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Courtesy University of Chicago

Dr. Sonia S. Kupfer recommends pancreatic ductal adenocarcinoma screening for BRCA carriers only if they have a family history of PDAC.

AGA releases BRCA risk guidance

BY WILL PASS
MDedge News

BRCA carrier status alone should not influence screening recommendations for colorectal cancer or pancreatic ductal adenocarcinoma, according to an American Gastroenterological Association clinical practice update.

Relationships between BRCA carrier status and risks of pancreatic ductal adenocarcinoma (PDAC) and colorectal cancer (CRC) remain unclear, reported lead author Sonia S. Kupfer, MD, AGAF, of the University of Chicago, and colleagues.

"Pathogenic variants in BRCA1 and BRCA2 have ... been associated with variable risk of GI cancer, including CRC, PDAC, biliary, and gastric cancers," the investigators wrote in Gastroenterology. "However, the magnitude of GI cancer risks is not well established and there is minimal evidence or guidance on screening for GI cancers among BRCA1 and BRCA2 carriers."

According to the investigators, personalized screening for CRC is well supported by evidence, as higher-risk individuals, such as those with a family history of CRC, have been shown

See **Risk** · *page 27*

Proton pump inhibitors tied to COVID-19 risk

BY LAIRD HARRISON

People who use proton pump inhibitors (PPIs) may be more likely to get COVID-19, researchers say.

In light of this finding, physicians should consider which patients truly need these powerful acid-lowering drugs, said Brennan Spiegel, MD, MSHS, AGAF, professor of medicine and public health at Cedars Sinai Medical Center in Los Angeles,

"All it means is that we're going to have a conversation with our patients," he said in an interview. "We don't normally have that conversation because we don't live in an environment with a high risk of enteric infection. But now we're in a pandemic."

The study by Dr. Spiegel and his colleagues was published in the American Journal of Gastroenterology.

Although studies have not borne out many of the other concerns raised about adverse reactions, they have shown that the drugs increase the risk for enteric infections, including infections by SARS-CoV-1, a virus that is related to the COVID-19 virus, SARS-CoV-2, Dr. Spiegel said.

SARS-CoV-2 uses the angiotensin-converting enzyme–2 receptor to invade enterocytes. Dr. Spiegel theorized that an increase in stomach pH above 3 as a result of use of PPIs might

See **PPIs** · *page 28*

AGA meta-analysis leads to new COVID-19 GI and liver guideline

BY WILL PASS
MDedge News

The American Gastroenterological Association has released a new guideline for consultative management of patients with COVID-19.

The recommendations, which were written by Shahnaz Sultan, MD, AGAF, chair of the AGA Clinical Guidelines Committee, of the University of Minnesota, Minneapolis, and colleagues, were based on a meta-analysis of data from 47 studies involving 10,890 unique patients.

"We seek to summarize international data on the GI and liver manifestations

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LETTER FROM THE EDITOR

Stay safe and please, wear a mask

"Beginning immediately, the University of Michigan will require all students, staff, faculty, and visitors to wear a face covering that covers the mouth and nose while anywhere on campus grounds," (Mark S. Schlissel MD, PhD – President, University of Michigan – July 15). Executive Order 2020-147 (Michigan's Governor Whitmer) mandated appropriate facial covering for all indoor spaces and crowded outdoor spaces. Additionally, businesses will be held responsible if they allow entry to anyone not wearing a mask.

While enforcement is proving to be a nightmare, masking combined with social distancing, hand washing, and staying home are the only effective levers we have to slow the spread of COVID-19. As of today, 138,000 Americans have died, and we anticipate 240,000 deaths by November 1. By now, most of us (myself included) have had a friend or relative die of this virus. America is not winning this battle and we have yet to see an effective, coordinated national response. Four forces are killing our citizens: COVID-19, structural racism, economic/health inequities, and divisive politics. We should do better.

Although Michigan and Minnesota (my home states) have slowed the virus enough to maintain resource capacity, just last weekend a single house party in a suburb near Ann Arbor resulted in 40 new infections. Thirty-nine states have rising case numbers, hospitalizations, and deaths. We are still in the early innings of this game. Michigan Medicine is actively planning our response to a second surge, which will be combined with increases of influenza and RSV infections.

This month we continue to cover the rapidly emerging information about COVID-19 and digestive implications. There are other interesting articles including guidance around BRCA risk for colorectal cancer, detection of IBD-related dysplasia, eosinophilic esophagitis, probiotics, and the emerging impact of AI on endoscopy. Enjoy – stay safe, wash hands, socially distance, and please, wear a mask.

Dr. Allen

Four forces are killing our citizens: COVID-19, structural racism, economic/health inequities, and divisive politics. We should do better.

"*Respect science, respect nature, respect each other*" (Thomas Friedman).

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

Top AGA Community patient cases

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

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

- Patient case: Elevated aminotransferases of unknown origin. (https://community.gastro.org/posts/21890)
- Patient case: Functional bowel obstruction. (https://community.gastro.org/posts/21888)
- Patient case: Autoimmune hepatitis with chronic hepatitis C. (https://community.gastro.org/posts/21880)
- Patient case: Immunosuppression in IBD (https://community.gastro.org/posts/21860)
- Is COVID-19 reinfection fact or fiction? (https://community.gastro.org/posts/21824)
- Experience with HALO procedures in ambulatory surgery centers. (https://community.gastro.org/posts/21812)

Roundtables (https://community.gastro.org/discussions/)

- GI COVID-19 Connection: Work-life balance in the COVID era.
- Trainee & early career networking connection.

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

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Combination probiotic formulations might improve outcomes in preterm infants

BY AMY KARON
MDedge News

For preterm, low-birth-weight infants, probiotic formulations containing *Lactobacillus* and *Bifidobacterium* strains appear to be superior to single-strain probiotics and to other multiple-strain formulations for reducing the risk of all-cause mortality, according to the findings of a network meta-analysis of randomized clinical trials.

See related story on page 29

A prior Cochrane review indicated that probiotics can help prevent severe necrotizing enterocolitis (NEC) and all-cause mortality in preterm infants, but the most effective formulations remained unclear. Therefore, Rebecca L. Morgan, PhD, MPH, and her associates searched MEDLINE, EMBASE, Science Citation Index Expanded, CINAHL, Scopus, Cochrane CENTRAL, BIOSIS Previews, and Google Scholar through Jan. 1, 2019, to identify studies of single-strain and multistrain probiotic formulations in preterm, low-birth-weight neonates. A total of 63 studies involving 15,712 infants met inclusion criteria. .

"High-certainty" evidence indicated that combination therapy with one or more *Lactobacillus* species and one or more *Bifidobacterium* species significantly reduced all-cause mortality, compared with placebo (odds ratio, 0.56; 95% confidence interval, 0.39-0.80), wrote Dr. Morgan, of McMaster University, Hamilton, Ont., and her coinvestigators. This was the only intervention to have moderate- or high-quality evidence for a reduction in mortality, the researchers wrote in Gastroenterology.

They added that, among the probiotic formulations with moderate- or high-quality evidence for efficacy, compared with placebo, those containing at least one species of *Lactobacillus* and at least one species of *Bifidobacterium*, and the single-strain probiotics containing *Bifidobacterium animalis* subspecies *lactis*, *Lactobacillus reuteri*, or *Lactobacillus rhamnosus* significantly reduced the risk of severe NEC (Bell stage II or higher), with statistically significant odds ratios of 0.35, 0.31, 0.55, and 0.44, respectively.

Three formulations were associated with "low-" or "very low–certainty" evidence for a reduction in risk for severe NEC, compared with placebo: *Bacillus* plus *Enterococcus* species, *Lactobacillus* plus *Bifidobacterium* plus *Enterococcus* species, and *Bifidobacterium* plus *Streptococcus salivarius* subspecies *thermophilus*. Estimated ORs were 0.23 (risk difference, –4.9%), 0.28 (RD, –4.9%), and 0.38 (RD, –3.9%), respectively.

"The combinations of *Bacillus* species and *Enterococcus* species, and one or more *Bifidobacterium* species and *S. salivarius* subspecies *thermophilus* might produce the largest reduction in [NEC] development," the investigators wrote.

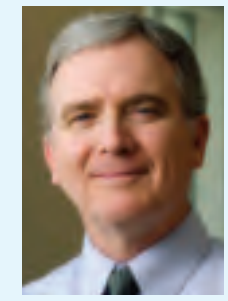
Several formulations were associated with moderate- or high-quality evidence for efficacy on secondary outcome measures. Compared with placebo, combinations of *Lactobacillus* and *Bifidobacterium* and *Saccharomyces boulardii* were associated with a significant decrease in the number of days to reach full feeding. Compared with placebo, single-strain therapy with *B. animalis* subspecies *lactis* or *Lactobacillus reuteri* was associated with a shorter duration of hospitalization, with mean reductions of 13.0 days and 7.9 days, respectively.

Partial support was provided by Mitacs Canada, in partnership with Nestlé Canada. The funder was not involved in designing or conducting the study or writing the manuscript. Dr. Morgan reported no conflicts of interest. One investigator disclosed ties to AbbVie, Ferring, Janssen, and Takeda.

ginews@gastro.org

SOURCE: Morgan RL et al. Gastroenterology. 2020 Jun 24. doi: 10.1053/j.gastro.2020.05.096.

The demonstration of decreased risks of both death and NEC in randomized placebo-controlled trials of probiotic microbes in very preterm babies is the most compelling case for administration of probiotics to date. Questions remain, including the optimal probiotic microbe(s) and dose for this population. Ideal studies would compare commercially available probiotic products and doses to each other (rather than to placebo).


Dr. Underwood

In the absence of these ideal studies, a network meta-analysis is a valuable tool to compare and rank multiple treatments. One of the drawbacks of a network meta-analysis is the assumption that all interventions have similar effects in all populations (a challenging assumption given the marked differences in the incidence of NEC between hospitals and populations).

The study conclusion that the combination of at least one *Lactobacillus* strain and at least one *Bifidobacterium* strain is most effective in preventing both death and NEC in very preterm infants is consistent with a previous network meta-analysis and with recent recommendations of the European Society for Paediatric Gastroenterology Hepatology and Nutrition and the AGA.

Administration of probiotics to very preterm infants remains uncommon in many countries, including the United States. Given an intervention with limited evidence of harm and significant evidence of benefit, it is incumbent upon neonatologists to discuss the available evidence with parents and include their wishes in the decision-making process.

Mark A. Underwood, MD, MAS, is a professor of pediatrics and chief of the division of neonatology in the department of pediatrics at the University of California, Davis. He received honoraria from Abbott and conducted a clinical trial of probiotics funded by Evolve Biosystems.

High-definition chromoendoscopy beats white-light endoscopy for detecting dysplasias in IBD

BY AMY KARON
MDedge News

High-definition chromoendoscopy significantly outperformed high-definition white-light endoscopy for detecting dysplastic lesions in patients with inflammatory bowel disease, according to the findings of a single-center prospective randomized trial.

In the intention-to-diagnose analysis, rates of dysplasia detection were 11% for high-definition chromoendoscopy and 5% for high-definition white-light endoscopy ($P = .032$). The per-protocol analysis produced a similar result (12% vs. 5%, respectively; $P = .027$). High-definition chromoendoscopy also detected significantly more dysplastic lesions per 10 minutes of colonoscope withdrawal time in the per-protocol analysis, although the difference did not reach statistical significance in the intention-to-diagnose analysis.

Overall, the findings "support the use of chromoendoscopy for surveillance of patients with inflammatory bowel diseases," Bjarki Alexandersson, a PhD student at Karolinska University Hospital in Solna, Stockholm, and his associates wrote in Clinical Gastroenterology and Hepatology.

Patients with inflammatory bowel disease are at increased risk for colorectal cancer. Most guidelines support chromoendoscopy for the surveillance of these patients, as do the results of two recent meta-analyses in which chromoendoscopy detected significantly more dysplasias among patients with inflammatory bowel disease than did white-light endoscopy. However, in subgroup analyses of these studies, the differ-

Continued on following page

Protocol requires 50% fewer biopsies

Targeting ascending, descending colon reveals microscopic colitis

BY AMY KARON
MDedge News

All patients with microscopic colitis who had biopsies of both the ascending and descending colon had positive slide review for at least one of the two sites, according to the findings of a single-center retrospective study.

"We propose a Western protocol (taking two biopsy specimens each from the ascending colon and the descending colon) in the evaluation of patients for microscopic colitis," wrote Boris Virine, MD, of London (Ont.) Health Sciences Centre, Western University, together with his associates in Clinical Gastroenterology and Hepatology.

That is half the minimum number of samples recommended by current guidelines, the researchers noted. "The American Society for Gastrointestinal Endoscopy recommends two or more biopsy specimens from the right, transverse, left, and sigmoid colons; however, these recommendations were based on expert opinion rather than scientific evidence, and these guidelines have not been validated," they wrote.

Microscopic colitis includes lymphocytic and collagenous subtypes, neither of which is grossly apparent on colonoscopy. "Endoscopists therefore often collect multiple random colonic biopsies, potentially oversampling, increasing times of colonoscopy and slide review," Dr. Virine and his associates wrote.

To better pinpoint optimal biopsy sites and specimen numbers, they studied 101 patients consecutively diagnosed with biopsy-confirmed microscopic colitis at London Health Sciences Centre from 2017 through 2018. Patients with other colonic diseases were excluded. Dr. Virine assessed all individual biopsy fragments, and another pathologist performed a second review of complex cases.

A total of 52 patients had biopsy-confirmed collagenous colitis – that is, normal crypt architecture, increased mononuclear inflammatory cells in the lamina propria, and a thickened subepithelial collagen band. Forty-two patients had lymphocytic colitis, defined as normal crypt architecture, increased mononuclear inflammatory cells in the lamina propria, and increased intraepithelial lymphocytosis. Seven patients had both disease subtypes.

For each patient, an average of nine (standard deviation, 4.9) biopsies had been collected. The most commonly sampled site was the ascending colon (biopsied in 47% of patients in whom at least one sample was labeled by site), followed by the descending colon (40%), rectum (21%), transverse colon (20%), sigmoid colon (15%), cecum (8%), and splenic and hepatic flexures (2% each). Diagnostic sensitivity was highest for the ascending colon (97%), transverse colon (96%), and sigmoid colon (91%) and lowest for the splenic flexure (75%), hepatic flexure (78%), and rectum (82%). The diagnostic sensitivity of the descending colon was 85%. However, all 39 patients with biopsies of both the ascending and descending colon had at least one biopsy that was positive for microscopic colitis (sensitivity, 100%).

"Based on the results of our study, collecting biopsy specimens from both the ascending and descending colons has the same overall sensitivity as following the guidelines," the researchers concluded.

Dr. Virine and the senior author reported having no conflicts of interest. One coauthor disclosed ties to AbbVie, Allergan, Ferring, Janssen, Lupin Pendopharm, Pfizer, Shire, and Takeda.

ginews@gastro.org

SOURCE: Virine B et al. Clin Gastroenterol Hepatol. 2020 Feb 25. doi: 10.1016/j.cgh.2020.02.036.

Microscopic colitis is a common cause of watery diarrhea. This debilitating disease is easy to treat, but the diagnosis can be challenging. Guidelines recommend colonoscopy with at least two biopsies from the right, transverse, descending, and sigmoid colon (total: eight-plus biopsies). With little evidence to guide this recommendation, this time-consuming protocol was proposed to minimize the risk of false-negative results.


Dr. Peery

This study by Virine and colleagues determined that a colonoscopy with two biopsies from the ascending and two biopsies from the descending colon (total: four biopsies) detects all patients with microscopic colitis. Biopsies of the rectosigmoid alone were insufficient. This work suggests that we can rule out a diagnosis of microscopic colitis by taking at least 50% fewer biopsies.

A more efficient and less invasive procedure is better for patients as sedation time and sampling the colon are associated with risks. In the future, a prospective, colonoscopy-based study in patients with diarrhea will allow us to confirm the optimal number and location of biopsies needed to establish a diagnosis of microscopic colitis. This work will be important to inform diagnostic guidelines and change practice.

Anne F. Peery, MD, MSCR, is assistant professor of medicine, division of gastroenterology and hepatology, University of North Carolina School of Medicine, Chapel Hill. She has no conflicts of interest.

Continued from previous page

ence emerged only when comparing chromoendoscopy with standard (not high-definition) white-light endoscopy. "Thus, the evidence in support of chromoendoscopy using high-definition endoscopes is weak," the researchers wrote.

For the study, they prospectively enrolled 305 patients with ulcerative colitis or Crohn's disease who were referred for surveillance colonoscopy at an academic hospital in Sweden from March 2011 through April 2016. Participants were randomly assigned to receive either high-definition chromoendoscopy with indigo carmine (152 patients) or high-definition white-light endoscopy (153 patients).

In the intention-to-diagnose analysis, dysplasias were detected in 17 (11%) patients evaluated by high-definition chromoendoscopy, compared with 7 (5%) patients evaluated by high-definition white-light endoscopy ($P = .032$). After excluding 20 patients for inadequate bowel preparation, 18 patients for protocol violations, and 4 patients for incomplete colonoscopies, the per-protocol population consisted of 263 patients. Dysplasias were detected in 12% of patients evaluated by high-definition chromoendoscopy and in 5% of those evaluated by high-definition white-light endoscopy ($P = .027$).

All patients also had 32 samples collected by random biopsy, which used to be standard for detecting dysplasia in inflammatory bowel disease but has become more controversial in the era of video endoscopy, the researchers noted. In all, random biopsy evaluation identified dysplasias in nine patients, including six in the high-definition chromoendoscopy group and three in the high-definition white-light endoscopy group. Random biopsies were low yield, identifying dysplasias in 0.092% of all specimens and 3% of colonoscopies. However, 20% of patients with dysplasias were identified only through random biopsy. This finding resembles that of another recent randomized trial in which 13% of patients with inflammatory bowel disease had dysplasias detected only through random biopsy (Gut. 2018;67:616-24), the researchers noted.

They also evaluated the number of macroscopic dysplastic lesions identified for every 10 minutes of colonoscope withdrawal time. These numbers were not significantly different in the intention-to-diagnose analysis (0.066 lesions in the high-definition chromoendoscopy group vs. 0.027 lesions in the high-definition white-light endoscopy group; $P = .056$). However, the per-protocol analysis revealed a significant difference (0.073 vs. 0.029 dysplastic lesions, respectively; $P = .031$).

"Based on our findings, we recommend the use of high-definition chromoendoscopy in inflammatory bowel disease surveillance," the researchers concluded. They acknowledged several limitations: The study included patients from only one center, most dyplastic lesions were small and, thus, had an unclear natural history, and the endoscopists included both experts and nonexperts.

The Stockholm City Council provided funding. The researchers reported having no conflicts of interest.

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SOURCE: Alexandersson B et al. Clin Gastroenterol Hepatol. 2020 Apr 27. doi: 10.1016/j.cgh.2020.04.049.

Real-time, computer-aided system significantly improved adenoma detection

BY AMY KARON
MDedge News

A real-time, computer-aided system using artificial intelligence significantly improved adenoma detection during high-definition colonoscopy in a multicenter, randomized clinical trial.

The adenoma detection rate was 55% in the intervention group and 40% in the control group, Alessandro Repici, MD, PhD, and his associates wrote in Gastroenterology. Improved detection of smaller adenomas explained the difference. After age, sex, and indication for colonoscopy were controlled for, computer-aided detection (CADe) increased the probability of adenoma detection by 30% (risk ratio, 1.30; 95% confidence interval, 1.14-1.45).

The CADe system did not increase the likelihood of resecting nonneoplastic lesions (26% versus 29% in the control group), said Dr. Repici, of Humanitas Research Hospital in Milano, Italy. "The per-protocol analysis produced similar results," he and his associates wrote. "The substantial improvement for adenoma detection rate and mean number of adenomas per colonoscopy, without increasing the removal of nonneoplastic lesions, is likely to improve the quality of colonoscopy without affecting its efficiency."

Screening colonoscopies miss about 25% of adenomas, increasing patients' risk for colorectal cancer. Although real-time CADe systems can identify colorectal neoplasias, comprehensive studies of the effect of CADe systems on adenoma detection and other colonoscopy quality measures are lacking.

The study included 685 adults from three centers in Italy who underwent screening colonoscopies for colorectal cancer, postpolypectomy surveillance, or workup based on a positive fecal immunochemical test or signs and symptoms of colorectal cancer. Patients were randomly assigned on a one-to-one basis to receive high-definition colonoscopies with or without the CADe system, which consists of an artificial intelligence–based medical device (GI Genius, Medtronic) that processes colonoscopy images in real time and superimposes a green box over suspected lesions. Six experienced endoscopists performed the colonoscopies; the minimum withdrawal time was 6 minutes, and histopathology was the reference standard.

The average number of adenomas detected per colonoscopy was 1.1 (standard deviation, 0.5) in the CADe group and 0.7 (SD, 1.2) in the control group, for an incidence rate ratio of 1.46 (95% CI, 1.15-1.86). The CADe system also significantly improved the detection of adenomas measuring 5 mm or less (34% vs. 27% in the control group; RR, 1.26; 95% CI, 1.01-1.52) and adenomas measuring 6-9 mm (11% vs. 6%, respectively; RR, 1.78; 95% CI, 1.09-2.86). Detection of larger adenomas did not significantly differ between groups. These findings did not vary based on adenoma morphology (polypoid or nonpolypoid) or location (proximal or distal colon), the researchers said.

Detection of multiple adenomas also was higher in the intervention group than in the control group (23% vs. 15%, respectively; RR, 1.50; 95% CI, 1.19-1.95). There were no significant differences in the detection of sessile serrated lesions (7% and 5%) and nonneoplastic lesions (20% and 17%). Average withdrawal times did not significantly differ between groups (417 seconds for CADe and 435 seconds for the control group).

The CADe system is a convolutional neural network that was trained and validated using a series of more than 2,600 histologically confirmed polyps from 840 participants in a prior clinical trial (Gastroenterology 2019;156:2198-207.e1). The system takes an average of 1.5 microseconds to output processed images.

"The addition of real-time CADe to colonoscopy resulted in a 30% and 46% relative increase in adenoma detection rate and the average number of adenomas detected per colonoscopy, demonstrating its efficacy in improving the detection of colorectal neoplasia at screening and diagnostic colonoscopy," the investigators wrote. "[The s]afety of CADe was demonstrated by the lack of increase of both useless resections and withdrawal time, as well as by the exclusion of any underskilling in the study period."

Medtronic loaned the equipment for the study. Dr. Repici and the senior author disclosed consulting fees from Medtronic.

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SOURCE: Repici A et al. Gastroenterology. 2020 May 3. doi: 10.1053/j.gastro.2020.04.062.

Characterization of norovirus immunity in nonsecretor adults

BY AMY KARON
MDedge News

Among nonsecretors – individuals who express a less diverse array of fucosylated histoblood group antigen carbohydrates (HBGAs) and consequently are less susceptible to some norovirus strains – natural infection with norovirus strain GII.2 induced cellular and antibody immunity that lasted for at least 30 days for T cells, monocytes, and dendritic cells and for at least 180 days for blocking antibodies, researchers reported.

"Multiple cellular lineages expressing interferon-gamma and tumor necrosis factor [TNF]–alpha dominated the response. Both T-cell and B-cell responses were cross-reactive with other GII strains, but not GI strains," Lisa C. Lindesmith of the University of North Carolina, Chapel Hill, and her associates wrote in Cellular and Molecular Gastroenterology and Hepatology. The researchers also found

Continued on following page

Noroviruses belonging to genogroup II.4 are the leading cause of acute gastroenteritis, but our understanding of norovirus immunity remains incomplete. Most studies have focused on humoral responses and have shown that antibodies may be short lived, strain specific, and not always protective against rechallenge. On the other hand, human innate and T-cell immunity have received little attention despite evidence from the mouse norovirus model that they are critical for limiting viral spread and clearing antigen.


Dr. Tomov

In this study, Lindesmith et al. conducted broad phenotypic and functional analysis of innate and adaptive immune responses following infection with a GII.2 strain of norovirus. Their cohort consists of "nonsecretors," subjects who express a limited repertoire of histoblood group antigens and are therefore naturally resistant to GII.4 infection. Since nonsecretors have no pre-existing immunity against GII.4 viruses, this system enables the authors to test cross-reactivity of GII.2-specific T cells against GII.4 virus-like particles (VLPs).

The authors showed broad immune activation against natural norovirus infection. Following GII.2 infection, T-cell responses persist for at least a month and, importantly, are cross-reactive against GII.4 VLPs. These findings suggest that T cells may target conserved viral epitopes and play an important role in long-term protection against reinfection.

Developing an effective norovirus vaccine will require a detailed understanding of immune correlates of protection, and this study is a step in the right direction. In future work, tracking epitope-specific T cells must further define the phenotype, functionality, and localization of the norovirus T-cell repertoire.

Vesselin Tomov, MD, PhD, is assistant professor of medicine at the Hospital of the University of Pennsylvania, Philadelphia. He has no conflicts of interest.

Continued from previous page

salts enable GII.2 to bind HBGAs produced by nonsecretors. "[I]n addition to HBGAs, one or more specific components of bile also is likely to be an essential co-factor for human norovirus attachment and infection," the researchers wrote.

Susceptibility to norovirus depends on whether individuals express secretor enzyme, which is encoded by the FUT2 gene. Nonsecretors (who are FUT2–/–) express less varied HBGA, are susceptible to fewer norovirus strains, and are resistant to the predominant norovirus strain, GII.4. "Because future human norovirus vaccines will comprise GII.4 antigen, and because secretor phenotype impacts GII.4 infection and immunity, nonsecretors may mimic young children immunologically in response to GII.4 vaccination," the researchers explained. But until now, most vaccines have focused on adult secretors, they said.

Their study focused on a familial norovirus outbreak in Chapel Hill that was the first to be characterized among nonsecretors who were naturally infected with norovirus GII.2. Four adults provided blood samples, and one provided a stool sample from which the researchers isolated and cloned the G11.2 capsid gene sequence. They used neutralization assays to study serologic immunity

Bile acids 'may override the genetic advantage of less-diverse HBGA expression in nonsecretors by improving the avidity of GII.2 binding to nonsecretor HBGAs, potentially paving the way for infection.'

and flow cytometry to assess cellular activation and cytokine production in blood samples from the four cases and from seven healthy donors.

Norovirus GII.2 infection activated both innate and adaptive immunity and typical production of antiviral helper T cell (Th)1 and Th2 cytokines. The cellular immune response lasted at least 30 days, "long after symptom resolution," the investigators wrote.

Compared with healthy donors, blood specimens from infected nonsecretors showed increases in non-class-switched memory, transitional B cells, and plasmablast B cells, and both naive and memory B cells also were positive for activation markers for at least 30 days after infection. Activated interferon-gamma+ T cells, natural killer cells, TNF-alpha+ monocytes, interleukin-10+, TNF-alpha+ myeloid dendritic cells, and TNF plasmacytoid dendritic cells also persisted for at least 30 days. Cross-reactive GII immunity was evident for at least 180 days. "GII.2 infection boosted cross-reactive blocking antibodies to GII.3, GII.14, and GII.17, as well as T-cell responses to GII.4, despite the lack of clear serologic evidence of previous GII.4 exposure," the investigators wrote.

Based on prior reports that bile enhances norovirus growth or ligand binding, they inoculated specimens with chenodeoxycholic acid (CDCA) and glycochenodeoxycholic acid (GCDCA), pig bile, ox bile, or

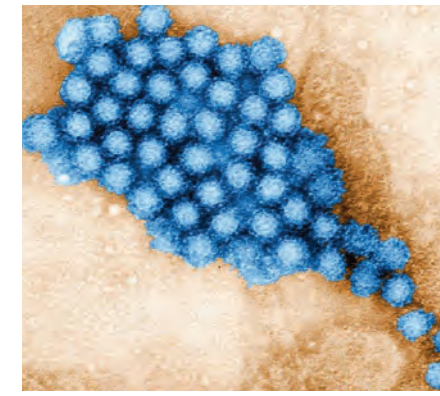

Photo Charles D. Humphrey, USCDCP/Pixnio

Norovirus is shown by electron micrograph.

human bile. "Strikingly, the addition of bile enabled GII.2 Chapel Hill outbreak virus-like particle to bind to saliva from the four nonsecretor donors," the researchers wrote. Bile acids "may override the genetic advantage of less-diverse HBGA expression in nonsecretors by improving the avidity of GII.2 binding to nonsecretor HBGAs, potentially paving the way for infection." However, bile salts did not enable the GII.2 strain to replicate in human intestinal enteroid cells, which suggests that additional factors play into how norovirus enters human cells, according to the researchers.

The findings, they wrote, "support development of within-genogroup, cross-reactive antibody and T-cell immunity, key outcomes that may provide the foundation for eliciting broad immune responses after GII.4 vaccination in individuals with limited GII.4 immunity, including young children."

The National Institutes of Health, the Wellcome Trust, the Centers for Disease Control and Prevention, and a Cancer Center Core support provided funding. Ms. Lindesmith and her associates reported having no relevant conflicts of interest.

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SOURCE: Lindesmith LC et al. Cell Molec Gastroenterol Hepatol. 2020 doi: 10.1016/j.jcmgh.2020.03.006.

AGA announces 6-point commitment to equity

With a long-standing interest in diversity, recent events in the United States have intensified the AGA Governing Board's interest in making a significant impact on the goals enumerated in our diversity policy.

Under the leadership of Dr. Sandra Quezada, AGA Diversity Committee chair, and Dr. Byron Cryer, director of the National Institutes od Health–funded Fostering Opportunities Resulting in Workforce and Research Diversity (FORWARD Program), the AGA Equity Project task force will develop a multi-year strategic plan to achieve the following aims:

- A just world free of health disparities in digestive diseases and inequities in access and effective health care delivery.
- State-of-the-art and well-funded research that aligns with the realities of the current multicultural patient population and disease states to achieve health equity for all.
- A world where it is expected and normal that both members and society leadership structures are diverse, and people of color and women are included in organizational decision-making.
- Recognition of accomplishments of diverse leaders. In addition, all leaders recognize, inspire, and cultivate the next generation of prominent, diverse leaders.
- An engaged AGA membership and staff educated about unconscious bias and committed to the eradication of racism and prejudice toward patients, colleagues, and communities.
- The existence of a diverse, culturally and socially aware, large and vocal early-career membership that leads the field toward achieving the vision.

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AGA journals' Impact Factors released: CMGH receives its first

AGA is proud to announce that its journals have maintained their excellent standing in the field of gastroenterology and hepatology, based on Impact Factor. The Impact Factor is a measure of the frequency with which articles published in the previous 2 years are cited and is commonly used to rank the significance of journals within their fields.

Particularly exciting is that *Cellular and Molecular Gastroenterology and Hepatology* (*CMGH*), AGA's basic and translational open-access journal has received its first Impact Factor – 7.076 – placing it 15th in a field of 88 journals in gastroenterology and hepatology, and second among nonclinical journals in that topic area. This outstanding debut is a testament to the rigor and dedication of the journal's founding editors Jerrold Turner, MD, PhD, AGAF, Jim Goldenring, MD, PhD, AGAF, Rebecca Wells, MD, AGAF; Maria Rescigno, PhD; and managing editor Lindsey Brounstein. Dr. Turner, his board, and many others worked tirelessly to publish only the highest-quality basic and translational digestive biology research.

Dr. Turner reflected, "At its inception, Jim, Becky, and I envisioned an author- and reader-friendly forum for the best translational and basic gastroenterology and hepatology research. The rapidity with which *CMGH* has grown reflects the intense need for such a venue and the contributions of authors, reviewers, and readers who were willing to 'bet' on the journal."

Michael Pack, MD, and Klaus Kaestner, PhD, add "We and our associate editors Alison Simmons, Thomas Luedde, and Jonathan Katz are extremely grateful to the prior *CMGH* board of editors for making *CMGH* an impactful platform for the rapid dissemination of high-quality peer-reviewed research in our field of digestive organ biology and disease. As we celebrate the remarkable success and achievement of *CMGH*, we remind our readers, contributors, reviewers, and friends that all credit goes to Jerry, Rebecca, Jim, and Maria. Thank you!"

Clinical Gastroenterology and Hepatology (*CGH*), AGA's clinically focused journal, hit its highest-ever Impact Factor at 8.549, ranking 10th in the field. Fasiha Kanwal, MD, MSHS, editor-in-chief of *CGH*, said, "We are delighted that *CGH* remains in a strong position in the top 10 GI journals in terms of Impact Factor. *CGH's* Impact Factor rose from 7.683 in 2017 to 8.549 in 2019 (11.3 percentage point increase). On behalf of the *CGH* board of editors, I want to extend a warm and most heartfelt thanks to our authors, reviewers, and readers! We would not have been able to achieve this milestone without your support, contributions and the faith that you place in us."

Gastroenterology, AGA's flagship journal, received an Impact Factor of 17.373, retaining its position among an elite group of journals focused on publishing original research spanning basic to clinical fields in gastroenterology and hepatology. Co-editors-in-chief Richard M. Peek Jr, MD, and Douglas A. Corley, MD, PhD, remark "We would like to thank our entire board of editors and reviewers, as well as the incredible AGA editorial staff, for their exceptional work as we continue to publish articles and reviews of outstanding quality that are widely used by our readership. It is an honor to be part of such a remarkable team."

AGA congratulates and thanks the boards of all three journals for their editorial leadership. We also thank our authors, readers, and reviewers for their continued support of AGA's journals.

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DDSEP 9
Digestive Diseases Self-Education Program

Quick Quiz

Q1. A 56-year-old woman presents for evaluation of right upper–quadrant pain. Her medical history is remarkable for obesity with a BMI of 31 kg/m^2, hyperlipidemia, diabetes mellitus, NASH cirrhosis, and a recent admission for melena. During her prior admission, she was treated with a proton pump inhibitor and octreotide. Esophagogastroduodenoscopy revealed a gastric ulcer with signs of recent bleeding and small esophageal varices without red wale signs.

Her lab evaluation is as follows: AST, 69 U/L; ALT, 35 U/L; total bilirubin, 1.6 mg/dL; alkaline phosphatase, 121 U/L; leukocytes 7,500/microL. An abdominal ultrasound is notable for a positive sonographic Murphy's sign, cholelithiasis, an 8-mm gallbladder wall, normal-appearing bile ducts, and a cirrhotic-appearing liver with splenomegaly. She undergoes cholecystectomy. Examination of the gallbladder reveals numerous hard gallstones, which are predominately composed of calcium bilirubinate.

Which of the following is the most likely risk factor for gallstones in this patient?

A. Cirrhosis
B. Obesity
C. Recent octreotide use
D. Gender
E. Hyperlipidemia

Q2. A 62-year-old man with hepatitis C cirrhosis is admitted with altered mental status. He had a recent dental procedure and was given pain medication and a short course of antibiotics. He is taking only spironolactone 50 mg for small ascites. Patient is alert but not oriented to place and time. He has evidence of asterixis. His mucous membranes are dry and he has no evidence of ascites on exam. His labs include WBC, 4.7 × 10^3 mm^3; AST, 45 U/L; ALT, 40 U/L; total bilirubin of 2.5 mg/dL; albumin, 3.7 g/dL; sodium, 142 mEq/L; and creatinine, 0.5 mg/dL.

What is the LEAST likely etiology of his encephalopathy?

A. Infection
B. Constipation
C. Narcotic use
D. Volume overload
E. Gastrointestinal bleeding

The answers are on page 30.

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

COVID-associated pancreatitis may be distinct

BY WILL PASS
MDedge News

Patients with COVID-19 develop a distinct subset of pancreatitis hallmarked by duodenal and periduodenal inflammation, according to a recent case series.

Although all five patients presented with many predictive markers of severe pancreatitis, the clinical pathway "was much more benign than anticipated," reported lead author Peter Szatmary, MB, BChir, PhD, of the University of Liverpool (England) and colleagues. Still, they noted long hospital stays because of inflammation and poor diabetic control.

For this series, Dr. Szatmary and colleagues restricted diagnosis of pancreatitis to international consensus guidelines, which require "abdominal pain consistent with pancreatitis, serum amylase/lipase greater than three times the upper limit of normal, and characteristic findings on cross-sectional imaging."

From the middle of March to late April, the investigators identified 35 patients with acute pancreatitis at Royal Liverpool University Hospital, 25 of whom tested negative for SARS-CoV-2, which resulted in study exclusion. "The remaining 5 patients, all with SARS-CoV-2, presented atypically yet homogenously with a distinct metabolic-pancreatitis phenotype," the investigators wrote.

All five patients were obese or overweight young men with a median body mass index of 30 kg/m^2 and age of 42 years. On presentation, all patients had elevated, but nondiagnostic, levels of amylase (median, 149 U/L). Contrast-enhanced abdominal CT revealed moderate to severe hepatic steatosis (less than 104 HU), which rapidly regressed within a week in patients who underwent repeat imaging.

The investigators described "mild pancreatic edema without significant pancreatic or peripancreatic necrosis, with distinct duodenal/periduodenal inflammation involving the second and third part of the duodenum."

According to Dr. Szatmary and colleagues, these findings were "accompanied by a profound systemic inflammatory response," including 1-2 criteria for systemic inflammatory response syndrome that increased to 2-4 criteria within 48 hours. During hospitalization, patients also exhibited a "dramatic elevation" of C-reactive protein, from a median of 31 mg/L on admission to 485 mg/L in 48 hours.

All patients were treated with IV fluids, four of five received broad-spectrum IV antibiotics for pneumonitis, three of five received fibrate or insulin therapy, and two of five received pancreatic enzyme replacement.

The investigators reported grants from NIHR, Wellcome Trust, Mylan, and others.

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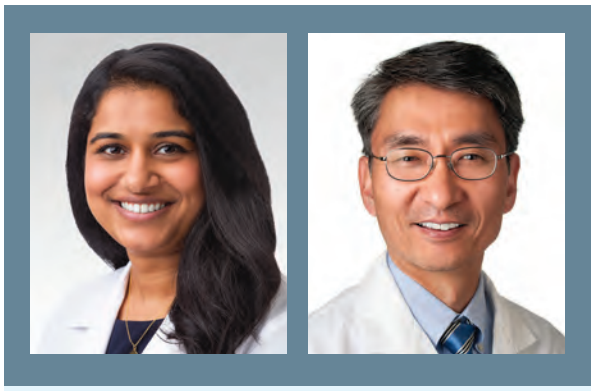
SOURCE: Szatmary P et al. Gastroenterology. 2020 Jun 1. doi: 10.1053/j.gastro.2020.05.069.

Eosinophilic esophagitis: Frequently asked questions (and answers) for the early-career gastroenterologist

BY RONAK PATEL, MD, AND IKUO HIRANO, MD, AGAF



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Dr. Hirano is professor of medicine, division of gastroenterology and hepatology, Northwestern University, Chicago.

Introduction

Eosinophilic esophagitis (EoE) has transformed over the past 3 decades from a rarely encountered entity to one of the most common causes of dysphagia in adults.[1] Given the marked rise in prevalence, the early-career gastroenterologist will undoubtedly be involved with managing this disease.[2] The typical presentation includes a young, atopic male presenting with dysphagia in the outpatient setting or, more acutely, with a food impaction when on call. As every fellow is keenly aware, the calls often come late at night as patients commonly have meat impactions while consuming dinner. Current management focuses on symptomatic, histologic, and endoscopic improvement with medication, dietary, and mechanical (i.e., dilation) modalities.

EoE is defined by the presence of esophageal dysfunction and esophageal eosinophilic inflammation with ≥15 eosinophils/high-powered field (eos/hpf) required for the diagnosis. With better understanding of the pathogenesis of EoE involving the complex interaction of environmental, host, and genetic factors, advancements have been made as it relates to the diagnostic criteria, endoscopic evaluation, and therapeutic options. In this article, we review the current management of adult patients with EoE and offer practical guidance to key questions for the young gastroenterologist as well as insights into future areas of interest.

What should I consider when diagnosing EoE?

Symptoms are central to the diagnosis and clinical presentation of EoE. In assessing symptoms, clinicians should be aware of adaptive "IMPACT" strategies patients often subconsciously develop in response to their chronic and progressive condition: **I**mbibing fluids with meals, **m**odifying foods by cutting or pureeing, **p**rolonging meal times, **a**voiding harder texture foods, **c**hewing excessively, and **t**urning away tablets/pills.[3] Failure to query such adaptive behaviors may lead to an underestimation of disease activity and severity.

An important aspect to confirming the diagnosis of EoE is to exclude other causes of esophageal eosinophilia. Gastroesophageal reflux disease (GERD) is known to cause esophageal eosinophilia and historically has been viewed as a distinct disease process. In fact, initial guidelines included lack of response to a proton pump inhibitor (PPI) trial or normal esophageal pH monitoring as diagnostic criteria.[4] However, as experience was garnered, it became clear that PPI therapy was effective at improving inflammation in 30%-50% of patients with clinical presentations and histologic features consistent with EoE. As such, the concept of PPI–responsive esophageal eosinophilia (PPI-REE) was introduced in 2011.[5] Further investigation then highlighted that PPI-REE and EoE had nearly identical clinical, endoscopic, and histologic features as well as eosinophil biomarker and gene expression profiles. Hence, recent international guidelines no longer necessitate a PPI trial to establish a diagnosis of EoE.[6]

The young gastroenterologist should also be mindful of other issues related to the initial diagnosis of EoE. EoE may present concomitantly with other disease entities including GERD, "extra-esophageal" eosinophilic gastrointestinal diseases, concomitant IgE-mediated food allergy, hypereosinophilic syndromes, connective tissue disorders, autoimmune diseases, celiac disease, and inflammatory bowel disease.[3] It has been speculated that some of these disorders share common aspects of genetic and environmental predisposing factors as well as shared pathogenesis. Careful history taking should include a full review of atopic conditions and GI-related symptoms and endoscopy should carefully inspect not only the esophagus, but also gastric and duodenal mucosa. The endoscopic features almost always reveal edema, rings, exudates, furrows, and strictures and can be assessed using the EoE Endoscopic Reference Scoring system (EREFS).[7] EREFS allows for systematic identification of abnormalities that can inform decisions regarding treatment efficacy and decisions on the need for esophageal dilation. When the esophageal mucosa is evaluated for biopsies, furrows and exudates should be targeted, if present, and multiple biopsies (minimum of five to six) should be taken throughout the esophagus given the patchy nature of the disease.

How do I choose an initial therapy?

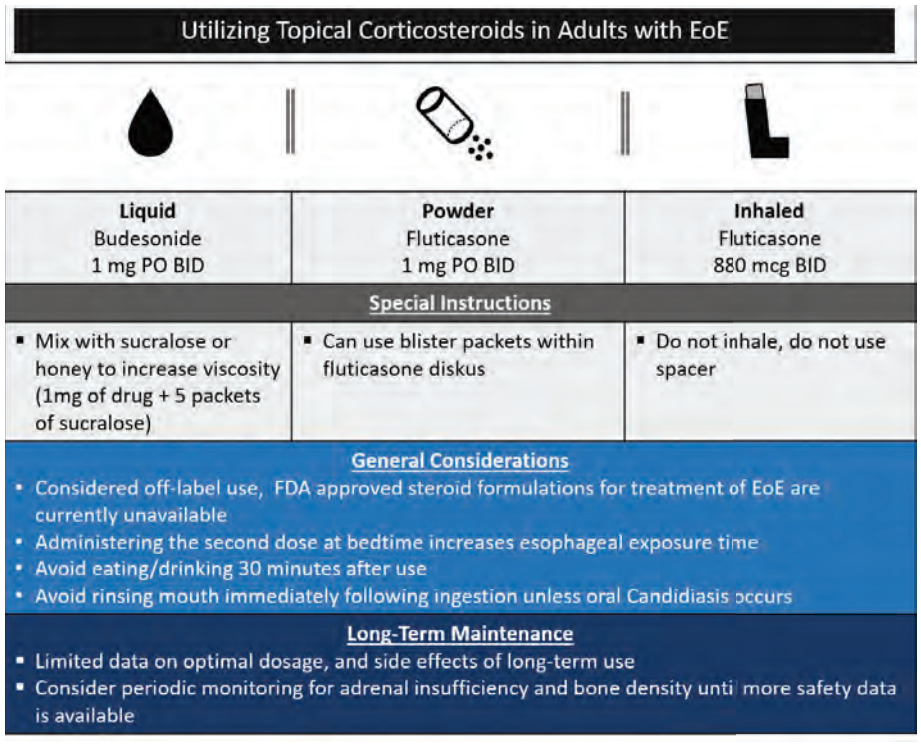
The choice of initial therapy considers patient preferences, medication availability, disease severity, impact on quality of life, and need for repeated endoscopies. While there are many novel agents currently being investigated in phase 2 and 3 clinical trials, the current mainstays of treatment include PPI therapy, topical steroids, dietary therapy, and dilation. Of note, there have been no head-to-head trials comparing these different modalities. A recent systematic review reported that PPIs can induce histologic remission in 42% of patients.[8] The ease of use and availability of PPI therapy make this an attractive first choice for patients. Pooled estimates show that topical steroids can induce remission in 66% of patients.[8] It is important to note that there is currently no Food and Drug Administration–approved formulation of steroids for the treatment of EoE. As such, there are several practical aspects to consider when instructing patients to use agents not designed for esophageal delivery (Figure 1).

Lack of insurance coverage for topical steroids can make cost of a prescription a deterrent to use. While topical steroids are well tolerated, concerns for candidiasis and adrenal insufficiency are being monitored in prospective, long-term clinical trials. Concomitant use of steroids with PPI would be appropriate for EoE patients with coexisting GERD (severe heartburn, erosive esophagitis, Barrett's esophagus). In addition, we often combine steroids with PPI therapy for EoE patients who demonstrate a convincing but incomplete response to PPI monotherapy (i.e.,

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease process triggered by food antigens. EoE has emerged in the last few decades as an entity distinct from gastroesophageal reflux disease, as eosinophils in the esophagus previously were considered to be a histologic feature only of reflux. It is now inevitably encountered by gastroenterologists as one of the most common etiologies of dysphagia and food impactions.

The In Focus article for this quarter, which is brought to you by *The New Gastroenterologist*, provides an excellent, high-yield review of EoE, written by Dr. Ronak Patel and Dr. Ikuo Hirano (Northwestern). This comprehensive piece seeks to answer frequently asked questions about EoE, specifically regarding diagnostic considerations and the approach to management by reviewing both pharmacologic and dietary interventions. It will certainly serve as a valuable guide to the young gastroenterologist.

Vijaya L. Rao, MD
Editor in Chief, The New Gastroenterologist



Dr. Ronak Patel and Dr. Ikuo Hirano, Northwestern University

Figure 1. Utilizing topical corticosteroids in adults with EoE.

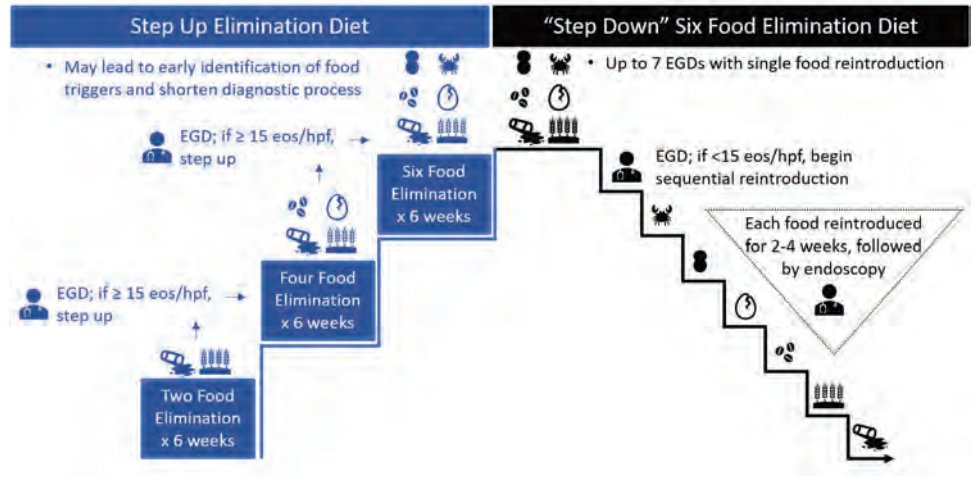
reduction of baseline inflammation from 75 eos/hpf to 20 eos/hpf).

Diet therapy is a popular choice for management of EoE by patients, given the ability to remove food triggers that initiate the immune dysregulation and to avoid chronic medication use. Three dietary options have been described including an elemental, amino acid–based diet which eliminates all common food allergens, allergy testing–directed elimination diet, and an empiric elimination diet. Though elemental diets have shown the most efficacy, practical aspects of implementing, maintaining, and identifying triggers restrict their adoption by most patients and clinicians.[9] Allergy-directed elimination diets, where allergens are eliminated based on office-based allergy testing, initially seemed promising, though studies have shown limited histologic remission, compared with other diet therapies as well as the inability to identify true food triggers. Advancement of office-based testing to identify food triggers is needed to streamline this dietary approach. In the adult patient, the empiric elimination diet remains an attractive choice of the available dietary therapies. In this dietary approach, which has shown efficacy in both children and adults, the most common food allergens (milk, wheat, soy, egg, nuts, and seafood) are eliminated.[9]

How do I make dietary therapy work in clinical practice?

Before dietary therapy is initiated, it is important that your practice is situated to support this approach and that patients fully understand the process. A multidisciplinary approach optimizes dietary therapy. Dietitians provide expert guidance on eliminating trigger foods, maintaining nutrition, and avoiding inadvertent cross-contamination. Patient questions may include the safety of consumption of non–cow-based cheese/milk, alcoholic beverages, wheat alternatives, and restaurant food. Allergists address concerns for a concomitant IgE food allergy based on a clinical history or previous testing. Patients should be informed that identifying a food trigger often takes several months and multiple endoscopies. Clinicians should be aware of potential food cost and accessibility issues as well as the reported, albeit uncommon, development of de novo IgE-mediated food allergy during reintroduction. Timing of diet therapy is also a factor in success. Patients should avoid starting diets during major holidays, family celebrations, college years, and busy travel months.

Particularly empiric elimination diets, frequently used in adults, several approaches have been described (Figure 2). Initially, a step-down approach was described, with patients pursuing a six-food elimination diet (SFED), which eliminates the six most common triggers: milk, wheat, soy/legumes, egg, nuts, and seafood. Once in histologic remission, patients then systematically reintroduce foods in order to identify a causative trigger. Given that many patients have only one or two identified food triggers, other approaches were created including a single-food elimination diet eliminating milk, the two-food elimination diet (TFED) eliminating milk and wheat, and the four-food elimination diet (FFED) eliminating milk, wheat, soy/legumes, and eggs. A novel step-up approach has also now been described where patients start with the TFED and progress to the FFED and then potentially SFED based on histologic response.[10] This approach has the potential to more readily identify triggers, decrease diagnostic time, and reduce endoscopic interventions. There are pros and cons to each elimination diet approach that should be discussed with patients. Many patients may find a one- or two-food elimination diet more feasible than a full SFED.



Dr. Ronak Patel and Dr. Ikuo Hirano, Northwestern University

Figure 2. Potential schema for empiric elimination diets.

What should I consider when performing dilation?

Esophageal dilation is frequently used to address the fibrostenotic complications of EoE that do not as readily respond to PPI, steroid, or diet therapy. The majority of patients note symptomatic improvement following dilation, though dilation alone does not address the inflammatory component of disease.[8] With a conservative approach, the complication rates of esophageal dilation in EoE are similar to that of benign, esophageal strictures. Endoscopists should be aware that endoscopy alone can miss strictures and consider both practical and technical aspects when performing dilations (Table 1).[11,12]

When should an allergist be consulted?

The role of the allergist in the management of patients with EoE varies by patient and practice. IgE serologic or skin testing have limited accuracy in identifying food triggers for EoE. Nevertheless, the majority of patients with EoE have an atopic condition which may include asthma, allergic rhinitis, atopic dermatitis, or IgE-mediated food allergy. Although EoE is thought to primarily occur from an immune response to ingested oral allergens, aeroallergens may exacerbate disease as evidenced by the seasonal variation in EoE symptoms in some patients. The allergist provides treatment for these "extraesophageal" atopic conditions which may, in turn, have synergistic effects on the treatment of EoE. Furthermore, allergists may prescribe biologic therapies that are FDA approved for the treatment of atopic dermatitis, asthma, and allergic rhinitis. While not approved for EoE, several of these agents have shown efficacy in phase 2 clinical trials in EoE. In some practice settings, allergists primarily manage EoE patients with the assistance of gastroenterologists for periodic endoscopic activity assessment.

What are the key aspects of maintenance therapy?

The goals of treatment focus on symptomatic, histologic, and endoscopic improvement, and the prevention of future or ongoing fibrostenotic complications.[2] Because of the adaptive eating behaviors discussed above, symptom response may not reliably correlate with histologic and/or endoscopic improvement. Moreover, dysphagia is related to strictures that often do not resolve in spite of resolution of mucosal inflammation. As such, histology and endoscopy are more objective and reliable targets of a successful response to therapy. Though studies have used variable esophageal density levels for response, using a cutoff of <15 eos/hpf as a therapeutic endpoint is reasonable for both initial response to therapy and long-term monitoring.[13] We advocate for standardization of reporting endoscopic findings to better track change over time using the EREFS scoring system.[7] While inflammatory features improve, the fibrostenotic features may persist despite improvement in histology. Dilation is

Continued on following page

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GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Cortisol levels may mark severity, hep C combo promising

BY LUCAS FRANKI
MDedge News

Cortisol levels at admission may mark COVID-19 severity

A study of patients admitted to major London hospitals for COVID-19 found that those with high levels of cortisol at admission were more likely to die from the disease.

Patients with COVID-19 had significantly higher levels of cortisol than those without COVID-19. Patients with COVID-19 who had a cortisol level at baseline above 744 nmol/L had a median survival of 15 days, while those with baseline cortisol below that level had a median survival of 36 days.

The study researchers noted that, while the steroid dexamethasone was shown in a trial to significantly reduce mortality among severely ill COVID-19 patients, those who suspect that they have the disease should not self-medicate because steroids increase cortisol levels and suppress the immune system.

Phase 3 COVID-19 vaccine trials underway

The Biomedical Advanced Research and Development Authority has awarded $2.5 billion to five different pharmaceutical companies to conduct phase 3 trials to test vaccines.

Some approaches for developing a vaccine include a whole, killed virus, or a live-attenuated vaccine, as well as novel approaches such as using a replication-defective adenovirus or injection of messenger RNA that codes for the coronavirus spike protein. The vaccines produced will not be licensed by the Food and Drug Administration, but will be approved through the Emergency Use Authorization program, and some will be mass produced at risk.

"These vaccines will be tested in tens of thousands of people, not tens of millions of people, so although you can disprove a relatively uncommon side effect preapproval, you're not going to disprove a rare side effect preapproval. You're only going to know that post approval," according to Paul A. Offit, MD, director of the Vaccine Education Center at the Children's Hospital of Philadelphia.

Sofosbuvir/daclatasvir combo promising for COVID-19

Sofosbuvir and daclatasvir, a combination whose safety for hepatitis C treatment has already been proven, significantly reduced time to recovery from COVID-19 and improved survival in people hospitalized with severe disease when taken for 14 days.

Patients treated with sofosbuvir/daclatasvir had a quicker recovery time than did those treated with hydroxychloroquine, and more patients in the sofosbuvir/daclatasvir group had recovered after 14 days. Patients who took sofosbuvir/daclatasvir were 70% more likely to survive.

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases, said that the study results are hopeful, "provocative, and encouraging," but that more data are needed before the sofosbuvir and daclatasvir combination can be added to the National Institutes of Health COVID-19 Treatment Guidelines.

MDedge associate editor Lucas Franki compiled this column from reports first published on MDedge.com and Medscape.com.

Continued from previous page

often performed in these situations, especially for symptomatic individuals.

During clinical follow-up, the frequency of monitoring as it relates to symptom and endoscopic assessment is not well defined. It is reasonable to repeat endoscopic intervention following changes in therapy (i.e., reduction in steroid dosing or reintroduction of putative food triggers) or in symptoms.[13] It is unclear if patients benefit from repeated endoscopies at set intervals without symptom change and after histologic response has been confirmed. In our practice, endoscopies are often considered on an annual basis. This interval is increased for patients with demonstrated stability of disease.

Table 1

Conservative approach to dilation in patients with eosinophilic esophagitis

Prior to dilation	
· Advise that dilation to a target of ≥16 mm may take multiple endoscopies, depending on initial diameter · Counsel patient on risks, including perforation · Discuss likelihood for significant postdilation odynophagia and/or chest pain	
During the dilation session	
· Know that proximal strictures or narrow caliber esophagus are difficult to appreciate by endoscopy · Know the diameter of endoscope and use retroflexion to estimate the diameter of distal esophagus · Determine your choice of dilator as below and start just below or at estimated diameter of the stricture	
Through the scope balloon	**Savary dilation**
· Focal, short-segment stricture · Position scope to view down barrel of balloon to assess for mucosal disruption · Consider balloon pullback to cervical esophagus to evaluate a possible missed proximal stricture	· Ideal for proximal or long strictures · Pay close attention to tactile resistance of dilator · Reintroduce endoscope to inspect mucosa after resistance if felt and/or after 1- to 2-mm increments in dilator size · Heme on the dilator is not a reliable marker of successful dilation
· Terminate session once significant mucosal disruption occurs · Biopsies should be taken after dilation, so mucosal disruption can be appropriately evaluated	
After the dilation	
· Assess the patient in recovery · Discuss findings and anticipated timing for future dilation · Counsel on warning signs and symptoms that would require prompt emergency room evaluation	

MDedge News

For patients who opt for dietary therapy and have one or two food triggers identified, long-term maintenance therapy can be straightforward with ongoing food avoidance. Limited data exist regarding long-term effectiveness of dietary therapy but loss of initial response has been reported that is often attributed to problems with adherence. Use of "diet holidays" or "planned cheats" to allow for intermittent consumption of trigger foods, often under the cover of short-term use of steroids, may improve the long-term feasibility of diet approaches.

In the recent American Gastroenterological Association guidelines, continuation of swallowed, topical steroids is recommended following remission with short-term treatment. The recurrence of both symptoms and inflammation following medication withdrawal supports this practice. Furthermore, natural history studies demonstrate progression of esophageal strictures with untreated disease.

There are no clear guidelines for long-term dosage and use of PPI or topical steroid therapy. Our practice is to down-titrate the dose of PPI or steroid following remission with short-term therapy, often starting with a reduction from twice a day to daily dosing. Although topical steroid therapy has fewer side effects, compared with systemic steroids, patients should be aware of the potential for adrenal suppression especially in an atopic population who may be exposed to multiple forms of topical steroids. Shared decision-making between patients and providers is recommended to determine comfort level with long-term use of prescription medications and dosage.

What's on the horizon?

Several areas of development are underway to better assess and manage EoE. Novel histologic scoring tools now assess characteristics on pathology beyond eosinophil density, office-based testing modalities have been developed to assess inflammatory activity and thereby obviate the need for endoscopy, new technology can provide measures of esophageal remodeling and provide assessment of disease severity, and several biologic agents are being studied that target specific allergic mediators of the immune response in EoE.[3,14-18] These novel tools, technologies, and therapies will undoubtedly change the management approach to EoE. Referral of patients into ongoing clinical trials will help inform advances in the field.

Conclusion

As an increasingly prevalent disease with a high degree of upper GI morbidity, EoE has transitioned from a rare entity to a commonly encountered disease. The new gastroenterologist will confront both straightforward as well as complex patients with EoE, and we offer several practical aspects on management. In the years ahead, the care of patients with EoE will continue to evolve to a more streamlined, effective, and personalized approach.

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

Look for these symptoms

Guideline *from page 1*

of COVID-19 infection and treatment," the panelists wrote in Gastroenterology. "Additionally, this document provides evidence-based clinical guidance on clinical questions that gastroenterologists may be consulted for."

The guideline includes seven best practice statements.

The first three statements relate to COVID-19–related GI symptoms, which are estimated to occur in less than 10% of patients, and rarely in the absence of other COVID-19–related symptoms, according to Dr. Sultan and her co-panelists.

"The overall prevalence of GI symptoms in the context of COVID-19, including nausea, vomiting, abdominal pain, and diarrhea, is lower than estimated previously," the panelists wrote, referencing a previous meta-analysis by Ka Shing Cheung, MBBS, and colleagues that showed a prevalence of 17.6% (Gastroenterology 2020 Apr 3. doi: 10.1053/j.gastro.2020.03.065).

Since GI issues may precede other symptoms of COVID-19, the guideline recommends questioning outpatients with new-onset GI symptoms about other symptoms of COVID-19, with viral testing recommended in areas of high prevalence. Conversely, the panelists recommended that patients with suspected or known COVID-19 should undergo thorough history taking for GI symptoms, "including onset, characteristics, duration, and severity."

The fourth practice statement advises against COVID-19 stool testing in routine clinical practice, either for diagnostic or monitoring purposes.

Although Dr. Cheung and colleagues reported that 48.1% of fecal specimens from patients with COVID-19 contained viral RNA, the panelists concluded that the practical relevance of this finding remains unknown.

The final three practice statements address liver concerns.

First, any patient with suspected or confirmed COVID-19 who has elevated liver function tests should be evaluated for alternative etiologies. Second, hospitalized patients with suspected or confirmed COVID-19 should undergo baseline liver function testing, followed by liver monitoring throughout their stay, "particularly in the context of drug treatment for COVID-19." And third, any patient receiving drugs to treat COVID-19 should be monitored for treatment-related hepatic and GI adverse effects.

Dr. Sultan and colleagues found that approximately 15% of patients with COVID-19 included in their meta-analysis had abnormal liver function tests, more often because of secondary effects rather than virally induced liver injury.

Although liver function test abnormalities were inconsistently reported across studies, and when available, often lacked relevant contextual data, such as information about underlying liver disease, published data suggest that abnormal liver values could predict more severe COVID-19, supporting baseline and serial liver testing, the panelists wrote.

Following these recommendations, the guideline includes a discussion of GI and hepatic adverse effects related to specific COVID-19 treatments.

According to the panelists, chloroquine and hydroxychloroquine may infrequently lead to GI disturbances, and rarely, liver injury,

The article was funded by the American Gastroenterological Association Institute.

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SOURCE: Sultan S et al. Gastroenterology. 2020 May 11. doi: 10.1053/j.gastro.2020.05.001.

BRCA role in PDAC may be small

Risk *from page 1*

to benefit from earlier and more frequent colonoscopies. Although the value of risk-based screening is less clear for other types of GI cancer, the investigators cited a growing body of evidence that supports screening individuals at high risk of PDAC.

Still, data illuminating the role of BRCA carrier status are relatively scarce, which has led to variability in clinical practice.

"Lack of accurate CRC and PDAC risk estimates in BRCA1 and BRCA2 leave physicians and patients without guidance, and result in a range of screening recommendations and practices in this population," wrote Dr. Kupfer and colleagues.

Subgroup analysis suggested that BRCA1 carriers drove this association, with a 49% increased risk of CRC, whereas no significant link was found with BRCA2.

To offer some clarity, they drafted the present clinical practice update on behalf of the AGA. The recommendations are framed within a discussion of relevant publications.

Data from multiple studies, for instance, suggest that BRCA pathogenic variants are found in 1.3% of patients with early-onset CRC, 0.2% of those with high-risk CRC, and 1.0% of those with any type of CRC, all of which are higher rates "than would be expected by chance.

"However," the investigators added, "this association is not proof that the observed BRCA1 and BRCA2 pathogenic variants play a causative role in CRC."

The investigators went on to discuss a 2018 meta-analysis by Oho et al., which included 14 studies evaluating risk of CRC among BRCA carriers. The analysis found that BRCA carriers had a 24% increased risk of CRC, which Dr. Kupfer and colleagues described as "small but statistically significant." Subgroup analysis suggested that BRCA1 carriers drove this association, with a 49% increased risk of CRC, whereas no significant link was found with BRCA2.

Dr. Kupfer and colleagues described the 49% increase as "very modest," and therefore insufficient to warrant more intensive screening, particularly when considered in the context of other risk factors, such as Lynch syndrome, which may entail a 1,600% increased risk of CRC. For PDAC, no such meta-analysis has been conducted; however, multiple studies have pointed to associations between BRCA and risk of PDAC.

For example, a 2018 case-control study by Hu et al. showed that BRCA1 and BRCA2 had relative prevalence rates of 0.59% and 1.95% among patients with PDAC. These rates translated to a 158% increased risk of PDAC for BRCA1, and a 520% increase risk for BRCA2; but Dr. Kupfer and colleagues noted that the BRCA2 carriers were from high-risk families, so the findings may not extend to the general population.

In light of these findings, the update recommends PDAC screening for BRCA carriers only if they have a family history of PDAC, with the caveat that the association between risk and degree of family involvement remains unknown.

Ultimately, for both CRC and PDAC, the investigators called for further BRCA research.

The investigators reported no relevant financial conflicts of interest.

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SOURCE: Kupfer SS et al. Gastroenterology. 2020 Apr 23. doi: 10.1053/j.gastro.2020.03.086.

Review the need for these drugs

PPIs *from page 1*

allow the virus to enter the GI tract more easily, leading to enteritis, colitis, and systemic spread to other organs, including the lungs.

To see how PPI use relates to COVID-19 infections, Dr. Spiegel and his colleagues surveyed online a nationally representative sample of Americans between May 3 and June 24, 2020, as part of a larger survey on gastroenterologic health.

Participants answered questions about gastrointestinal symptoms, current use of PPIs, and COVID-19 test results. They also answered questions about histamine-2 receptor agonists (H_2RAs), also known as H_2 blockers, which are used to treat some of the same conditions as PPIs but do not reduce stomach acid as much.

The surveying firm, Cint, contacted 264,058 people. Of the 86,602 eligible participants who completed the survey, 53,130 said they had experienced abdominal discomfort, acid reflux, heartburn, or regurgitation. These survey participants were subsequently asked about PPI and H_2RA use.

Of these, 6.4% reported testing positive for SARS-CoV-2. The researchers adjusted for age, sex, race/ethnicity, education, marital status, household income, body mass index, smoking, alcohol consumption, U.S. region, insurance status, and the presence of irritable bowel syndrome, celiac disease, gastroesophageal reflux disease, liver cirrhosis, Crohn's disease, ulcerative colitis, diabetes, and HIV/AIDS.

After adjusting for these factors, the researchers found that those who took PPIs up to once a day were twice as likely to have had a positive COVID-19 test result than those who did not take the drugs (odds ratio, 2.15; 95% confidence interval, 1.90-2.44).

Those who took PPIs twice a day were almost four times as likely to have tested positive for the disease (OR, 3.67; 95% CI, 2.93-4.60).

By contrast, those taking H_2RA drugs once daily were 15% less likely to report a positive COVID-19 test result (OR, 0.85; 95% CI, 0.74-0.99). Research is currently underway to determine whether H_2RAs might protect against the disease for reasons unrelated to pH balance.

Dr. Spiegel cautioned that the current data show only an association between PPI use and COVID-19 positivity; it cannot prove cause and effect.

Nevertheless, Dr. Spiegel said the findings should encourage physicians to prescribe PPIs only when clearly indicated. "If somebody is not yet on a PPI and you're considering whether to start them on a PPI, it's a good idea to consider H_2 blockers," he said.

People who need a daily dose of a PPI to control a severe condition can safely continue doing so, but such patients should take care to follow standard public health recommendations for avoiding exposure to the virus. These recommendations include wearing a mask, maintaining social distance, and washing hands frequently.

"People who are older, comorbid, or smokers – if they get infected, it could be severe," he said. "[For] someone like that, it's reasonable to ask, do we really need to be on twice-daily PPIs? There is good evidence that they are no better off than if they are taking once-daily doses."

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

Brian Lacy, MD, PhD, a professor of medicine at the Mayo Clinic in Jacksonville, Fla., agreed that the study should prompt physicians to take a second look at their patients' PPI prescriptions. "My view is that PPIs are frequently overused." On the other hand, the drugs are important for treating conditions such as erosive esophagitis and healing ulcers, he said. The overall risk of contracting COVID-19 is low, so even this finding of a 3.7-fold increased risk should not lead patients or providers to stop taking or prescribing PPIs.

The study lends support to the idea that the gastrointestinal tract could be involved in SARS-CoV-2 transmission, and it supports warnings about aerosols emitted from flushing toilets and through exhalation, Dr. Spiegel said. There is less evidence of the virus being transmitted through food. "It may not be fecal-oral; it may be fecal-respiratory," he said.

The study was part of a larger project funded by Ironwood. Dr. Spiegel reported relationships with Alnylam, Arena, Ironwood, Salix, Shire, Synergy, and Takeda. Dr. Lacy disclosed no relevant financial relationships.

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

AGA probiotic guidelines reveal shortage of data

BY WILL PASS
MDedge News

The role of probiotics in the management of gastrointestinal disorders remains largely unclear, according to clinical practice guidelines published by the American Gastroenterological Association (AGA).

Out of eight disorders reviewed by the guideline panel, four had enough relevant data to support conditional recommendations, while the other four were associated with knowledge gaps that precluded guidance, reported lead author Grace L. Su, MD, AGAF, of the University of Michigan, Ann Arbor, and colleagues.

"It is estimated that 3.9 million American adults used some form of probiotics or prebiotics ... in 2015," the guideline panelists wrote in Gastroenterology. "Given widespread use and often biased sources of information, it is essential that clinicians have objective guidance for their patients about the appropriate use of and indications for probiotics."

The creation of such guidance, however, proved a challenging task for the panel, who faced an "extremely varied" evidence base.

Dr. Su and colleagues encountered "differences in the strain of microbe(s) used, dose, and route of administration." They noted that such differences can significantly affect clinical outcomes.

"Within species, different strains can have widely different activities and biologic effects," they wrote. "Many immunologic, neurologic, and biochemical effects of gut microbiota are likely not only to be strain specific, but also dose specific. Furthermore, combinations of different microbial strains may also have widely different activity as some microbial activities are dependent on interactions between different strains."

Beyond differences in treatments, the investigators also reported wide variability in endpoints and outcomes, as well as relatively small study populations compared with pharmacologic trials.

Still, data were sufficient to provide some conditional recommendations.

The guidelines support probiotics for patients with pouchitis, those receiving antibiotic therapy, and preterm/low-birth-weight infants. (See related story on page 9.) In contrast, the panel recommended against probiotics for children with acute infectious gastroenteritis, noting that this recommendation differs from those made by other medical organizations.

"While other society guidelines have previously recommended the use of probiotics in [children with acute infectious gastroenteritis], these guidelines were developed without utilizing GRADE methodology and also relied on data outside of North America which became available after the recommendations were made," wrote Dr. Su and colleagues.

For *Clostridioides difficile* infection, Crohn's disease, ulcerative colitis, and irritable bowel syndrome, the panel recommended probiotics only in the context of a clinical trial, citing knowledge gaps in these areas.

They also noted that probiotics may not be suitable for those at high risk of infection. "[F]or patients who place a high value on avoidance of potential harms, particularly those with severe illnesses or immunosuppression, it would be reasonable to select not to use probiotics," the panelists wrote.

Concluding their discussion, Dr. Su and colleagues called for more high-quality research.

The investigators disclosed relationships with Nestex, AbbVie, Takeda, and others.

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SOURCE: Su GL et al. Gastroenterology. 2020 doi: 10.1053/j.gastro.2020.05.059.

Endoscopic full-thickness resection of colorectal lesions appears safe and effective

BY WILL PASS
MDedge News

Endoscopic full-thickness resection (eFTR) of complex colorectal lesions appears safe and effective, based on prospective data from 20 Dutch hospitals.

Macroscopic complete en bloc resection was achieved in 83.9% of procedures with an adverse event rate of 9.3%, reported lead author Liselotte W. Zwager, a PhD candidate at the University of Amsterdam, and colleagues.

"With the advantage of enabling a transmural resection, eFTR offers an alternative to radical surgery in lesions considered incurable with current resection techniques such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)," the investigators wrote in Endoscopy.

But more data are needed for widespread adoption, they noted. "Several studies have reported encouraging results on the short-term safety and efficacy of eFTR for numerous indications. However, firm conclusions on clinical results will require analysis of large prospective series of patients in everyday clinical practice."

The present study provided data from 362 patients who underwent 367 procedures at 5 academic and 15 nonacademic centers in the Netherlands.

Patients were eligible for eFTR if polyps were nonlifting or in difficult-to-reach locations, or if T1 colorectal cancer (CRC) was suspected. In addition, eFTR was performed for subepithelial tumors, and as secondary completion treatment after incomplete endoscopic resection of T1 CRC with a positive or nonassessable resection margin. Lesions greater than 30 mm were excluded because of device diameter constraints.

The primary outcome was macroscopic complete en bloc resection. Secondary outcomes included adverse events, full-thickness resection rate, and clinical success, the latter of which was defined by tumor-free resection margins (R0).

Out of 367 procedures, eFTR was most frequently conducted because of incomplete resection of T1 CRC (41%), followed by nonlifting or difficult-to-reach polyps (36%), suspected T1 CRC (19%), and least often, subepithelial tumors (4%).

'The presented data highlight some of the limitations of the full-thickness resection device, including the relatively small size of the lesion [median diameter, 23 mm] that can be resected, and challenges related to accessing and capturing the lesion due to the limited visibility and maneuverability of the device.'

Complete en bloc resection was achieved in 83.9% of procedures. Excluding 21 procedures in which eFTR was not performed because of inaccessibility of the lesion (n = 7) or immobility of tissue prohibiting retraction of the lesion into the cap (n = 14), R0 was achieved in 82.4% of cases. Among the same group, full-thickness resection rate was comparable, at 83.2%.

Adverse events occurred in 34 patients (9.3%), among whom 10 (2.7%) underwent emergency surgery for perforations or appendicitis.

"In conclusion," the investigators wrote, "eFTR is an exciting, innovative resection technique that is clinically feasible and safe for complex colorectal lesions, with the potential to obviate the need for surgical resection. Further efficacy studies on eFTR as a primary and secondary treatment option for T1 CRC are needed, focusing on both the short- and long-term oncologic results."

Peter V. Draganov, MD, of the University of Florida, Gainesville, called the R0 resection rate "respectable," and suggested that the study "reconfirms on a larger scale that eFTR with the full-thickness resection device is successful in the majority of cases."

"The full-thickness resection device expands our armamentarium to remove difficult polyps and early CRC," he said.

Still, Dr. Draganov, who has previously advised careful patient selection for eFTR, noted certain drawbacks of the technique. "The presented data highlight some of the limitations of the full-thickness resection device, including the relatively small size of the lesion [median diameter, 23 mm] that can be resected, and challenges related to accessing and capturing the lesion due to the limited visibility and maneuverability of the device."

Ultimately, Dr. Draganov supported the investigators' call for more data. "Before eFTR becomes a primary modality for management of T1 CRC, we do need follow-up data on long-term cancer-related outcomes," he said.

The study was supported by Ovesco Endoscopy. The investigators disclosed additional relationships with Cook, Ethicon, Olympus, and others.

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SOURCE: Zwager LW et al. Endoscopy. 2020 Jun 4. doi: 10.1055/a-1176-1107.

DDSEP 9
Digestive Diseases Self-Education Program

Quick Quiz answers

Q1. Correct answer: A

Rationale

In the United States, pigmented stones (black and brown) are less common than cholesterol gallstones. Both types of pigmented stones contain an excess of unconjugated bilirubin and are composed of calcium hydrogen bilirubinate, which is oxidized and polymerized in the hard black stones but unpolymerized in softer brown stones.

Black pigmented gallstones are frequently radiopaque and form in sterile bile. Risk factors for black pigmented stones include hemolysis (example, sickle cell disease), cirrhosis, cystic fibrosis, and diseases affecting the ileum (example, Crohn's disease). In contrast, brown stones are more likely to occur in the bile ducts, are radiolucent, and form secondary to biliary stasis (example, biliary stricture) and infection (example, *Clonorchis sinensis*).

Obesity, female sex, and hyperlipidemia are risk factors for cholesterol gallstone formation. Octreotide decreases gallbladder motility and long-term use can increase the risk of cholelithiasis.

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Q2. Correct answer: D

Rationale

Episodic hepatic encephalopathy is usually precipitant induced in over 80% of cases and includes dehydration, infections, over diuresis, gastrointestinal bleeding, constipation, and the use of narcotics and sedatives. Key is to identify and treat the precipitant. A diagnostic work-up to rule out other disorders that can alter brain function and mimic hepatic encephalopathy should also be performed.

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Hemospray: High efficacy, but rebleeding concerns remain

BY WILL PASS
MDedge News

Hemospray is highly effective for initial gastrointestinal hemostasis, but not long-term therapy, based on a recent meta-analysis.

In 814 patients with GI bleeding who were treated with Hemospray, respective rates of clinical success and early rebleeding were 92% and 20%, reported lead author Andrew Ofosu, MD, of the Brooklyn Hospital Center, New York, and colleagues.

"Since its introduction, multiple studies have evaluated the efficacy of Hemospray for endoscopic hemostasis in a wide array of bleeding disorders in either the upper and/or lower GI tract," the investigators wrote in the Journal of Clinical Gastroenterology.

The present review and meta-analysis included 19 of those studies, including randomized controlled trials, case series, and case-control studies. Of 814 adult patients, 212 were treated with Hemospray as monotherapy, while 602 were treated with Hemospray combined with conventional hemostatic techniques.

Clinical success, defined by endoscopically observed initial hemostasis, was achieved in 91% of patients who were treated with Hemospray as monotherapy, a rate that did not significantly differ from the 93% success rate achieved by a combination approach. Early rebleeding, defined by rebleeding within 7 days, was comparable between monotherapy (21%) and combination therapy (20%), a finding maintained in subgroup analysis. Similarly, no statistical difference was found between rates of rebleeding within 30 days, which were 22% and 24%, for monotherapy and combination therapy, respectively.

"Our study showed the rate of rebleeding increased with time after the application of Hemospray, likely due to the limited duration of action of the hemostatic powder at the site of bleeding," wrote Dr. Ofosu and colleagues. "Second-look endoscopy performed in some studies has shown Hemospray is eliminated from the GI tract in as few as 24 hours after use, which potentially increases the risk of recurrent bleeding."

The investigators reported no conflicts of interest.

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SOURCE: Ofosu A et al. J Clin Gastroenterol. 2020 Jul 3. doi: 10.1097/MCG.0000000000001379.

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