtle movements of the legs and increased blood flow to reduce foot and leg injuries. We attempt an athletic stance (the endo-athlete) during endoscopy: shoulders back, chest out, knees bent, and feet hip-width apart pointed at the endoscopy screen (Figure 1). These mats help prevent pelvic girdle twisting and turning that may lead to awkward positions and instead leave the endoscopist in an optimized position for the procedure. We encourage endoscopists to keep the scope in the most neutral position possible to reduce overuse of torque and the forces on the wrists and thumbs. When possible, we use two-piece lead aprons for procedures

Continued on following page

Continued from previous page

that require fluoroscopy, which transfers some of the weight of the apron from the shoulders to the hips and reduces upper-body strain. Optimization of the room for therapeutic procedures is even more important (with dual screens both fulfilling the criteria we have listed earlier) given the extra weight of the lead on the body. We suggest that if procedures are performed in cramped endoscopy rooms, placement of additional monitors can help alleviate neck strain and rotation.

Working with our nurses was imperative. We first had our nurses watch videos on appropriate ergonomics in the endoscopy suite. Given that endoscopists usually are concentrating their attention on the screens in the suite, we tasked our nurses to not only monitor our patients, but also to observe the physical stance of the endoscopists. Our nurses are encouraged to help our endoscopists focus on their working stance: The nurses help with monitor positioning, and give verbal cues when endoscopists are contorting their bodies unnaturally. This intervention requires open two-way communication in the endoscopy suite. We are fortunate to be at an institution that trains fellows; we have two endoscopists in the suite at any time, which allows for additional two-way feedback between fellows and attendings to improve ergonomic positioning.

We also encourage preventative exercises of the upper extremities to reduce pain and injuries. Stretches should emphasize finger, wrist, forearm, and shoulder flexion and extension. Even a minute of stretching between procedures allows for muscle relaxation and may lead to a decrease in overuse injuries. Adding these elements may seem inefficient and unnecessary if you have never had an injury, but we suggest the following paradigm: Think of yourself as an endo-athlete. Similar to an athlete, you have worked years to gain the skills you possess. Taking a few moments to reduce your chances of a career-slowing (or career-ending) injury can pay long-term dividends.

Future remedies

Although there have been substantial advances in endoscopic imaging technology, the process of endoscope rotation and tip deflection has changed little since the development of flexible endoscopy. A freshman engineering student tasked with designing a device to navigate, examine, and provide therapy in the human colon likely would create a device that does not resemble the scope that we use daily. Numerous investigators currently are working on novel devices designed to examine and deliver therapy to the digestive tract. These devices may diminish an endoscopist's injury risk though the use of better ergonomic principles. This section is not intended to be a comprehensive review and is not an endorsement of any particular product. Rather, we hope it provides a glimpse into a possible future.

Reduction of gravitational load

The concept of a mechanical device to hold some or all of the weight of the endoscope was first published in 1974.[13] Since then, a number of products have been described for this purpose.[14-17] In general, these consist of a simple metal tube with a hemicylindrical plastic clip, similar to a microphone stand, or a yoke/strap with a plastic scope holder in the front akin to what a percussionist in a marching band might wear. For a variety of reasons, including limited mobility and issues with disinfection, these devices have not gained traction.

Novel control mechanisms

Some of the largest forces on the endoscopist relate to moving the wheels on the scope head to effect tip deflection via a cable linkage. Because the wheels rotate only in one axis, the options for altering and adjusting load are few. One proposed solution is the use of a system with a fully detachable endoscope handle with a joystick style control deck (E210; Invendo Medical, Kissing, Germany). The control deck uses electromechanical assistance – as opposed to pure mechanical force – to transmit energy to the shaft of the instrument. Such assistive technologies have the potential to decrease injuries by decreased load, particularly on the carpometacarpal joint. Other devices seek to decrease the need for torque and high-load tip deflection though the use of self-propelled, disposable colonoscopes that use an aviation-style joystick (Aero-scope; GI View, Kissing, Germany). Although interesting and potentially useful, neither product is currently available for clinical use in the United States.

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Robots and magnets

Magnetically controlled wireless capsules have been studied in vivo in human beings on several occasions in the United Kingdom and Asia. Wired colonic capsules are currently under development in the United States. These products use joystick-style controls to direct movement of the capsule. Optimal visualization often requires the patient to rotate through numerous positions and, at least in the stomach, to drink significant quantities of fluid to ensure adequate distention. At present, these devices provide only diagnostic capabilities.

Conclusions

The performance of endoscopy inherently places its practitioners at risk of biomechanical injury. Fortunately, there are numerous ways we can optimize our environment and ourselves. We should treat our bodies as professional athletes do: Use good form, encourage colleagues to observe and provide feedback on our actions, optimize our practice facilities, and stretch our muscles. In the future, technological innovations, such as ergonomically designed endoscope handles and self-propelled colonoscopes, may reduce the inherent physical stresses of endoscopy. In doing so, we hope can preserve our own health and continue to better the health of our patients as well.

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Take away points

1. Optimize room design, including adjustable height monitors. In my informal survey of endoscopy units, this seems to be the most violated principle.
2. Stretch briefly (30-60 seconds) after each case. Surgical literature on microbreaks suggests enhanced performance without a loss of efficiency.
3. Empower your team to correct poor ergonomics practices when they see them. We are often so focused on the patient that we are unaware of our body position.

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