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GI&Hepatology News

November 2021

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Courtesy Dr. C. Prakash Gyawali

The combination of metrics better classifies nonresponders to PPI than the individual metrics, said Dr. C. Prakash Gyawali.

GERD: Composite pH impedance identifies escalation need

BY BRANDON MAY
MDedge News

Combinations of abnormal pH–impedance metrics better predicted nonresponse to proton pump–inhibitor therapy, as well as benefit of treatment escalation, than individual metrics in patients with gastroesophageal reflux disease (GERD) on twice-daily PPI.

The researchers found a higher proportion of nonresponders to PPI in a group of patients that had combinations of abnormal reflux burden, characterized as acid exposure time greater than 4%, more than 80 reflux episodes, and/or mean nocturnal baseline impedance (MNBI) less than 1,500 ohms, with 85% of these patients improving following initiation of invasive GERD management such as antireflux surgery or magnetic sphincter augmentation.

Not only does the combination of metrics offer more value in identifying responders to PPI than individual metrics, but the com-

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MRE plus FIB-4 beats FAST for detecting NAFLD-related fibrosis

BY JIM KLING
MDedge News

A combination of magnetic resonance elastography and blood levels of fibrosis-4 index (MEFIB) outperformed Fibro-Scan-AST (FAST) in determining the presence of significant fibrosis among patients with nonalcoholic fatty liver disease (NAFLD), according to a new prospective cohort analysis.

Liver fibrosis is the most important prognostic factor for NAFLD, but the invasiveness, propensity for sampling error, and interoperator variability of biopsy have prompted efforts to develop alternatives.

FAST, which uses vibration-controlled transient elastography (VCTE), controlled attenuation parameter (CAP), and aspartate aminotransferase levels, and MEFIB have been developed as candidates, but until now they had not been directly compared in screening. The findings of this analysis suggest that MEFIB may be a better tool for identifying NAFLD patients at heightened risk of nonalcoholic

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Do alcohol, obesity impact cirrhosis?

BY JIM KLING
MDedge News

Alcohol intake and obesity are independent risk factors for morbidity among patients with cirrhosis, but the two factors do not appear to combine for a stronger effect (supra-additive), according to conclusions from a new analysis of participants in the UK Biobank study published in Hepatology (2021 Aug. doi: 10.1002/hep.32123).

The researchers analyzed data from the records of 489,285 individuals in the UK Biobank from May 2006 to July 2010. Researchers defined morbidity as first-time hospitalization for cirrhosis and calculated the cumulative incidence at 10 years among included individuals. The researchers de-

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INSIDE

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LETTER FROM THE EDITOR

Giving thanks

Thanksgiving has long been my favorite holiday: a chance to reconnect with family and friends as well as time for reflection, gratitude, and hope. While Thanksgiving 2020 (sadly) was spent eating takeout turkey on the couch due to the pandemic, I am hopeful that Thanksgiving 2021 will for most of us bring a return to the holiday traditions that sustain us.


Dr. Adams

I am hopeful that Thanksgiving 2021 will for most of us bring a return to the holiday traditions that sustain us.

In this month's issue of GIHN, we highlight several important studies impacting frontline clinical practice. Relevant to patients with liver disease, we highlight work evaluating the potential supra-additive effects of alcohol intake and obesity in impacting cirrhosis incidence and assessing the comparative performance of noninvasive screening tests in detecting NAFLD-related fibrosis. Another study of note, relevant to clinical management of GERD, suggests that combinations of abnormal pH-impedance monitoring metrics may predict PPI nonresponders better than individual metrics and could be used to identify patients more likely to respond to invasive GERD management.

We also wish to acknowledge in this issue the outstanding work that AGA and its fellow societies do on behalf of the gastroenterology community in developing and harmonizing ACGME Reporting Milestones for GI and Transplant Hepatology fellowship programs to assist with trainee assessment. Our fellowship trainees represent the future of our profession, and it is of critical importance that we train competent, compassionate professionals who will provide outstanding clinical care to our patients. Kudos to the team, including Dr. Brijen Shah, GI & Hepatology News associate editor Dr. Janice Jou, and others, for their hard work on Milestones 2.0!

Megan A. Adams, MD, JD, MSc
Editor in Chief


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Top case

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. Here's a preview of a recent popular clinical discussion: *Vikrant Parihar, MD, wrote the following in "COVID-19 and UC":*

A 43-year-old man with an index presentation of distal colitis (Montreal E2) (Mayo endoscopic score 2-3) was discharged home on tapering doses of oral steroids. He was being worked up to commence anti-TNF likely initially as combo therapy. Fully vaccinated against COVID – had both doses of vaccine way back in May. Attended a match and looks to have got mild symptoms and on testing turned out to be COVID+. Rx himself by self-quarantine.

What would be the optimal strategy?
1. Stop steroids completely and immediately given the adverse signal in registry data?
2. When can anti-TNF's be safely started?
3. How to manage him in the interim?

See how AGA members responded and join the discussion: https://community.gastro.org/posts/25172.

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Combo predicts escalation response

Impedance *from page 1*

also offer greater value in "subsequently predicting response to escalation of antireflux management," study authors C. Prakash Gyawali, MD, AGAF, of Washington University, St. Louis, and colleagues wrote in Gastroenterology (2021 Jul. doi: 10.1053/j.gastro.2021.07.004).

Currently in question is the applicability of thresholds for metrics from pH-impedance monitoring for studies performed on PPI. According to Dr. Gyawali and colleagues, thresholds from the Lyon Consensus may be too high and likewise lack optimal sensitivity for detecting refractory acid burden in patients on PPI, while thresholds based on pH-metry alone, as reported in other publications, may also lack specificity.

To determine which metrics from "on PPI" pH-impedance studies predict escalation therapy needs, the researchers analyzed deidentified pH-impedance studies performed in healthy volunteers (n=66; median age, 37.5 years) and patients with GERD (n = 43; median age, 57.0 years); both groups were on twice-daily PPI. The investigators compared median values for pH-impedance metrics between healthy volunteers and patients with proven GERD using validated measures.

Data were included from a total of three groups: tracings from European and North American healthy volunteers who received twice-daily PPI for 5-7 days; tracings from European patients with heartburn-predominant proven GERD with prior abnormal reflux monitoring off PPI who subsequently received twice-daily PPI; and tracings from a cohort of patients with regurgitation-predominant, proven GERD and prior abnormal reflux monitoring off PPI who subsequently received twice-daily PPI.

An improvement in heartburn of at least 50%, as recorded on 4-point Likert-type scales, defined PPI responders and improvements following antireflux surgery in the European comparison group. Additionally, an improvement of at least 50% on the GERD Health-Related Quality of Life scale also characterized PPI responders and improvements following magnetic sphincter augmentation in the North American comparison group.

There was no significant difference between PPI responders and nonresponders in terms of individual conventional and novel reflux metrics. The combinations of metrics associated with abnormal reflux burden and abnormal mucosal integrity (acid exposure time >4%, >80 reflux episodes, and MNBI <1,500 ohms) were observed in 32.6% of patients with heartburn and 40.5% of patients with regurgitation-predominant GERD, but no healthy volunteers. The combinations were also observed in 57.1% and 82.4% of nonresponders, respectively.

The authors defined a borderline category (acid exposure time, >0.5% but <4%; >40 but <80 reflux episodes), which accounted for 32.6% of patients with heartburn-predominant GERD and 50% of those regurgitation-predominant

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GERD. Nonresponse among these borderline cases was identified in 28.6% and 81%, respectively.

"Performance characteristics of the presence of abnormal reflux burden and/or abnormal mucosal integrity in predicting PPI nonresponse consisted of sensitivity, 0.50; specificity, 0.71; and area under the curve (AUC), 0.59 (P = .15)," the authors explained. "Performance characteristics of abnormal and borderline reflux burden categories together in predicting PPI nonresponse consisted of sensitivity, 0.86; specificity, 0.36; and AUC, 0.62 (P = .07)."

Limitations of this study included its retrospective nature, small sample sizes for the healthy volunteer and GERD populations, and the lack of data on relevant clinical information, including body mass index, dietary patterns, and PPI types and doses. Additionally, the findings may lack generalizability because of the inclusion of only patients with GERD who underwent surgical management.

Despite these limitations, the researchers wrote that the findings and identified "thresholds will be useful in planning prospective outcome studies to conclusively determine when to escalate antireflux therapy when GERD symptoms persist despite bid PPI therapy."

The study researchers reported conflicts of interest with several pharmaceutical companies. No funding was reported for the study.

ginews@gastro.org

The management of gastroesophageal reflux disease is the most common referral for a gastroenterologist; however, metrics to determine dose escalation for persistent symptoms in patients with proven GERD is an unmet need. The Lyon consensus aimed to standardize abnormal pH parameters but used similar thresholds for off– and on–proton pump inhibitor testing; these thresholds for on-PPI testing are likely too high to detect refractory reflux on PPI therapy. The use of pH-impedance results is an optimal test for patients with persistent symptoms in the setting of proven GERD to determine escalation of antireflux therapy.

Dr. Naik

In this multicenter, international cohort study, Gyawali and colleagues rigorously challenged the definition of abnormal pH-impedance testing with an evaluation of pH-impedance parameters comparing controls (n = 66) versus proven GERD (n = 43) on twice-daily PPI dosing to define pH-impedance parameters.

In the era of easy access and overprescription of PPI countered by the unfounded, but perceived, fears of PPI or surgery, testing prior to antireflux escalation is now more easily standardized with this data to help guide our patients. Abnormal pH-impedance parameters also help support of the utility of surgery for the carefully selected patient and these cutoffs highlight success rates for patients with heartburn or regurgitation. Limitations of pH impedance include careful examination of the original tracings and center expertise/availability, but with improved definitions of abnormal thresholds, providers should feel empowered to test prior to escalation. Prospective studies using these cutoffs will enhance and hopefully continue an iterative process to define this plurality approach to reflux metrics.

Rishi D. Naik, MD, MSCI, is an assistant professor in the department of medicine in the section of gastroenterology & hepatology at the Esophageal Center at Vanderbilt University Medical Center, Nashville, Tenn. He has no conflicts.

AGA leaders met with federal regulators

AGA President John Inadomi, MD, AGAF, and former AGA President David Lieberman, MD, AGAF, along with American Cancer Society Cancer Action Network and Fight CRC, met with Assistant Secretary of Labor, Ali Khawar, and representatives from the U.S. Department of Health & Human Services and U.S. Department of Treasury to request they direct private health plans to cover colonoscopy after a positive noninvasive colorectal cancer (CRC) screening test.

The meeting was in response to an appeal sent to the three agencies, which provided guidance to health plans to ensure that workers have the benefits that have been agreed upon by their employers. As part of the Affordable Care Act, plans are mandated to cover colorectal cancer screening without cost sharing.

In May 2021, when the United States Preventive Services Task Force lowered the recommended CRC screening age to 45, it also stated that "positive results on stool-based screening tests require follow-up with colonoscopy for the screening benefits to be achieved."

To ensure that privately insured Americans receive proper CRC screening, AGA, ACS, and Fight CRC are pushing the government to provide written guidance to private plans clarifying that follow-up colonoscopies conducted after a positive noninvasive screening test are part of the colorectal cancer screening process and, therefore, patients should not face out-of-pocket costs when completing colorectal cancer screening.

Colorectal cancer remains the second leading killer in cancer in the United States despite the availability of preventive screening options. In 2018, just 68.8% of those eligible were screened for colorectal cancer. The challenge of getting people screened was exacerbated in 2020 when it is estimated that colorectal cancer screening declined by 86% during the first few months of the COVID-19 pandemic.

Introducing Gastroenterology's new DEI editor

Chyke Doubeni, MD, MPH, will spearhead the efforts at Gastroenterology and across our portfolio of journals to develop a scientific publishing enterprise that is diverse, equitable, and inclusive. Check out a few questions we asked the new editor below:

What are you most looking forward to in this role?

This is a unique opportunity to advance diversity, equity, and inclusion through the scientific publication process.

Describe your ideal DEI-focused submission.

Articles that address the critical importance of workforce diversity, health equity, the use of race and the effect of racism in GI research and practice. Other important topics are identifying and explicating biases in risk assessment tools and algorithms in GI, promotion of inclusive research, and interventions that demonstrate elimination or reduction of health disparities.

What are you looking for when identifying and recruiting colleagues that are underrepresented in medicine to serve as a thoughtful reviewer or contributor?

We recognize the contributions and sacrifice made by our colleagues who serve as reviewers to advance the science of health equity and antiracism. We greatly value reviewers who provide additional contextual information or data to highlight the importance of health equity as a priority in the field, conclusions that are supported by the data, feedback for peers on the appropriate use of language on race/ethnicity, attention to sex as a biological variable, and avoidance of potentially stigmatizing language.

Be sure to follow Dr. Doubeni on Twitter, @ChykeDoubeni.

Lesion morphology drives optical evaluation's accuracy for predicting SMIC

BY BRANDON MAY
MDedge News

The diagnostic performance of optical evaluation for submucosal invasive cancer (SMIC) in patients with large (≥20 mm) nonpedunculated colorectal polyps (LNPCPs) may be dependent on lesion morphology. While optical evaluation featured excellent performance in the assessment of flat lesions, the assessment only featured decent performance in nodular lesions, underscoring the need for additional evaluation algorithms for these lesions.

Endoscopists rely on the accuracy of real-time optical evaluation to facilitate appropriate selection of treatment; however, in studies focusing on LNPCPs, the performance of optical evaluation is modest (Gut. 2019 Feb;68[2]:271-9).

The stratification of optical evaluation by lesion morphology may enable more accurate "implementation of a selective resection algorithm by identifying lesion subgroups with accurate optical evaluation performance characteristics," first authors Sergei Vosko, MD, and Neal Shahidi, MD, of the department of gastroenterology and hepatology, Westmead Hospital, Sydney, and colleagues wrote in Clinical Gastroenterology and Hepatology (2021 May. doi: 10.1016/j.cgh.2021.05.017).

Given the potential importance of stratification in optical evaluation, Dr. Vosko and colleagues assessed the performance of the optical assessment modality based on lesion morphology in a prospective cohort of 1,583 LNPCPs measuring at least 20 mm in patients (median age, 69 years) referred for endoscopic resection.

In the observational cohort, centers performed optical evaluation before endoscopic resection. The optical prediction of SMIC was based on several different established features, including Kudo V pit pattern, depressed morphology, rigidity/fixation, and ulceration. The researchers calculated optical evaluation performance outcomes, which were reported by the dominant morphology, namely nodular (Paris 0–Is/0– IIaDIs) versus flat (Paris 0–IIa/0–IIb).

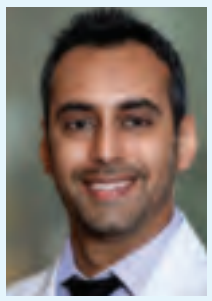
Across the overall cohort, the median lesion size was 35 mm. The investigators identified a total of 855 flat LNPCPs and 728 nodular LNPCPs, with 63.9% of LNPCPs considered granular. Additionally, the researchers reported submucosal invasive cancer in 146 LNPCPs (9.2%).

According to the investigators, the overall sensitivity of optical evaluation to diagnose submucosal invasive cancer was 67.1% (95% confidence interval, 59.2%-74.2%), while the overall specificity was 95.1% (95% CI, 93.9%-96.1%). The investigators reported significant differences between flat vs. nodular LNPCPs in terms of sensitivity (90.9% vs. 52.7%, respectively; *P* <.001) and specificity (96.3% vs. 93.7%; *P* =.027).

Overall, the SMIC miss rate was 3.0% (95% CI, 2.3%-4.0%). There was a significant difference in the SMIC miss rate between flat and nodular LNPCPs (0.6% vs. 5.9%, respectively; *P* < .001).

Continued on following page

Because endoscopists are becoming more proficient with endoscopic mucosal resection (EMR) and are pushing the bounds with endoscopic submucosal dissection (ESD), there is a need for high-quality endoscopic markers of submucosal invasion (SMI) to help guide decision-making for management.


Dr. Sheikh

This study by Dr. Vosko and colleagues demonstrated a high degree of accuracy in predicting SMI via optical evaluation for a select group of large nonpedunculated colorectal polyps (LNPCP). The features associated with SMI were Kudo Pit Pattern V, ulceration, depression (Paris 0-IIc morphology), and rigidity or fixation.

The authors demonstrated that optical evaluation was highly accurate in detecting submucosal invasion for flat LNPCP with a high sensitivity and specificity. The sensitivity was considerably lower when evaluating nodular LNPCPs with a higher miss rate in polyps >4.0 cm and those located in the rectosigmoid colon. Of the endoscopic features assessed, Kudo pit pattern had the highest reliability in predicting SMI.

These data further tip the scale in favor of EMR as the appropriate therapeutic option for flat LNPCP in absence of features of SMI outlined by the authors. It also highlights the need for all endoscopists to be well versed in Kudo Pit classification and proficient in assessing for rigidity, fixation, and depression as the therapeutic decision (namely EMR vs. ESD vs. surgery) is often made by the endoscopist discovering the polyp. More studies are needed to identify endoscopic characteristics that provide a high sensitivity and specificity for SMI in nodular LNPCPs.

Rehman Sheikh, MD, is a gastroenterologist at the Baylor College of Medicine in Houston. He has no conflicts to declare.

NEWS FROM THE AGA

AGA says stay the course, despite the Delta variant

As COVID-19 cases rise in the United States because of the Delta variant, there is renewed concern about infection and transmission of SARS-CoV-2 during endoscopy. In May 2021, AGA released updated recommendations on preprocedure testing post vaccination in the setting of ongoing population-wide vaccination programs for the prevention of COVID-19–related morbidity. In vaccinated individuals, breakthrough infections occurred very infrequently. Weighing the evidence demonstrating extremely low rates of infection and transmission with vaccination and personal protective equipment, and considering the downsides of routine testing (burden, cost, false test results, increased disparities), AGA made a conditional recommendation against routine preprocedure testing for elective cases. The highly contagious Delta variant has now emerged as the predominant SARS-CoV2 virus in the United States and some data suggest that it may cause more severe illness than previous strains. While more breakthrough infections may develop in fully vaccinated individuals, the greatest risk of infection, transmission, and hospitalizations is among those who are unvaccinated.

- AGA suggests against reinstituting routine preprocedure testing prior to elective endoscopy. The downsides (delays in patient care, burden, inaccurate results) outweigh potential benefits. Infection and transmission of SARS-CoV-2 from asymptomatic individuals is rare especially among vaccinated health care workers using personal protective equipment (PPE), even with the emergence of the Delta variant.
- If PPE is available, AGA recommends using N95 for upper endoscopy and suggests using N95 or surgical masks for lower endoscopy (acknowledging that upper endoscopy is more aerosolizing than lower endoscopy) and continuation of elective and nonelective endoscopy.
- Based on local prevalence rates, PPE, and test availability, in intermediate- and high-prevalence settings, preprocedure testing may be used to inform PPE decisions (N95 versus surgical mask). Additional benefits to testing are small and include deferring elective endoscopy in individuals testing positive and reducing anxiety among staff and patients.

UC relapse associated with impaired luminal control of macrophage maturation

BY BRANDON MAY
MDedge News

Patients with ulcerative colitis (UC) who are in remission from their disease lack luminal signals capable of inducing macrophage hyporesponsiveness, which may contribute to a patient's persistent vulnerability to relapse, according to a new study.

"Together with the distinct fecal metabolomic profile of UC patients in remission, our data suggest that UC patients may lack the signals required for proper macrophage education, rendering them vulnerable to relapse," wrote study authors Lujain Maasfeh, PhD, of the University of Gothenburg (Sweden) and colleagues in Cellular and Molecular Gastroenterology and Hepatology (2021 Jun. doi: 10.1016/j.jcmgh.2021.06.004).

Macrophages found in the lamina propria play a role in sustaining intestinal homeostasis. Through education by local signals, intestinal macrophages adopt a hyporesponsive phenotype and tolerogenic nature and are replenished constantly from monocytes. In patients with UC who are in remission, however, the lack of proper macrophage maturation may result in gut inflammation.

Current evidence has yet to define fully the immunomodulating determinants in the education of intestinal macrophages; however, Dr. Maasfeh and associates wrote that "intestinal microbiota and microbiota-derived metabolites increasingly are recognized for their role in imprinting tissue-specific features of intestinal macrophages."

The researchers added that previous evidence has established that patients with UC demonstrate dysbiosis, which may impact maturation of intestinal macrophages (Metabolomics. 2015;11:122-33). The hyporesponsive state of intestinal lamina propria macrophages induced by the microbiota may be lost in patients with UC who are in remission, ultimately resulting in disease relapse.

To gauge the effects of fecal luminal factors on macrophage phenotype and function, the researchers extracted fecal supernatants (FS) from the fecal samples of 10 healthy volunteers and 17 patients with UC who were in remission. Following maturation of monocytes to macrophages in the presence of granulocyte-macrophage colony-stimulating factor without and with FS, the researchers assessed macrophage phenotype and function. The investigators also used gas chromatography and mass spectrometry to analyze fecal metabolomic profiles.

In healthy donors, fecal luminal factors effectively downregulated Toll-like receptor signaling, cytokine signaling, as well as antigen presentation in macrophages. In contrast, the fecal luminal factors in patients with UC demonstrated less potency in their ability to induce lipopolysaccharide hyporesponsiveness. An immune pathway–scoring analysis also showed a consistently higher reaction potential among UC remission FS-treated macrophages vs. healthy FS-treated macrophages.

While FS treatment did not seem to affect the phagocytic and bactericidal abilities of macrophages, the researchers observed that the healthy FS-treated macrophages better suppressed a cluster of differentiation 4^+ T-cell activation as well as interferon-gamma secretion vs. FS-treated macrophages from patients with UC in remission. The FS-treated macrophages in the UC remission population also featured less potency in their ability to suppress CD4+ T-cell activation and cytokine secretion.

The authors acknowledged a few limitations, including the small sample size and the effects from using in vitro system.

"Identification of the factors involved in intestinal macrophage education is important to maintain/reestablish gut homeostasis in patients with UC," they concluded.

The study received financial support from Swedish Research Council-Medicine, in addition to funding from a Region Västra Götaland ALF-agreement, the Knut och Alice Wallenberg Foundation Wallenberg Centre for Molecular and Translational Medicine at the University of Gothenburg, Ruth and Richard Julin's foundation, Adlerbertska Foundation, Wilhelm and Martina Lundgren Foundation, and Apotekare Hedberg's Foundation. The authors disclose no conflicts.

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Current therapies for ulcerative colitis, including anti-inflammatory drugs and biologics such as anti–tumor necrosis factor therapies and anti-interleukin-12/23 antibodies, are aimed at inducing and maintaining remission. However, approximately 20%-40% of patients are primary nonresponders and about 23%-46% patients lose response within 12 months of treatment, which suggests an unmet need to look for new therapeutic targets.


Dr. Pandey

Intestinal macrophages are essential in the maintenance of intestinal immune homeostasis by acquiring a hyporesponsive state in response to microbial stimuli. This study by Maasfeh and colleagues highlights the role of luminal factors in shaping the macrophage response. The authors show that human monocyte–derived macrophage treated with fecal luminal factors derived from patients with ulcerative colitis in remission are less hyporesponsive to lipopolysaccharide stimulation. They are also less efficient in modulating cytokine and Toll-like receptor signaling pathway genes and have a dampened ability to suppress CD4+ T-cell activation and interferon-gamma secretion compared to controls.

Luminal factors derived from gut microbiota (short-chain fatty acids, indole derivatives, polyamines, and bile acids) can shape macrophage differentiation and antibacterial response. This study points toward key luminal factors, which might be playing pivotal roles in maintaining homeostasis. However, the current study needs further validation in a larger cohort of patients and in the lamina propria macrophages. In addition, it will be important to know the physiologically relevant concentration to achieve functional effect. The identification of specific metabolites responsible for inducing hyporesponsiveness in macrophages could be an approach for mining potential therapeutic targets.

Sumeet Pandey, PhD, is in the Translational Gastroenterology Unit at John Radcliffe Hospital at the University of Oxford (England). He has no conflicts of interest.

Continued from previous page

Independent predictors of missed SMIC on optical evaluation, as identified in the multiple logistic regression analysis, included nodular morphology (odds ratio, 7.2; 95% CI, 2.8-18.9; $P < .001$), rectosigmoid location (OR, 2.0; 95% CI, 1.1-3.7; P =.026), and size of at least 40 mm (OR, 2.0; 95% CI, 1.0-3.8; $P = .039$).

Based on the findings, the researchers suggested that all flat lesions, in the absence of optical features consistent with submucosal invasive cancer, should subsequently be removed by high-quality endoscopic mucosal resection, in conjunction with the application of "site-specific modifications and ancillary techniques where needed."

One limitation of this study is how lesion morphology was classified, which can in some cases be subjective.

The researchers added that additional refinement is required "to robustly apply a selective resection algorithm irrespective of lesion morphology" given the modest performance value of optical evaluation in nodular lesions. "Nevertheless, it is imperative that all endoscopists embrace optical evaluation in everyday clinical practice, thus harnessing its proven ability to influence resection technique selection and the associated clinical and economic ramifications," they concluded.

The study received financial support the Cancer Institute of New South Wales, in addition to funding from the Gallipoli Medical Research Foundation. One author reported receiving research support from Olympus Medical, Cook Medical, and Boston Scientific. The remaining authors disclosed no conflicts.

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AGA Clinical Practice Update: Expert Review

How to manage GI perforations

BY JIM KLING
MDedge News

A clinical practice update expert review from the American Gastroenterological Association gives advice on management of endoscopic perforations in the gastrointestinal tract, including esophageal, gastric, duodenal and periampullary, and colon perforation.


Dr. Lee

There are various techniques for dealing with perforations, including through-the-scope clips (TTSCs), over-the-scope clips (OTSCs), self-expanding metal stents (SEMS), and endoscopic suturing. Newer methods include biological glue and esophageal vacuum therapy. These techniques have been the subject of various retrospective analyses, but few prospective studies have examined their safety and efficacy.

In the expert review, published in Clinical Gastroenterology and Hepatology (2021 Jul 2. doi: 10.1016/j.cgh.2021.06.045), authors led by Jeffrey H. Lee, MD, MPH, AGAF, of the department of gastroenterology at the University of Texas MD Anderson Cancer Center, Houston, emphasized that gastroenterologists should have a perforation protocol in place and practice procedures that will be used to address perforations. Endoscopists should also recognize their own limits and know when a patient should be sent to experienced, high-volume centers for further care.

In the event of a perforation, the entire team should be notified immediately, and carbon dioxide insufflation should be used at a low flow setting. The endoscopist should clean up luminal material to reduce the chance of peritoneal contamination, and then treat with an antibiotic regimen that counters gram-negative and anaerobic bacteria.

Esophageal perforation

Esophageal perforations most commonly occur during dilation of strictures, endoscopic mucosal resection (EMR), and endoscopic submucosal dissection (ESD). Perforations of the mucosal flap may happen during so-called third-space endoscopy techniques like peroral endoscopic myotomy (POEM). Small perforations can be readily addressed with TTSCs. Larger perforations call for some combination of TTSCs, endoscopic suturing, fibrin glue injection, or esophageal stenting, though the latter is discouraged because of the potential for erosion.

A more concerning complication of POEM is delayed barrier failure, which can cause leaks, mediastinitis, or peritonitis. These complications have been estimated to occur in 0.2%-1.1% of cases.

In the event of an esophageal perforation, the area should be kept clean by suctioning, or by altering patient position if required. Perforations 1-2 cm in size can be closed using OTSCs. Excessive bleeding or larger tears can be addressed using a fully covered SEMS.

Leaks that occur in the ensuing days after the procedure should be closed using TTSCs, OTSCs, or endosuturing, followed by putting in a fully covered stent. Esophageal fistula should be addressed with a fully covered stent with a tight fit.

Endoscopic vacuum therapy is a newer technique to address large or persistent esophageal perforations. A review found it had a 96% success rate for esophageal perforations (Surg Endosc. 2017 Sep;31[9]:3449-58).

Gastric perforations

Gastric perforations often result from peptic ulcer disease or ingestion of something caustic, and it is a high risk during EMR and ESD procedures (0.4%-0.7% intraprocedural risk). The proximal gastric wall isn't thick as in the gastric antrum, so proximal endoscopic resections require extra care. Lengthy procedures should be done under anesthesia. Ongoing gaseous insufflation during a perforation may worsen the problem because of heightened intraperitoneal pressure. OTSCs may be a better choice than TTSCs for 1- to 3-cm perforations, while endoloop/TTSC can be used for larger ones.

Duodenal and periampullary perforations

Duodenal and periampullary perforations occur during duodenal stricture dilation, EMR, endoscopic submucosal dissection, endoscopic ultrasound, and endoscopic retrograde cholangiopancreatography (ERCP). The thin duodenal wall makes it more susceptible to perforation than the esophagus, stomach, or colon.

Endoscopists should also recognize their own limits and know when a patient should be sent to experienced, high-volume centers for further care.

Closing a duodenum perforation can be difficult. Type 1 perforations typically show sudden bleeding and lumen deflation, and often require surgical intervention. Some recent reports have suggested success with TTSCs, OTSCs, band ligation, and endoloops. Type 2 perforations are less obvious, and the endoscopist must examine the gas pattern on fluoroscopic beneath the liver or in the area of the right kidney. Retroperitoneal air following ERCP, if asymptomatic, doesn't necessarily require intervention.

The challenges presented by the duodenum mean that, for large duodenal polyps, EMR should be done only by experienced endoscopists who are skilled at mucosal closure, and only experts should attempt ESD. Proteolytic enzymes from the pancreas can also pool in the duodenum, which can degrade muscle tissue and lead to delayed perforations. TTSC, OTSC, endosuturing, polymer gels or sheets, and TTSC combined with endoloop cinching have been used to close resection-associated perforations.

Colon perforation

Colon perforation may be caused by diverticulitis, inflammatory bowel disease, or occasionally colonic obstruction. Iatrogenic causes are more common and include endoscopic resection, hot forceps biopsy, dilation of stricture resulting from radiation or Crohn's disease, colonic stenting, and advancement of colonoscope across angulations or into diverticula with without straightening the endoscope

Large perforations are usually immediately noticeable and should be treated surgically, as should hemodynamic instability or delayed perforations with peritoneal signs.

Endoscopic closure should be attempted when the perforation site is clean, and endoscopic rectal perforations can generally be repaired with TTSC, OTSC, or endoscopic suturing. In the cecum, or in a torturous or unclean colon, it may be difficult or dangerous to remove the colonoscope and insert an OTSC, and endoscopic suturing may not be possible, making TTSC the only procedure available for right colon perforations. The X-Tack Endoscopic HeliX Tacking System is a recently introduced, through-the-scope technology that places suture-tethered tacks into tissue surrounding the perforation and cinches it together. The system in principle can close large or irregular colonic and small bowel perforations using gastroscopes and colonoscopes, but no human studies have yet been published.

Conclusion

This update was a collaborative effort by four endoscopists who felt that it was timely to review the issue of perforations since they can be serious and challenging to manage. The evolution of endoscopic techniques over the last few years, however, has made the closure of spontaneous and iatrogenic perforations much less fear provoking, and we wished to summarize the approaches to a variety of such situations in order to guide practitioners who may encounter them.

"Although perforation is a serious event, with novel endoscopic techniques and tools, the endoscopist should no longer be paralyzed when it occurs," the authors concluded.

Some authors reported relationships, such as consulting for or royalties from device companies such as Medtronic and Boston Scientific. The remaining authors disclosed no conflicts.

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AGA Section: Gastroenterology and hepatology training milestones updated

BY JIM KLING
MDedge News

Updated milestones for professional development aim to help specialists in gastroenterology and transplant hepatology achieve knowledge, skills, and attitudes that will help them establish their own practices.

The new version, Milestones 2.0, represents the latest milestones created by the Accreditation Council for Graduate Medical Education, including six core competencies developed initially in 1999: patient care (PC), medical knowledge (MK), interpersonal and communication skills (ICS), professionalism (PROF), systems-based practice (SBP), and practice-based learning and improvement (PBLI).

In 2013, the Oversight Working Network, working together with gastroenterology societies, developed a companion document of 13 entrustable professional activities (EPAs) aimed at gastroenterologists: These include management of various individual disorders such as liver or pancreatic diseases, performance of specific diagnostic procedures, and management of patient adverse events and nutritional status.

Milestones 1.0 encountered some resistance from the graduate medical education community. It was felt that many of the milestones were too vague or were described using language that was too complex. Some viewed the milestones as burdensome, and a review suggested hundreds of different ways to describe ICS and PROF, leading to confusion.

In an effort to improve matters, the ACGME made some changes. The first involved standardizing milestones used for ICS, PROF, SBP, and PBLI so that they could be used across disciplines. They also developed PC and MK milestones tailored to each specialty.

In the latest article on the topic, appearing in Gastroenterology (2021 Oct;161[4]:1318-24), the authors led by Brijen J. Shah, MD, AGAF, of the Icahn School of Medicine at Mount Sinai, New York, outlined a second group of changes, which included development of specialty-specific milestones aimed at gastroenterology and transplant hepatology.

Development

The new set of milestones includes 17 for gastroenterology and 16 for transplant hepatology.

There are four PC milestones, which include taking a history and conducting patient examinations, patient management, and two more related to cognitive and technical components of procedures. The MK milestones include competency in gastrointestinal and liver diseases (MK1) and medical reasoning (MK2). These milestones are different from the internal medicine milestones met by graduating residents. MK1 includes specialty-specific disorders and diagnostic, therapeutic, and pharmacologic options for treatment or prevention. MK2 encompasses differential diagnoses and how cognitive bias can influence decision-making, a new concept introduced in Milestones 2.0.

Because the skills represented in the four other core milestones (ICS, PROF, SBP, and PBLI) are "common across specialties," the authors drafted subcompetencies for these four areas with "harmonized" language for use by every specialty. These harmonized milestones were then tailored for each specialty. An important change occurred with SBP because transplant hepatology poses unique challenges in this domain. They ultimately split SBP into two, with SBP1 focusing on unique liver transplant regulatory requirements and SBP2 covering organ allocation and Model for End-Stage Liver Disease (MELD) score exceptions.


Dr. Shah

The previous milestones encountered some resistance from the graduate medical education community. It was felt that many of the milestones were too vague or were described using language that was too complex.

Public response

The researchers sought out comment on the updated milestones from program directors and coordinators, and published on the ACGME website, and members of the working group also shared it with faculty, fellows, and specialty societies. Overall, 48 respondents assessed "whether the updated milestone provided a realistic measure of knowledge, skills, and behavior; whether it discriminated between different levels of competency; whether the respondent knew how to assess the milestone effectively; and whether the Supplemental Guide was a useful resource in understanding the milestone." They rated each on a scale of 1 (strongly disagree) to 4 (strongly agree). They could also provide free-text comments.

Respondents agreed that milestones realistically measure progression (mean, 3.49), could distinguish levels of competency (mean, 3.41), could be used accurately (mean, 3.43), and were explained well by the supplemental guide (mean, 3.42). No trends that suggested a need for additional action were found in the free-text comments.

Role of milestones

The milestones can be used to develop learning objectives, which in turn can be worked into clinical rotations and learning activities. For instance, the inpatient consult rotation could be used to address the SBP2 (organ allocation/MELD score exemptions), SBP3 (the physician's role in the health care system), PBLI1 (evidence-based medicine), and some of the PC (patient care) milestones.

The milestones should not be used as an assessment method by supervisors, the authors cautioned, but rather should be used by the Clinical Competency Committee to assess trainees at various time points. The committee may combine milestones with direct observation, chart-simulated recall, multiple evaluations, and other factors to determine a trainee's progress.

An institution's program directors can use the milestones to adjust curriculum development and ensure that any gaps are filled. Milestones can be used at multiple times throughout training: When trainees repeat rotations, they can be used to determine year-to-year progress. Trainees who are not progressing adequately may be identified earlier on, then offered supplemental learning opportunities. On the other hand, trainees who exceed expectations may be offered additional opportunities.

Trainees can also use milestones in self-directed learning, though they should work with the program director and clinical faculty to identify gaps in their learning as well as any deficiencies.

The authors have no relevant financial disclosures.

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AGA Giving Day

On Oct. 26, AGA and the AGA Research Foundation brought together the GI community in an effort to help spark diverse students' interest in GI research and launch underrepresented investigators' academic research careers.

In alignment with AGA's Diversity Policy and the AGA Equity Project codifying our commitment to diversity, equity, and inclusion, the AGA Research Foundation's 2021 AGA Giving Day Campaign focused on recruiting and retaining GI investigators from diverse backgrounds. We did this by collecting donations to strengthen and diversify the investigator pipeline and address equity in gastroenterology by offering support through the GI Pipeline Fund and the Fellow-to-Faculty Transition Fund.

AGA Giving Day was the opportunity to help the Foundation foster and support the careers of underrepresented researchers. With money raised through this campaign, the Foundation will provide undergraduate students from groups underrepresented in biomedical research with summer experiences in GI research and help fellows to pursue academic research careers, particularly those from groups underrepresented in medicine.

Thank you to all our donors who supported this effort. Learn more at foundation.gastro.org/aga-giving-day.

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GI & HEPATOLOGY NEWS

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No supra-additive effect seen

Cirrhosis *from page 1*

fined obesity as body mass index of at least 30 kg/m^2 and healthy BMI as 20-25. Safe drinking was defined as having fewer than 22 units per week for males or fewer than 15 units for females, harmful drinking was defined as more than 50 units per week for males or more than 35 for females, and hazardous drinking was defined as 22-49 units per week for males and 15-35 for females. The researchers assumed 2 units in a pint of beer or cider, 1.5 units in a glass of wine and "other" drinks, and 1 unit per measure of spirits.

The mean age was 57.0 years, and 45.4% were male. Overall, 24.3% of subjects were obese, 76.5% had safe levels of alcohol consumption, 19.7% had hazardous alcohol consumption, and 3.8% were classified as harmful drinkers.

The findings contradict previous studies, which suggested that high BMI and harmful drinking combined may produce much higher risk than either factor alone.

Overall, harmful drinking was associated with 5.0 times the 10-year cumulative incidence of cirrhosis morbidity among harmful versus safe drinkers (1.51% vs. 0.30%). However, among those with a healthy BMI, harmful was associated with an 8.6-fold increase of cirrhosis morbidity, compared with safe drinkers (1.38% vs. 0.16%). On the other hand, obese patients with harmful drinking habits had a 3.6-fold increase over obese safe drinkers (1.99% vs. 0.56%).

When looked at according to BMI, 10-year cumulative incidence was 3.1 times higher in patients with obesity versus those with healthy BMI (0.65% vs. 0.21%). This varied strongly with drinking: Safe drinkers with obesity had 3.7 times the incidence, compared with safe drinkers with healthy BMI (0.56% vs. 0.15%), and harmful drinkers who were obese had a 1.4-fold increased incidence, compared with harmful drinkers of a healthy weight (1.99% vs. 1.38%).

"In contrast to some previous studies, we found little evidence that [obesity and drinking] interacted supra-additively to modulate the risk of cirrhosis morbidity," the authors wrote. "On the contrary, through a relative risk lens, the association between alcohol intake and cirrhosis morbidity was actually weaker for individuals with obesity than for individuals with a healthy BMI (indicating a sub-additive relationship)."

Fine-Gray regression modeling seemed to confirm that the relationship was sub-additive. After controlling for various factors, researchers found that harmful drinkers had a 6.84-fold increased risk at a healthy BMI, while the risk was only 3.14 times higher in obese patients ($P_{\text{interaction}} = 3.53 \times 10^{-6}$).

The findings contradict previous studies, which suggested that high BMI and harmful drinking combined may produce much higher risk than either factor alone, possibly because obesity might "prime" the liver to be vulnerable to the effects of alcohol.

The authors suggest that the differences in findings may be caused by methodological limitations of the earlier studies, such as reliance on self-reported BMI data; small sample sizes and a relatively small number of liver events among those with obesity and harmful alcohol consumption; and the failure to use a competing risk perspective. The latter is relevant because alcohol and obesity are risk factors for other potentially fatal health conditions.

But the current study is not without its own limitations, according to Nancy Reau, MD, AGAF, who is a professor of medicine and chair of hepatology at Rush University Medical Center in Chicago, who was asked to comment on the findings. Dr. Reau pointed out that the authors found the highest frequency of complications was observed in people with harmful alcohol intake whose BMI was under 20. That group may be composed of subjects with sarcopenia and end-stage liver disease from alcohol use. "Until you can separate these from the truly healthy BMI but [with harmful alcohol use], you can't interpret this arm," said Dr. Reau.

Beyond that, the researchers found increased risks of harm among individuals regardless of BMI, but the risks were highest among those with BMI over 30. Dr. Reau posited that the frequency might have been significantly greater at BMI higher than 35 and 40, but the researchers didn't report results among these subcategories.

THINKSTOCK

"In no way does this suggest that we need to ignore alcohol use in our patients with NAFLD [nonalcoholic fatty liver disease] or [nonalcoholic steatohepatitis]," said Dr. Reau.

In fact, she pointed to a figure in the paper that showed the highest increase in frequency among those with harmful alcohol use and obesity. "It's clear that both conditions are much more serious than just obesity alone. It is incredibly important to council our NAFLD patients on appropriate alcohol use, [since] problematic drinking increases their risk. Problematic drinking remains a serious problem and increased awareness and linking to addiction services is important," she said.

The authors reported no conflicts of interest. Dr. Reau has no relevant financial disclosures.

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MEFIB could help identify patients for clinical trials

NAFLD *from page 1*

steatohepatitis, as well as which patients might or might not be candidates for pharmacotherapy interventions and clinical trials down the line.

Although there are no drugs currently approved for high-risk NAFLD patients, many clinical trials are underway. Patients with stage 2 or higher fibrosis are candidates for clinical trials, but many trials experience a high screening failure rate. A noninvasive method that can identify clinical trial candidates while avoiding liver biopsy

Dr. Zobair M. Younossi

"It seems like the combination of FIB-4 and MRE has very good performance for identifying and excluding NAFLD patients with moderate to advanced fibrosis."

would be a welcome addition, Nobuharu Tamaki, MD, PhD, of the NAFLD Research Center, division of gastroenterology and hepatology, department of medicine, at the University of California, San Diego, and colleagues explained in Hepatology (2021 Sep. doi: 10.1002/HEP.32145).

"We suspect that these are the patients; if there is going to be a drug approved, it will be for this patient population. So it's important for prognosis, but it's also important potentially for future treatment with new drugs," said Zobair M. Younossi, MD, who was asked to comment on the study.

The researchers examined a cohort of 234 consecutive adults at UCSD and a second cohort of 314 consecutive adults at Yokohama (Japan) City University; both cohorts underwent liver biopsy, magnetic resonance elastography (MRE), VCTE, and CAP assessment.

Significant fibrosis was found in 29.5% of the Yokohama cohort and 66.2% of the UCSD cohort. MEFIB had a higher area under the receiver operating characteristic curve than FAST in the UCSD cohort (0.860 vs. 0.757; $P = .005$) and the Yokohama cohort (0.899 vs. 0.724; $P < .001$).

When the researchers employed MEFIB as a rule-in criteria (MRE

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MEFIB, which combines magnetic resonance elastography with FIB-4, outperformed FAST in determining the presence of significant fibrosis among patients with NAFLD.

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value ≥3.3 kPa and FIB-4 ≥1.6), MEFIB had a positive predictive value of 91.2% in the UCSD cohort and 96.0% in the Yokohama cohort, versus 74.2% and 89.2% for FAST (≥0.67), respectively. Rule-out criteria included MRE less than 3.3 kPa and Fib-4 less than1.6 for MEFIB, as well as FAST of 0.35 or less; with those parameters, negative predictive value for significant fibrosis was 92.8% in the UCSD group and 85.6% in the Yokohama group for MEFIB, and 88.3% and 57.8% for FAST, respectively.

Most of the existing noninvasive tests do a pretty good job of excluding advanced fibrosis, but they don't perform quite as well at identifying patients with cirrhosis, according to Dr. Younossi. He added that MEFIB isn't suitable for general population screening, but rather, it's better suited for case finding in which it can be used to identify patients who are likely to have high risk for fibrosis.

The approach also relies on magnetic resonance technology, which is costly and may not be readily available.

"Nevertheless, it seems like the combination of FIB-4 and MRE has very good performance for identifying and excluding NAFLD patients with moderate to advanced fibrosis, at least in the two cohorts that were looked at," said Dr. Younossi.

However, Dr. Younossi noted some potential limitations to the study. Both cohorts were from referral centers, making it likely that the included patients have higher prevalences of fibrosis than a typical practice patient population, making it important to validate the findings in a real-world setting. The approach also relies on magnetic resonance technology, which is costly and may not be readily available. "We need to potentially find other, simpler noninvasive test combinations that are easier to do than MRE," said Dr. Younossi.

Several authors disclosed ties with numerous pharmaceutical and device companies, including Pfizer, AstraZeneca, and Siemens. Dr. Younossi has no relevant financial disclosures.

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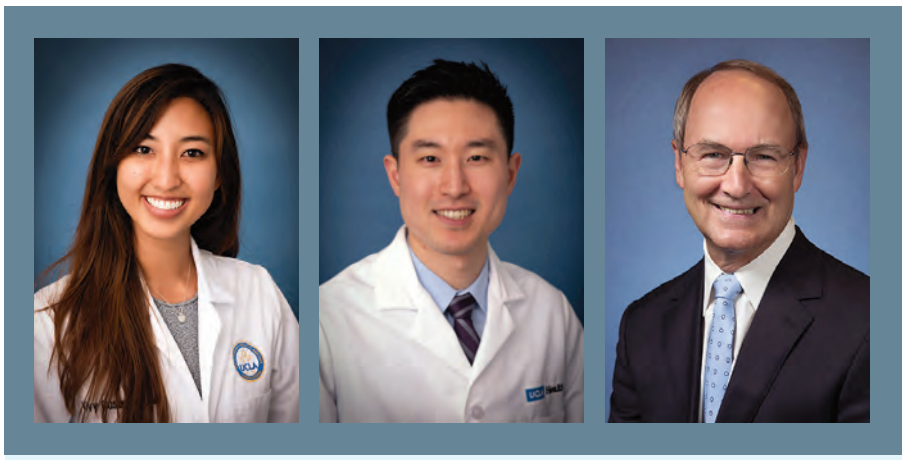
Definitive diverticular hemorrhage: Diagnosis and management

BY VIVY T. CUSUMANO, MD; CHRISTOPHER L. PAIJI, MD; AND DENNIS M. JENSEN, MD

Diverticular hemorrhage is the most common cause of colonic bleeding, accounting for 20%-65% of cases of severe lower-intestinal bleeding in adults.[1] Urgent colonoscopy after purging the colon of blood, clots, and stool is the most accurate method of diagnosing and guiding treatment of definitive diverticular hemorrhage.[2-5] The diagnosis of definitive diverticular hemorrhage depends upon identification of some stigmata of recent hemorrhage (SRH) in a single diverticulum (TIC), which can include active arterial bleeding, oozing, nonbleeding visible vessel, adherent clot, or flat spot.[2-4] Although other approaches, such as nuclear medicine scans and angiography of various types (CT, MRI, or standard angiography), for the early diagnosis of patients with severe hematochezia are utilized in many medical centers, only active bleeding can be detected by these techniques. However, as subsequently discussed, this SRH is documented in only 26% of definitive diverticular bleeds found on urgent colonoscopy, so diagnostic yields of these techniques will be low.[2-5]

The diagnosis of patients with severe hematochezia and diverticulosis, as well as triage of all of them to specific medical, endoscopic, radiologic, or surgical management, is facilitated by an urgent endoscopic approach.[2-5] Patients who are diagnosed with definitive diverticular hemorrhage on colonoscopy represent about 30% of all true TIC bleeds when urgent colonoscopy is the management approach.[2-5] That is because approximately 50% of all patients with colon diverticulosis and first presentation of severe hematochezia have incidental diverticulosis; they have colonic diverticulosis, but another site of bleeding is identified as the cause of hemorrhage in the gastrointestinal tract.[2-4] Presumptive diverticular hemorrhage is diagnosed when colonic diverticulosis without TIC stigmata are found but no other GI bleeding source is found on colonoscopy, anoscopy, enteroscopy, or capsule endoscopy.[2-5] In our experience with urgent colonoscopy, the presumptive diverticular bleed group accounts for about 70% of patients with documented diverticular hemorrhage (e.g., not including incidental diverticulosis bleeds but combining subgroups of patients with either definitive or presumptive TIC diagnoses as documented TIC hemorrhage).



Dr. Cusumano and Dr Paiji are fellow physicians in the Vatche and Tamar Manoukian Division of Digestive Diseases at University of California Los Angeles. Dr. Jensen is a professor of medicine in Vatche and Tamar Manoukian Division of Digestive Diseases and is with the CURE Digestive Diseases Research Center at the VA Greater Los Angeles Healthcare System. All authors declare that they have no competing interests or disclosures.

Clinical presentation

Patients with diverticular hemorrhage present with severe, painless large-volume hematochezia. Hematochezia may be self-limited and spontaneously resolve in 75%-80% of all patients but with high rebleeding rates up to 40%.[5-7] Of all patients with diverticulosis, only about 3%-5% develop diverticular hemorrhage.[8] Risk factors for diverticular hemorrhage include medications (e.g., nonsteroidal anti-inflammatory drugs – NSAIDs, antiplatelet drugs, and anticoagulants) and other clinical factors, such as older age, low-fiber diet, and chronic constipation.[9,10] On urgent colonoscopy, more than 70% of diverticulosis in U.S. patients are located anatomically in the descending colon or more distally. In contrast, about 60% of definitive diverticular hemorrhage cases in our experience had diverticula with stigmata identified at or proximal to the splenic flexure.[2,4,11]

Pathophysiology

Colonic diverticula are herniations of mucosa and submucosa with colonic arteries that penetrate the muscular wall. Bleeding can occur when there is asymmetric rupture of the vasa recta at either the base of the diverticulum or the neck.[4] Thinning of the mucosa on the luminal surface (such as that resulting from impacted fecaliths and stool) can cause injury to the site of the penetrating vessels, resulting in hemorrhage.[12]

Initial management

Patients with acute, severe hematochezia should be triaged to an inpatient setting with a monitored bed. Admission to an intensive care unit should be considered for patients with hemodynamic instability, persistent bleeding, and/or significant comorbidities. Patients with TIC hemorrhage often require resuscitation with crystalloids and packed red blood cell transfusions for hemoglobin less than 8 g/dl.[4] Unlike upper-GI hemorrhage, which has been extensively reported on, data regarding a more restrictive transfusion threshold, compared with a liberal transfusion threshold, in lower-intestinal bleeding are very limited. Correction of underlying coagulopathies is recommended but should be individualized, particularly in those patients on antithrombotic agents or with underlying bleeding disorders.

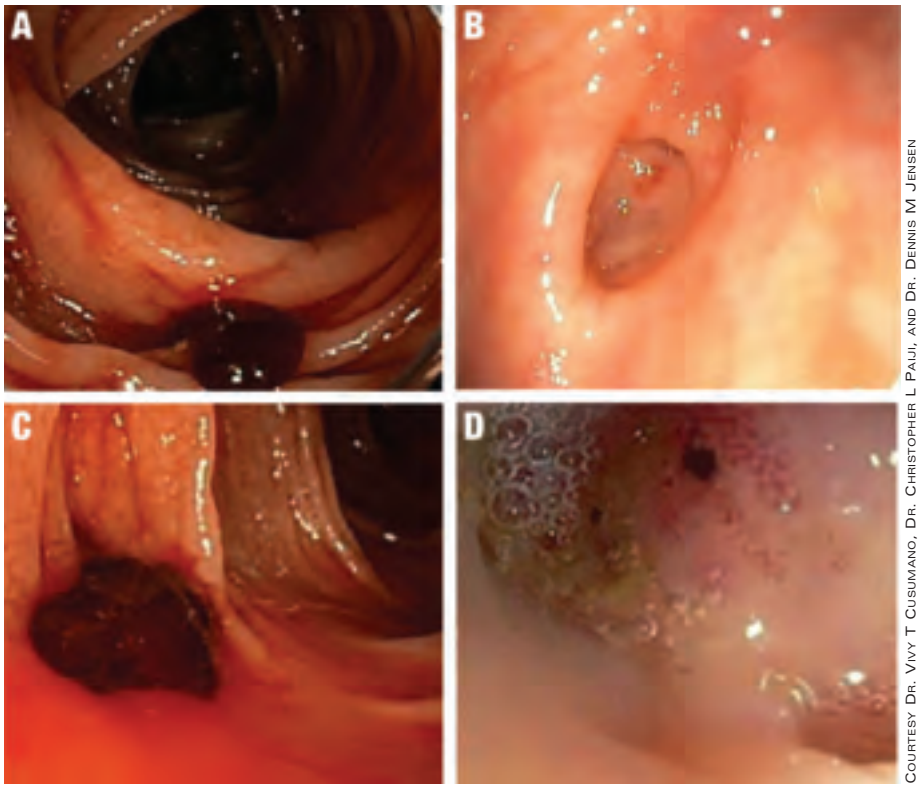
Urgent diagnosis and hemostasis

Urgent colonoscopy within 24 hours is the most accurate way to make a diagnosis of definitive diverticular hemorrhage and to effectively and safely treat them.[2-4,10,11] For patients with severe hematochezia, when the colonoscopy is either not available in a medical center or does not reveal the source of bleeding, nuclear scintigraphy or angiography (CT, MRI, or inversion recovery [IR]) are recommended. CT angiography may be particularly helpful to diagnose patients with hemodynamic instability who are suspected to have active TIC bleeding and are not able to complete a bowel preparation. However, these imaging techniques require active bleeding at the time of the study to be diagnostic. This SRH is also uncommon for definitive diverticular hemorrhage, so the diagnostic yield is usually quite

Colonic diverticular bleeding is the most common etiology of overt lower-gastrointestinal bleeding and one of the most frequent consults we receive as gastroenterologists. Classically, diverticular bleeding is characterized by painless hematochezia which often self-resolves without intervention. While this specific constellation of symptoms raises suspicion for diverticular bleeding, obtaining a definitive diagnosis can often be difficult.

The In Focus article for November, which is brought to you by The New Gastroenterologist, provides a comprehensive review of the management of definitive diverticular hemorrhage and is written by Dr. Vivy T. Cusumano, Dr. Christopher L. Paiji, and Dr. Dennis M. Jensen. This excellent piece details the pathophysiology, diagnosis, and treatment, but importantly also provides an in-depth review of the therapeutic utility and limitations of available diagnostic modalities, namely colonoscopy and angiography.

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



Courtesy Dr. Vivy T Cusumano, Dr. Christopher L Paiji, and Dr. Dennis M Jensen

Figure: Stigmata of recent hemorrhage in definitive TIC hemorrhage is shown, as well as prevalence on urgent colonoscopy when diagnosed: A. Active arterial bleeding, 26%; B. Nonbleeding visible vessel, 24%; C. Adherent clot, 37%; and D. Flat spot, 13%.

low.[2-5,10,11] An additional limitation of scintigraphy and CT or MRI angiography is that, if active bleeding is found, some other type of treatment, such as colonoscopy, IR angiography, or surgery, will be required for definitive hemostasis.

For urgent colonoscopy, adequate colon preparation with a large-volume preparation (6-8 liters of polyethylene glycol–based solution) is recommended to clear stool, blood, and clots to allow endoscopic visualization and localization of the bleeding source. Use of a nasogastric tube should be considered if the patient is unable to drink enough prep.[2-4,13] Additionally, administration of a prokinetic agent, such as Metoclopramide, may improve gastric emptying and tolerance of the prep. During colonoscopy, careful inspection of the colonic mucosa during insertion and withdrawal is important since lesions may bleed intermittently and SRH can be missed. An adult or pediatric colonoscope with a large working channel (at least 3.3 mm) is recommended to facilitate suctioning of blood clots and stool, as well as allow the passage of endoscopic hemostasis accessories. Targeted water-jet irrigation, an expert colonoscopist, a cap attachment, and adequate colon preparation are all predictors for improved diagnosis of definitive diverticular hemorrhage.[4,14]

SRH in definitive TIC bleeds all have a high risk of TIC rebleeding,[2-4,10,11] including active bleeding, nonbleeding visible vessel, adherent clot, and a flat spot (See Figure).

Based on CURE Hemostasis Group data of 118 definitive TIC bleeds, 26% had active bleeding, 24% had a nonbleeding visible vessel, 37% had an adherent clot, and 13% had a flat spot (with underlying arterial blood flow by Doppler probe monitoring).[4] Approximately 50% of the SRH were found in the neck of the TIC and 50% at the base, with actively bleeding cases more often from the base. In CURE Doppler endoscopic probe studies, 90% of all stigmata had an underlying arterial blood flow detected with the Doppler probe.[4,10] The Doppler probe is reported to be very useful for risk stratification and to confirm obliteration of the arterial blood flow underlying SRH for definitive hemostasis.[4,10]

Endoscopic treatment

Given high rates of rebleeding with medical management alone, definitive TIC hemorrhage can be effectively and safely treated with endoscopic therapies once SRH are localized.[4,10] Endoscopic therapies that have been reported in the literature include electrocoagulation, hemoclip, band ligation, and over-the-scope clip. Four-quadrant injection of 1:20,000 epinephrine around the SRH can improve visualization of SRH and provide temporary control of bleeding, but it should be combined with other modalities because of risk of rebleeding with epinephrine alone.[15] Results from studies reporting rates of both early rebleeding (occurring within 30 days) and late rebleeding (occurring after 30 days) are listed in the Table.

Multipolar electrocoagulation (MPEC), which utilizes a focal electric current to generate heat, can coaptively coagulate small TIC arteries.[16] For SRH in the neck of TIC, MPEC is effective for coaptive coagulation at a power of 12-15 watts in 1- to 2-second pulses with moderate laterally applied tamponade pressure. MPEC should be avoided for treating SRH at the TIC base because of lack of muscularis propria and higher risk of perforation.

Hemoclip therapy has been reported to be safe and efficacious in treatment of definitive TIC hemorrhage, by causing mechanical hemostasis with occlusion of the bleeding artery.[16] Hemoclips are recommended to treat stigmata in the base of TICs and should be targeted on either side of visible vessel in order to occlude the artery underneath it.[4,10] With a cap on the tip of the colonoscope, suctioning can evert TICs, allowing more precise placement of hemoclip on SRH in the base of the TIC.[17] Hemoclip retention rates vary with different models and can range from less than 7 days to more than 4 weeks. Hemoclips can also mark the site if early rebleeding occurs; then, reintervention (e.g., repeat endoscopy or angioembolization) is facilitated.

Another treatment is endoscopic band ligation, which provides mechanical hemostasis. Endoscopic band ligation has been reported to be efficacious for TIC hemorrhage.[18] Suctioning the TIC with the SRH into the distal cap and deploying a band leads to obliteration of vessels and potentially necrosis and disappearance of banded TIC.[16] This technique carries a risk of perforation because of the thin walls of TICs. This risk may be higher for right-sided colon lesions since an ex vivo colon specimen study reported serosal entrapment and inclusion of muscularis propria postband ligation, both of which may result in ischemia of intestinal wall and delayed perforation.[19]

Over-the-scope clip (OTSC) has been reported in case series for treatment of definitive TIC hemorrhage. With a distal cap and large clip,

Continued on page 27

Study results of endoscopic therapies for definitive diverticular hemorrhage

Study	Design	Treatment modality	N	Hemostasis achieved	Early rebleeding (less than 30 days)	Late rebleeding (greater than 30 days)
Prakash et al. (1999)[28]	Retrospective	Epinephrine injection and/or thermal coagulation	5	5 (100%)	0	0
Jensen et al. (2000)[2]	Prospective	Epinephrine injection and/or bipolar coagulation	10	10 (100%)	0	0
Yen et al. (2008)[29]	Retrospective	Hemoclip	11	11 (100%)	0	2 (18.2%)
Kaltenbach et al. (2012)[17]	Retrospective	Epinephrine injection and/or hemoclip	24	21 (88%)	0	5 (21%)
Ishii et al. (2012)[30]	Retrospective	Band ligation	31	27 (87%)	3 (10%)	0
Nakano et al. (2015)[18]	Retrospective	Hemoclip	39	39 (100%)	15 (38%)	7 (28%)
Nakano et al. (2015)[18]	Retrospective	Band ligation	61	61 (100%)	9 (15%)	12 (20%)
Jensen (2018)[4]	Prospective	Hemoclip or multipolar electrocoagulation	81	81 (100%)	4 (5%)	Not available
Nagata et al. (2018)[31]	Prospective	Hemoclip	47	47 (100%)	10 (21%)	8 (17%)
Nagata et al. (2018)[31]	Prospective	Band ligation	61	61 (100%)	6 (10%)	4 (7%)
Kaltenbach et al. (2020)[20]	Retrospective	OTSC	7	7 (100%)	0	0
Wongpongsalee et al. (2020)[26]	Prospective	Hemoclip or MPEC	74	74 (100%)	6 (8.1%)	23 (31.1%)

Source: Dr. Cusumano, Dr. Paiji, Dr. Jensen

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suctioning can evert TICs and facilitate deployment over the SRH.[20,21] OTSC can grasp an entire TIC with the SRH and obliterate the arterial blood flow with a single clip.[20,21] No complications have been reported yet for treatment of TIC hemorrhage. However, the OTSC system is relatively expensive when compared with other modalities.

After endoscopic treatment is performed, four-quadrant spot tattooing is recommended adjacent to the TIC with the SRH. This step will facilitate localization and treatment in the case of TIC rebleeding.[4,10]

Outcomes following endoscopic treatment

Following endoscopic treatment, patients should be monitored for early and late rebleeding. In a pooled analysis of case series composed of 847 patients with TIC bleeding, among the 137 patients in which endoscopic hemostasis was initially achieved, early rebleeding occurred in 8% and late rebleeding occurred in 12% of patients.[22] Risk factors for TIC rebleeding within 30 days were residual arterial blood flow following hemostasis and early reinitiation of antiplatelet agents.

Remote treatment of TIC hemorrhage distant from the SRH is a significant risk factor for early TIC rebleeding.[4,10] For example, using hemoclips to close the mouth of a TIC when active bleeding or an SRH is located in the TIC base often fails because arterial flow remains open in the base and the artery is larger there.[4,10] This example highlights the importance of focal obliteration of arterial blood flow underlying SRH in order to achieve definitive hemostasis.[4,10]

Salvage treatments

For TIC hemorrhage that is not controlled by endoscopic therapy, transcatheter arterial embolization (TAE) is recommended. If bleeding rate is high enough (at least 0.5 milliliters per minute) to be detected by angiography, TAE can serve as an effective method of diagnosis and immediate hemostasis.[23] However, the most common major complication of embolization is intestinal ischemia. The incidence of intestinal ischemia has been reported as high as 10%, with highest risk with embolization of at least three vasa recta.[24]

Surgery is also recommended if TIC hemorrhage cannot be controlled with endoscopic therapy or TAE. Segmental colectomy is recommended if the bleeding site can be localized before surgery with colonoscopy or angiography resulting from significantly lower perioperative morbidity than subtotal colectomy.[25] However, subtotal colectomy may be necessary if preoperative localization of bleeding is unsuccessful.

There are very few reports of short- or long-term results that compare endoscopy, TAE, and surgery for management of TIC bleeding. However, a recent retrospective study reported better outcomes with endoscopic treatment of definitive TIC bleeding.[26] Patients who underwent endoscopic treatment had fewer RBC transfusions, shorter hospitalizations, and lower rates of postprocedure complications.

Management after cessation of hemorrhage

Medical management is important following an episode of TIC hemorrhage. A mainstay is daily fiber supplementation every morning and stool softener in the evening. Furthermore, patients are advised to drink an extra liter of fluids (not containing alcohol or caffeine) daily. By reducing colon transit time and increasing stool weight, these measures can help control constipation and prevent future complications of TIC disease.[27]

Patients with recurrent TIC hemorrhage should undergo evaluation for elective surgery, provided they are appropriate surgical candidates. If preoperative localization of bleeding site is successful, segmental colectomy is preferred. Segmental resection is associated with significantly decreased rebleeding rate, with lower rates of morbidity compared with subtotal colectomy.[32]

Chronic NSAIDs, aspirin, and antiplatelet drugs are risk factors for recurrent TIC hemorrhage, and avoiding these medications is recommended if possible.[33,34] Although anticoagulants have shown to be associated with increased risk of all-cause gastrointestinal bleeding, these agents have not been shown to increase risk of recurrent TIC hemorrhage in recent large retrospective studies. Since antiplatelet and anticoagulation agents serve to reduce risk of thromboembolic events, the clinician who recommended these medications should be consulted after a TIC bleed to re-evaluate whether these medications can be discontinued or reduced in dose.

Conclusion

The most effective way to diagnose and treat definitive TIC hemorrhage is to perform an urgent colonoscopy within 24 hours to identify and treat TIC SRH. This procedure requires thoroughly cleansing the colon first, as well as an experienced colonoscopist who can identify and treat TIC SRH to obliterate arterial blood flow underneath SRH and achieve definitive TIC hemostasis. Other approaches to early diagnosis include nuclear medicine scintigraphy or angiography (CT, MRI, or IR). However, these techniques can detect only active bleeding which is documented in only 26% of colonoscopically diagnosed definitive TIC hemorrhages. So, the expected diagnostic yield of these tests will be low. When urgent colonoscopy fails to make a diagnosis or TIC bleeding continues, TAE and/or surgery are recommended. After definitive hemostasis of TIC hemorrhage and for long-term management, control of constipation and discontinuation of chronic NSAIDs and antiplatelet drugs (if possible) are recommended to prevent recurrent TIC hemorrhage.

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

CLINICAL CHALLENGES AND IMAGES

What's your diagnosis?

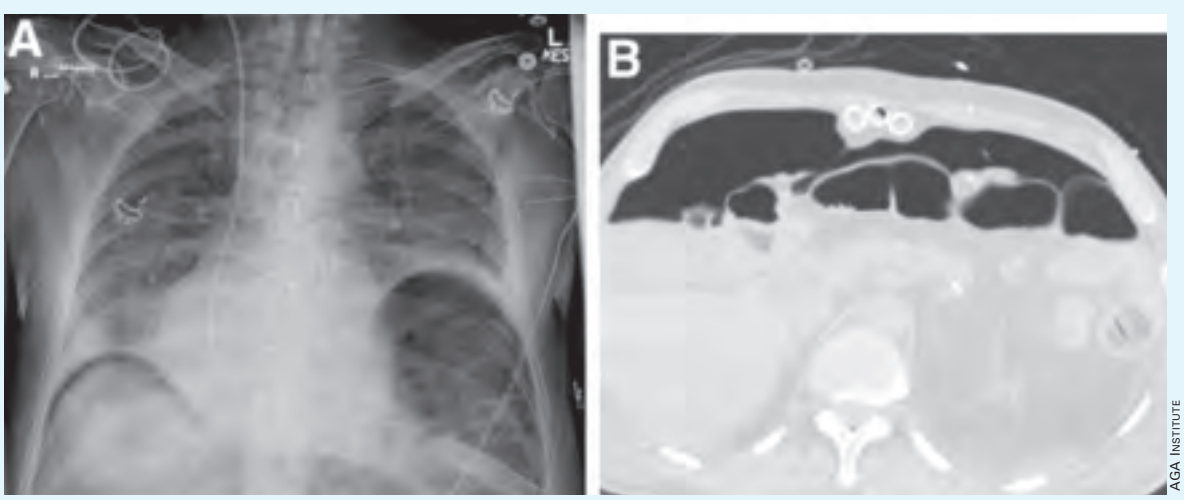
BY CHARLES MEADE, MD, AND MAGNUS HALLAND, MD, B.MED

Previously published in Gastroenterology (2019 Nov;157[5]:1199-200).

Question: An 82-year-old man was admitted for urgent coronary artery bypass and concurrent mitral valve repair. Intraoperatively, he underwent cardiopulmonary bypass, epicardial pacing, and placement of two anterior mediastinal and one pleural chest tubes. After a relatively unremarkable initial postoperative course and nonnarcotic pain control, concern for ileus developed on postoperative day 4. A nasogastric tube was placed out of concern for worsening somnolence, nausea, and the inability to safely tolerate oral intake. The patient had been passing flatus but had yet to have a bowel movement since the operation. Physical examination at the time was notable for a soft abdomen with diffuse tenderness and voluntary guarding. Subsequent plain film imaging to confirm nasogastric tube placement (Figure A) and follow-up computed tomography imaging (Figure B) are shown.

What's the diagnosis?

The answer is on page 28.



Is telemedicine here to stay?

It holds promise


Dr. Hernaez

The Federation of State Medical Boards defines telemedicine as "the practice of medicine using electronic communication, information technology, or other means between a physician in one location, and a patient in another location, with or without an intervening health care provider." What my patient was asking was to use a mode of telemedicine – a video visit – to receive the same quality of care. He brought up three critical points that I will discuss further: access to specialty care (such as transplant hepatology), reduction of costs (time and money), and improved patient satisfaction.

Ruben Hernaez, MD, MPH, PhD, is with the section of gastroenterology and the Center for Innovations in Quality, Effectiveness and Safety at the Michael E. DeBakey VA Medical Center and in the section of gastroenterology and hepatology in the department of medicine Baylor College of Medicine, both in Houston. He has no relevant conflicts of interest.

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

Dear colleagues and friends,

I am fortunate to receive the baton from Charles Kahi, MD, in facilitating the fascinating and timely debates that have characterized the AGA Perspective series. Favorable reimbursement changes and the need for social distancing fast-tracked telemedicine, a care delivery model that had been slowly evolving. In this month's Perspective column, Dr. Hernaez and Dr. Vaughn discuss the pros and cons of telemedicine in GI. Is it the new office visit? Or simply just good enough for when we really need it? I look forward to hearing your thoughts and experiences on the AGA Community forum and by email (ginews@gastro.org).


Dr. Ketwaroo

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

It has its limits


Dr. Vaughn

The post-pandemic world will include telehealth. Technology disrupts business-as-usual and often brings positive change. But there are consequences. To employ telehealth into routine care equitably and effectively into a gastroenterology practice, we should consider two general questions: "Was the care I provided the same quality as if the patient was seen in person?" and more broadly, "am I satisfied with my practice's implementation of telehealth?" This perspective will highlight several areas affecting gastroenterology care: lack of physical exam, disproportionate impact on certain populations, development of a patient-provider relationship, impact on physician wellbeing, and potential financial ramifications. We will all have to adapt to telemedicine to some extent. Understanding the tradeoffs of this technology can help us position effectively in a gastroenterology practice.

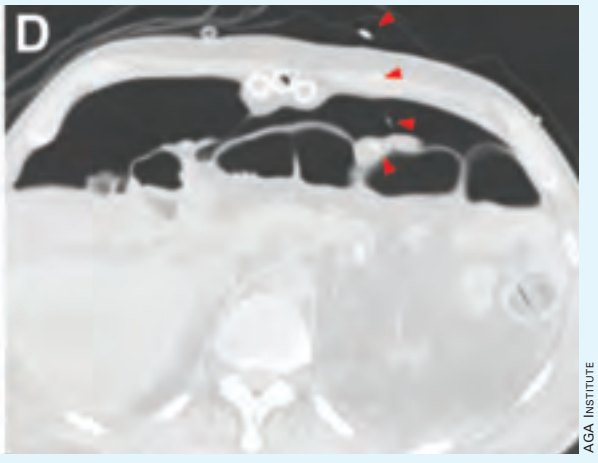
Byron P. Vaughn, MD, MS, is an associate professor of medicine and codirector, The Inflammatory Bowel Disease Program in the division of gastroenterology, hepatology, and nutrition at University of Minnesota, Minneapolis. He has received consulting fees from Prometheus and research support from Roche, Takeda, Celgene, Diasorin, and Crestovo.

CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What's your diagnosis?" from page 27: Sigmoid colon perforation secondary to transcutaneous epicardial pacer wires.

A plain film image (Figure A) shows diffusely dilated loops of bowel with subdiaphragmatic air concerning for GI viscous perforation. Dedicated cross-sectional imaging confirms intra-abdominal free air, and in representative cross section, the epicardial pacing wires can be visualized within the gastrointestinal lumen (Figure D, arrows). At the time of surgical consultation, the radiology report was notable for concern regarding possible disruption of peritoneum secondary to the difficult surgical chest tube placement in a patient with a high-riding left hemidiaphragm. Urgent laparoscopic exploration secondary to these findings unexpectedly revealed that the transcutaneous epicardial pacing wires had been inadvertently placed through the sigmoid colon (Figure C). The pacer wires were cut and removed intraoperatively. Unfortunately, 4 days after removal of pacer wires, the patient continued to have ongoing distension and was found to have sigmoid volvulus necessitating endoscopic decompression. After a prolonged hospitalization and recovery, he was discharged with a normal bowel pattern and tolerating oral intake to a skilled nursing facility.



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Temporary transcutaneous epicardial pacing wires are often placed after complex cardiovascular surgical procedures. Complications from wire placement are thought to be relatively rare and are typically associated with migration into local structures after wire placement and infectious complications secondary to retained wires.[1,2] Perforation of local structures during placement is less common, and GI viscous perforation in particular is not a well characterized cause of associated morbidity.[3]

Our case demonstrates that, in patients with hemidiaphragm elevation, epicardial wire placement risks GI viscous perforation. Furthermore, given the frequency of concomitant surgical hardware in this patient population, identification of malpositioned epicardial wires on plain film and even cross-sectional imaging can be difficult and can delay diagnosis.

References

1. Del Nido P and Goldman BS. J Card Surg. 1989 Mar;4(1):99-103.
2. Kapoor A et al. Interact Cardiovasc Thorac Surg. 2011 Jul;13(1):104-6.
3. Haba J et al. Can Assoc Radiol J. 2013 Feb;64(1):77-80.

AGA Clinical Practice Update: Expert Review

Diagnosing and managing atrophic gastritis

BY JIM KLING
MDedge News

A new clinical practice update expert review for the diagnosis and management of atrophic gastritis (AG) from the American Gastroenterological Association focuses on cases linked to *Helicobacter pylori* infection or autoimmunity.


Dr. Shah

This update (Gastroenterology. 2021 Oct;161[4]:1325-32.E7) addresses a sparsity of guidelines for AG in the United States and should be seen as complementary to the AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia (Gastroenterology. 2020 Feb;158[3]:693-702), according to the authors led by Shailja C. Shah, MD, MPH, of the gastroenterology section at Veterans Affairs San Diego Healthcare System and the division of gastroenterology at the University of California, San Diego.

The 2020 guidelines didn't specifically discuss diagnosis and management of AG; however, a diagnosis of intestinal metaplasia based on gastric histopathology indicates the presence AG since metaplasia occurs in atrophic mucosa. Nevertheless, AG often goes unmentioned in histopathology reports. Such omissions are important because AG is an important stage in the potential development of gastric cancer.

AG is believed to result from genetic and environmental factors. The two primary triggers for the condition are *H. pylori* infection (HpAG) and autoimmunity (AIG). The condition results from chronic inflammation and replacement of normal gastric glandular structures with connective tissue or nonnative epithelium. It can proceed to other precancerous conditions, including gastric intestinal metaplasia and dysplasia. An estimated 15% of the U.S. population has AG, according to the authors, although this prevalence could be higher in populations with higher rates of *H. pylori* infection. AIG is rare, occurring in 0.5%-2% of the U.S. population.

Among individuals with AG, 0.1%-0.3% per year go on to develop gastric adenocarcinoma, though additional factors could heighten this risk. Furthermore, 0.4%-0.7% per year go on develop type 1 neuroendocrine tumors.

HpAG and AIG have different patterns of mucosal involvement. During diagnosis, the authors advised careful mucosal visualization with air insufflation and mucosal cleansing. High-definition white-light endoscopy is more sensitive than traditional WLE in the identification of premalignant mucosal changes.

The condition results from chronic inflammation and replacement of normal gastric glandular structures with connective tissue or nonnative epithelium.

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Gastric cancer: Family history–based *H. pylori* strategy would be cost effective

BY JIM KLING
MDedge News

Testing for and treating *Helicobacter pylori* infection among individuals with a family history of gastric cancer could be a cost-effective strategy in the United States, according to a new model published in the journal Gastroenterology (2021 Aug. doi: 10.1053/j.gastro.2021.08.042).

As many as 10% of gastric cancers aggregate within families, though just why this happens is unclear, according to Sheila D. Rustgi, MD, and colleagues. Shared environmental or genetic factors, or combinations of both, may be responsible. First-degree family history and *H. pylori* infection each raise gastric cancer risk by roughly 2.5-fold.

In the United States, universal screening for *H. pylori* infection is not currently recommended, but some studies have suggested a possible benefit in some high-risk populations. American Gastroenterological Association clinical practice guidelines suggest that a patient's family history should be a factor when considering surveillance strategies for intestinal metaplasia (Gastroenterology. 2020 Feb;158[3]:693-702).

Furthermore, a study by Il Ju Choi, MD, and colleagues in 2020 (Jan 30. N Engl J Med. doi: 10.1056/NEJMoa1909666) showed that *H. pylori* treatment with bismuth-based quadruple therapy reduced the risk of gastric cancer by 73% among individuals with a first-degree relative who had gastric cancer. The combination included a proton pump inhibitor, bismuth, metronidazole, and tetracycline for 10 days.

"We hypothesize that, given the dramatic reduction in GC demonstrated by Choi et al., that the screening strategy can be a cost-effective intervention," Dr. Rustgi and colleagues wrote.

In the new study, the researchers used a Markov state-transition mode, employing a hypothetical cohort of 40-year-old U.S. men and women with a first-degree relative with gastric cancer. It simulated a follow-up period of 60 years or until death. The model assumed a 7-day treatment with triple therapy (proton pump inhibitor, clarithromycin, and amoxicillin) followed by a 14-day treatment period with quadruple therapy if needed. Although the model was analyzed from the U.S. perspective, the trial that informed the risk reduction was performed in a South Korean population.

No screening had a cost of $2,694.09 and resulted in 21.95 quality-adjusted life-years (QALYs). 13C-Urea Breath Test screening had a cost of $2,105.28 and led to 22.37 QALYs. Stool antigen testing had a cost of $2,126.00 and yielded 22.30 QALYs.

In the no-screening group, an estimated 2.04% of patients would develop gastric cancer, and 1.82% would die of it. With screening, the frequency of gastric cancer dropped to 1.59%-

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AG diagnosis should be confirmed by histopathology. The updated Sydney protocol should be used to obtain biopsies (Am J Surg Pathol. 1996 Oct;20[10]:1161-81), and serum pepsinogens can be used to identify extensive atrophy, though this testing is not generally available in the United States for clinical use. When histology results are suggestive of AIG, the presence of parietal cell antibodies and intrinsic factor antibodies can contribute to a diagnosis, although the former can be prone to false positives because of *H. pylori* infection, and the latter has low sensitivity.

Patients identified with AG should be tested for *H. pylori* and treated for infection, followed by nonserologic testing to confirm treatment success. If *H. pylori* is present, successful eradication may allow for reversal of AG to normal gastric mucosa; however, some patients may have irreversible changes. This could leave them at elevated risk of further progression, though elimination of *H. pylori* does appear to blunt that risk somewhat.

Neoplastic complications from AG are rare, and the benefits of surveillance among those with AG have not been demonstrated in prospective trials. Observational trials show that severe AG is associated with greater risk of gastric adenocarcinoma, and other factors, such as comorbidities and patient values and priorities, should inform decision-making. When called for, providers should consider surveillance endoscopies every 3 years, though the authors noted that the optimal surveillance interval is unknown. Factors such as the quality of the original endoscopy, family history of gastric cancer, and a history of immigration from regions with high rates of *H. pylori* infection may impact decisions on surveillance intervals.

AG can lead to iron or vitamin B_{12} deficiency, so patients with AG, especially those with corpus-predominant AG, should be evaluated for both. AG should also be considered as a differential diagnosis in patients presenting with either deficiency.

A diagnosis of AIG should be accompanied by screening for autoimmune thyroid disease, and type 1 diabetes or Addison's disease may also be indicated if clinical presentation is consistent.

Because AG is commonly underdiagnosed, the authors advise that gastroenterologists and pathologists should improve coordination to maximize diagnosis of the condition, and they call for comparative clinical trials to improve risk stratification algorithms and surveillance strategies.

The authors disclose no relevant conflicts of interest.

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1.65%, with a gastric cancer mortality rate of 1.41%-1.46%. Overall, screening was modeled to lead to a 19.1%-22.0% risk reduction.

The researchers validated their model by an assumption of an *H. pylori* infection rate of 100% and then compared the results of the model to the outcome of the study by Dr. Choi and colleagues. In the trial, there was a 55% reduction in gastric cancer among treated patients at a median of 9 years of follow-up. Those who had successful eradication of *H. pylori* had a 73% reduction. The new model estimated reductions from a testing and treatment strategy of 53.3%-64.5%.

The findings aren't surprising, according to Joseph Jennings, MD, of the department of medicine at Georgetown University, Washington, and director of the Center for GI Bleeding at MedStar Georgetown University Hospital, who was not involved with the study. "Even eliminating one person getting gastric cancer, where they will then need major surgery, chemotherapy, all these very expensive interventions [is important]," said Dr. Jennings. "We have very efficient ways to test for these things that don't involve endoscopy."

One potential caveat to identifying and treating *H. pylori* infection is whether elimination of *H. pylori* may lead to some adverse effects. Some patients can experience increased acid reflux as a result, while others suffer no ill effects. "But when you're dealing with the alternative, which is stomach cancer, those negatives would have to stack up really, really high to outweigh the positives of preventing a cancer that's really hard to treat," said Dr. Jennings.

Dr. Jennings pointed out that the model also projected testing and an intervention conducted in a South Korean population, and extrapolated it to a U.S. population, where the incidence of gastric cancer is lower. "There definitely are some questions about how well it would translate if applied to the general United States population," said Dr. Jennings.

That question could prompt researchers to conduct a U.S.-based study modeled after the test and treat study in South Korea to see if the regimen produced similar results. The model should add weight to that argument, said Dr. Jennings: "This is raising the point that, at least from an intellectual level, it might be worth now designing the study to see if it works in our population," said Dr. Jennings.

The authors and Dr. Jennings have no relevant financial disclosures.

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