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Member SPOTLIGHT

In a Parallel Universe, I'd Be a Concert Pianist Says Tennessee GI

Courtesy Dr. Stephanie D. Pointer

Dr. Stephanie D. Pointer

BY JENNIFER LUBELL
MDedge News

Whether it's playing her piano, taking on a sewing project, or performing a colonoscopy, Stephanie D. Pointer, MD, enjoys working with her hands. She also relishes opportunities to think, to analyze, and solve problems for her patients.

One of her chief interests is inflammatory bowel disease (IBD). It's reassuring to focus on a field of work "where I know exactly what's causing the issue, and I can select a therapeutic approach (medication and lifestyle changes) that help a patient achieve remission," said Dr. Pointer, co-owner and managing partner of Digestive and Liver Health Specialists in Hendersonville, Tenn. She's also the medical director and a principal investigator of Quality Medical Research in Nashville, and currently serves as chair of the AGA Trainee and Early Career Committee.

Starting her own practice has been just as challenging and rewarding as going through medical school. Medical training does not prepare you for starting your own practice, Dr. Pointer said, so she and her business partner have had to learn as they go. "But I think we've done very well. We've taken the ups

See **Tennessee** · *page 18*

Cold Snare Resection Safe for Large Nonpedunculated Colorectal Polyps

BY DIANA SWIFT

FROM GASTROENTEROLOGY

Cold snare endoscopic mucosal resection (EMR) may be a safe therapeutic option for selected large colorectal polyps, thanks to a safety profile superior to that of hot EMR.

In findings from Germany's randomized controlled CHRONICLE trial, published in *Gastroenterology* (2024 May. doi: 10.1053/j.gastro.2024.05.013), the cold technique almost eliminated major adverse events (AEs) — but at the cost of higher rates of recurrence and residual adenoma at first follow-up.

"The exact definition of the ideal lesions requires further research," wrote investigators led by Ingo Steinbrück, MD, of the Department of Medicine and Gastroenterology at the Academic Teaching Hospital of the University of Freiburg, Freiburg im Breisgau, Germany. "Further studies have to confirm to what extent polyp size and histology can determine an individualized approach."

The researchers noted that while hot snare resection is the gold standard for larger nonpedunculated polyps of ≥ 2 cm, previous research has found the cold technique, which resects without cutting and cauterizing current, to be superior for small polyps (Ann Intern Med. 2023 Feb 21. doi: 10.7326/M22-2189).

"Our study suggests that sessile serrated lesions larger than 2 cm should be resected with the cold snare. Selected cases of lateral spreading tumors may also be good candidates for cold snare resection

See **Polyps** · *page 23*

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LETTER FROM THE EDITOR

Following the Light

Percutaneous endoscopic gastrostomy (PEG) was first introduced in the early 1980s by surgeons Michael Gauderer and Jeffrey Ponsky as a less-invasive alternative to surgical gastrostomy via open laparotomy. The concept was born after the pair observed that the light from an endoscope in an infant undergoing endoscopy caused the abdominal wall to glow in the darkened operating room.

In fact, PEG was among the first procedures that defined minimally invasive surgery, a concept that has now revolutionized the surgical field. Since that time, PEG has evolved as a preferred method for patients needing long-term nutritional support for various indications. By 2001, approximately 216,000 PEGs were placed annually in the United States. While the volume of PEG procedures has declined in recent years at some institutions as practice patterns have shifted toward interventional radiology–placed gastrostomy tubes, evaluation of patients for PEG insertion, removal, or management of PEG complications remains a core area of gastroenterology practice.

ROMASET/ISTOCK/GETTY IMAGES

Among the most important roles of the gastroenterologist in considering potential PEG candidates is to determine whether an appropriate indication exists, a decision that requires a detailed understanding of a patient's overall clinical condition, goals of care, values, and preferences. This month's Ethics Corner column provides important expert insights on navigating the complex ethical and clinical issues relating to PEG placement, a common GI consultation that deserves thoughtful consideration and demands effective communication among members of the multidisciplinary team and with patients.

Dr. Adams

This month's Ethics Corner column provides important expert insights on navigating the complex ethical and clinical issues relating to PEG placement.

Also in our October issue, we highlight a recently published large multicohort study from *Gastroenterology* elucidating clinical, serologic, and genetic factors associated with extraintestinal manifestations in IBD. We also review key updates to colonoscopy quality indicators, including modifications to existing indicators such as ADR and the addition of two new "priority indicators" — rate of inadequate bowel prep and sessile serrated lesion detection rate.

In this month's Member Spotlight, Dr. Stephanie Pointer of Digestive & Liver Health Specialists in Tennessee, shares the many ways in which she has given back to her community through music and mentoring while leading a thriving GI practice. We hope you enjoy this, and all the coverage included in our October issue. ■

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

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GI&Hepatology News

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Meet Our 10 Editorial Fellows

The AGA editorial fellowship program, currently in its seventh year, selects several outstanding individuals who are interested in scientific publishing to take part in the year-long program.

We are excited to announce the 2024-2025 participants, who will gain hands-on experience and mentorship working closely with the editors and staff at the AGA journals over the next year.

The 10 editorial fellows (2 per journal) will learn about the entire editorial process, from manuscript submission to peer review to acceptance. They will participate in discussions and conferences with the boards of editors, assist with manuscript review, and help disseminate articles via their social media platforms. ■

AGA

The 2024-2025 participants in the AGA editorial fellowship program will gain hands-on experience and mentorship working closely with editors and staff at the AGA journals over the next year.

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Creating a Planned Gift That's Meaningful to You

As an AGA member, you can help fund discoveries that will continue to improve GI practice and better patient care.

The AGA Research Foundation has helped make significant strides in advancing the treatment and cure of digestive diseases by funding talented investigators.

Planning your gift to benefit AGA Research Foundation in the future is an opportunity to express what matters to you. As an AGA member, you can work with the AGA Research Foundation to ensure that your planned gift is designated for a purpose that meets your goals for leaving a legacy — such as research awards, support for specific programs, or unrestricted gifts to help meet the Foundation's mission.

In as little as one sentence in your will and/or trust, you can complete your gift: "I give to AGA Research Foundation, a nonprofit corporation currently located at 4930 Del Ray Avenue, Bethesda, MD 20814, or its successor thereto, _____ [written amount or percentage of the estate or description of property] for its unrestricted charitable use and purpose."

If you have named the AGA Research Foundation in your will or trust, please let us know so we can ensure that your gift is used according to your wishes. Notifying us of your plans will enable us to plan for the use of your future gift. However, if you prefer to remain anonymous, we will keep your name and gift in strict confidence.

Please contact foundation@gastro.org for more information. If you are considering a planned gift, consult with your own legal and tax advisers. ■

2025 Crohn's & Colitis Congress® Abstract Submissions

The 2025 Crohn's & Colitis Congress®, a partnership of the Crohn's & Colitis Foundation and AGA, is now accepting original inflammatory bowel disease (IBD) research abstract submissions through Oct. 16. Abstracts are free to submit and may be selected for in-person lectures or poster presentations. Accepted abstracts will also be co-published in AGA's *Gastroenterology* (https://www.gastrojournal.org/) and the Crohn's & Colitis Foundation's *Inflammatory Bowel Diseases* (https://academic.oup.com/ibdjournal).

Be sure to review the abstract submission guidelines (crohnscolitiscongress.org/abstracts-2/submit-an-abstract/) and submit by 9 pm EDT, Wednesday, Oct. 16.

Presenting authors will receive notification of acceptance on Monday, Dec. 9.

The Crohn's & Colitis Congress will take place Feb. 6-8, 2025, in San Francisco, California. It brings together the community of multidisciplinary experts and colleagues to revolutionize prevention, care and outcomes for IBD patients.

Learn alongside your colleagues and discover how to provide the absolute best care to those suffering with Crohn's disease and ulcerative colitis. ■

Subcutaneous Infliximab Beats Placebo for IBD Maintenance Therapy

BY WILL PASS
MDedge News

FROM GASTROENTEROLOGY

Subcutaneous (SC) infliximab is safe and effective, compared with placebo, for maintenance therapy in patients with inflammatory bowel disease (IBD), based on results of the phase 3 LIBERTY trials.

These two randomized trials should increase confidence in SC infliximab as a convenient alternative to intravenous (IV) delivery, reported co–lead authors Stephen B. Hanauer, MD, AGAF, of Northwestern Feinberg School of Medicine, Chicago, Illinois, and Bruce E. Sands, MD, AGAF, of Icahn School of Medicine at Mount Sinai, New York City, and colleagues.

Specifically, the trials evaluated CT-P13, an infliximab biosimilar, which was Food and Drug Administration approved for IV use in 2016. The SC formulation was approved in the United States in 2023 as a new drug, requiring phase 3 efficacy confirmatory trials.

"Physicians and patients may prefer SC to IV treatment for IBD, owing to the convenience and flexibility of at-home self-administration, a different exposure profile with high steady-state levels, reduced exposure to nosocomial infection, and health care system resource benefits," the investigators wrote in *Gastroenterology* (2024 May. doi: 10.1053/j.gastro.2024.05.006).

One trial included patients with Crohn's disease (CD), while the other enrolled patients with ulcerative colitis (UC). Eligibility depended upon inadequate responses or intolerance to corticosteroids and immunomodulators.

All participants began by receiving open-label IV CT-P13, at a dosage of 5 mg/kg, at weeks 0, 2, and 6. At week 10, those who responded to the IV induction therapy were randomized in a 2:1 ratio to continue with either the SC formulation of CT-P13 (120 mg) or switch to placebo, administered every 2 weeks until week 54.


Dr. Hanauer


Dr. Sands

The CD study randomized 343 patients, while the UC study had a larger cohort, with 438 randomized. Median age of participants was in the mid-30s to late 30s, with a majority being White and male. Baseline disease severity, assessed by the Crohn's Disease Activity Index (CDAI) for CD and the modified Mayo score for UC, was similar across treatment groups.

The primary efficacy endpoint was clinical remission at week 54, defined as a CDAI score of less than 150 for CD and a modified Mayo score of 0-1 for UC.

In the CD study, 62.3% of patients receiving CT-P13 SC achieved clinical remission, compared with 32.1% in the placebo group, with a treatment difference of 32.1% (95% CI, 20.9-42.1; $P < .0001$). In addition, 51.1% of CT-P13 SC-treated patients achieved endoscopic response, compared with 17.9% in the placebo group, yielding a treatment difference of 34.6% (95% CI, 24.1-43.5; $P < .0001$).

In the UC study, 43.2% of patients on CT-P13 SC achieved clinical remission at week 54, compared with 20.8% of those on placebo, with a treatment difference of 21.1% (95% CI, 11.8-29.3; $P < .0001$). Key secondary endpoints, including endoscopic-histologic mucosal improvement, also favored CT-P13 SC over placebo with statistically significant differences.

The safety profile of CT-P13 SC was comparable with that of IV infliximab, with no new safety concerns emerging during the trials.

"Our results demonstrate the superior efficacy of CT-P13 SC over placebo for maintenance therapy in patients with moderately to severely active CD or UC after induction with CT-P13 IV," the investigators wrote. "Importantly, the findings confirm that CT-P13 SC is well tolerated in this population, with no clinically meaningful differences in safety profile, compared with placebo. Overall, the results support CT-P13 SC as a treatment option for maintenance therapy in patients with IBD."

The LIBERTY studies were funded by Celltrion. The investigators disclosed relationships with Pfizer, Gilead, Takeda, and others. ■

Intravenous (IV) infliximab-dyyb, also called CT-P13 in clinical trials, is a biosimilar that was approved in the United States in 2016 under the brand name Inflectra. It received approval in Europe and elsewhere under the brand name Remsima.

The study from Hanauer and colleagues represents a milestone in biosimilar development as the authors studied an injectable form of the approved IV biosimilar, infliximab-dyyb. How might efficacy compare among the two formulations? The LIBERTY studies did not include an active IV infliximab comparator to answer this question. Based on a phase 1, open-label trial, subcutaneous (SC) infliximab appears noninferior to IV infliximab.


Dr. Velayos

The approval of SC infliximab-dyyb is notable for highlighting the distinct process for approving "modified" biosimilars in the United States, compared with elsewhere. For SC infliximab, the Food and Drug Administration required a new drug application and additional trials (the LIBERTY trials). As a result, SC infliximab-dyyb has a different name (Zymfentra) than its IV formulation (Inflectra) in the United States. This contrasts with other areas of the globe, where the SC formulation (Remsima-SC) was approved as a line-extension to the IV biosimilar (Remsima-IV).

It is remarkable that we have progressed from creating highly similar copies of older biologics whose patents have expired, to reimagining and modifying biosimilars to potentially improve on efficacy, dosing, tolerability, or as in the case of SC infliximab-dyyb, providing a new mode of delivery. For SC infliximab, whether the innovator designation will cause different patterns of use based on cost or other factors, compared with places where the injectable and intravenous formulations are both considered biosimilars, remains to be seen.

Fernando S. Velayos, MD, MPH, AGAF, is director of the Inflammatory Bowel Disease Program, The Permanente Group Northern California; adjunct investigator at the Kaiser Permanente Division of Research; and chief of Gastroenterology and Hepatology, Kaiser Permanente San Francisco Medical Center. He reported no conflicts of interest.

Crohn's Strictures and Cancer Risk Reevaluated in New Study

BY WILL PASS
MDedge News

FROM GASTRO HEP ADVANCES

Colonic strictures in patients with Crohn's disease (CD) may not increase long-term risk of colorectal cancer (CRC), offering support for a conservative approach to stricture management, according to investigators.

Although 8% of patients with strictures in a multicenter study were diagnosed with CRC, this diagnosis was made either simultaneously or within 1 year of stricture diagnosis, suggesting that cancer may have driven stricture development, and not the other way around, lead author Thomas Hunaut, MD, of Université de Champagne-Ardenne, Reims, France, and colleagues reported.

"The occurrence of colonic stricture in CD always raises concerns about the risk for

Continued on following page

Optimize Biologic Therapy Early in Pediatric Crohn's

BY WILL PASS
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Pediatric patients with Crohn's disease (CD) are less likely to discontinue biologic therapy if they take concomitant immunomodulatory drugs and undergo therapeutic drug monitoring (TDM), according to investigators.

These findings, and others concerning a lack of high-dose therapy and poor follow-up, suggest that more work is needed to optimize biologic therapy in this patient population, reported lead author Sabina Ali, MD, of UCSF Benioff Children's Hospital, Oakland, California, and colleagues.

"With few medications available for treating CD, limited therapeutic longevity places patients at risk of exhausting treatment options," the investigators wrote in *Clinical Gastroenterology and Hepatology* (2024 May 7. doi: 10.1016/j.cgh.2024.03.043). "This is especially problematic for children, for whom infliximab and adalimumab remain the only medications approved by the Food and Drug Administration (FDA), and who require effective long-term therapy to maintain remission and prevent morbidity and disability for decades to come."

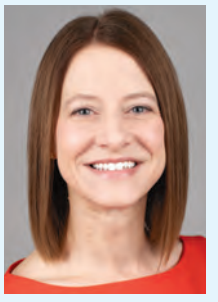
Despite these concerns, reasons behind biologic discontinuation in the pediatric CD population have been poorly characterized, prompting the present study.

Dr. Ali and colleagues analyzed prospectively collected data from 823 patients treated at seven pediatric inflammatory bowel disease centers. Median age was 13 years, with slightly more male than female patients (60% vs 40%).

Within this group, 86% started biologics, most often infliximab

Continued on following page

As pediatric gastroenterologists, our practice has significantly changed over time, including the approach of using more effective medications sooner and adoption of therapeutic drug monitoring (TDM) as standard of care to optimize dosing. This study found the use of TDM during the induction phase of biologic therapy increased over the study duration from 2% to 70%, which is remarkable. Pediatric patients tend to have more extensive and severe disease, often necessitating higher dosing. With limited Food and Drug Administration–approved medications to treat children with inflammatory bowl disease (IBD), it is imperative that we position these medications appropriately and be assertive with dose optimization to improve patient outcomes.


Dr. Dotson

Alarmingly, one third of patients discontinued their biologic after 2.2 years. Concerningly, half discontinued their biologics without a trial of high-dose therapy and 14% without any evaluation. Trough levels > 10 µg/mL may be associated with improved efficacy and low antibody levels can be overcome; however, many of these patients had levels lower than this. This is likely a missed opportunity to capture response and increase durability with dose escalation.

Biologic discontinuation was reduced by 60% with the use of proactive TDM and 32% with concomitant immunomodulators (on > 12 months, compared with monotherapy). Pediatric data supporting the use of concomitant immunomodulators has been mixed.

As pediatric IBD physicians, we need to increase our diligence to optimize biologic therapy early. Early dose optimization could negate the observed protective impact from concomitant immunomodulator use in many cases, thereby decreasing risk of potential side effects. This highlights the importance of a shared decision-making discussion with our patients and families.

Further research is needed to address strategies to increase drug durability including TDM and dose optimization, adherence, health literacy, engagement, and the role for patient education to enhance medication optimization and durability.

Jennifer L. Dotson, MD, MPH, is chief of pediatric gastroenterology, hepatology, and nutrition at Arkansas Children's Hospital and professor of pediatrics at the University of Arkansas for Medical Sciences, both in Little Rock. She declares no conflicts of interest.

Continued from previous page

dysplasia/cancer," the investigators wrote in *Gastro Hep Advances* (2024 May. doi: 10.1016/j.gastha.2024.05.003), noting that no consensus approach is currently available to guide stricture management. "Few studies with conflicting results have evaluated the frequency of CRC associated with colonic stricture in CD, and the natural history of colonic stricture in CD is poorly known."

The present retrospective study included 88 consecutive CD patients with 96 colorectal strictures who were managed at three French referral centers between 1993 and 2022.

Strictures were symptomatic in 62.5% of cases, not passable by scope in 61.4% of cases, and ulcerated in 70.5% of cases. Colonic resection was needed in 47.7% of patients, while endoscopic balloon dilation was performed in 13.6% of patients.

After a median follow-up of 21.5 months, seven patients (8%) were diagnosed with malignant stricture, including five cases of colonic adenocarcinoma, one case of neuroendocrine carcinoma, and one case of B-cell lymphoproliferative neoplasia.

Malignant strictures were more common among older patients with longer disease duration and frequent obstructive symptoms; however, these factors were not supported by multivariate analyses, likely because of sample size, according to the investigators.

Instead, Dr. Hunaut and colleagues highlighted the timing of the diagnoses. In four out of seven patients with malignant stricture, both stricture and cancer were diagnosed at the same time. In the remaining three patients, cancer was diagnosed at 3 months, 8 months, and 12 months after stricture diagnosis. No cases of cancer were diagnosed later than 1 year after the stricture diagnosis.

'Systematic colectomy is probably no longer justified. Factors such as a long disease duration, primary sclerosing cholangitis, a history of dysplasia, and nonpassable and/or symptomatic stricture despite endoscopic dilation tend to argue in favor of surgery — especially if limited resection is possible.'

"We believe that this result is important for the management of colonic strictures complicating CD in clinical practice," Dr. Hunaut and colleagues wrote.

The simultaneity or proximity of the diagnoses suggests that the "strictures observed are already a neoplastic complication of the colonic inflammatory disease," they explained.

In other words, common concerns about strictures causing cancer at the same site could be unfounded.

This conclusion echoes a recent administrative database study (Inflamm Bowel Dis. 2022 Jun. doi: 10.1093/ibd/izab177) that reported no independent association between colorectal stricture and CRC, the investigators noted.

"Given the recent evidence on the risk of cancer associated with colonic strictures in CD, systematic colectomy is probably no longer justified," they wrote. "Factors such as a long disease duration, primary sclerosing cholangitis, a history of dysplasia, and nonpassable and/or symptomatic stricture despite endoscopic dilation tend to argue in favor of surgery — especially if limited resection is possible."

In contrast, patients with strictures who have low risk of CRC may be better served by a conservative approach, including endoscopy and systematic biopsies, followed by close endoscopic surveillance, according to the investigators. If the stricture is impassable, they recommended endoscopic balloon dilation, followed by intensification of medical therapy if ulceration is observed.

The investigators disclosed relationships with MSD, Ferring, Biogen, and others. ■

Agency Grants Livdelzi Accelerated Approval for Primary Biliary Cholangitis

BY MEGAN BROOKS

The US Food and Drug Administration (FDA) granted accelerated approval for Livdelzi (seladelpar, Gilead Sciences) for primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who fail to respond adequately to UDCA, or as monotherapy in those who can't tolerate UDCA.

Livdelzi, a selective agonist of peroxisome proliferator–activated receptor delta, is not recommended in adults who have or develop decompensated cirrhosis.

PBC is a rare, chronic, autoimmune disease of the bile ducts that affects roughly 130,000 Americans, primarily women, and can cause liver damage and possible liver failure if untreated. The disease currently has no cure.

The FDA approved Livdelzi based largely on results of the phase 3 RESPONSE study, in which the drug significantly improved liver biomarkers of disease activity and bothersome symptoms of pruritus in adults with PBC.

The primary endpoint of the trial was a biochemical response, defined as an alkaline phosphatase (ALP) level < 1.67 times the upper limit of the normal range, with a decrease of 15% or more from baseline, and a normal total bilirubin level, at 12 months.

The FDA approved Livdelzi based largely on results of the phase 3 RESPONSE study, in which the drug significantly improved liver biomarkers of disease activity and bothersome symptoms of pruritus in adults with PBC.

After 12 months, 62% of patients taking Livdelzi met the primary endpoint vs 20% of patients taking placebo.

In addition, significantly more patients taking Livdelzi than placebo had normalization of the ALP level (25% vs 0%). The average decrease in ALP from baseline was 42.4% in the Livdelzi group vs 4.3% in the placebo group.

At 12 months, alanine aminotransferase and gamma-glutamyl transferase levels were reduced by 23.5% and 39.1%, respectively, in the Livdelzi group compared with 6.5% and 11.4%, respectively, in the placebo group.

A key secondary endpoint was change in patient-reported pruritus.

At baseline, 38.3% of patients in the Livdelzi group and 35.4% of those in the placebo group had moderate to severe pruritus, with a daily numerical rating scale (NRS) score ≥ 4 out of 10.

Among these patients, the reduction from baseline in the pruritus NRS score at month 6 was significantly greater with Livdelzi than with placebo (change from baseline, -3.2 vs -1.7 points). These

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(78%), followed by adalimumab (21%), and distantly, others (less than 1%). Most patients (86%) underwent TDM at some point during the treatment process, while one quarter (26%) took concomitant immunomodulators for at least 1 year.

Slightly less than one third of patients (29%) discontinued their first biologic after a median of approximately 2 years. The most common reason for discontinuation was inefficacy (34%), followed by nonadherence (12%), anti-drug antibodies (8%), and adverse events (8%).

Among those who discontinued because of inefficacy, 85% underwent prediscontinuation evaluation. When TDM of adalimumab or infliximab was performed prior to discontinuation, almost two out of three patients (62%) had drug levels lower than 10 µg/mL.

"We cannot determine the reasons dose escalation was not attempted," the investigators wrote. "However, trough levels greater than 10 µg/mL may be associated with improved efficacy."

Most patients (91%) who stopped their first biologic started a second, and more than one third (36%) also discontinued that second option, usually after about 1 year. After 4 years, only 10% of patients remained on their second biologic therapy. By study end, almost 1 out of 12 patients were on their third or fourth biologic, and 17% of patients were on a biologic currently not approved by the FDA.

Beyond characterizing these usage and discontinuation rates, the investigators also assessed factors associated with discontinuation or therapeutic persistence.

Proactive TDM was the strongest factor driving therapeutic persistence, as it reduced risk of discontinuation by 63%. Concomitant immunomodulatory therapy also reduced discontinuation risk, by 30%. Conversely, usage of 5-aminoasalicylate in the first 90 days of diagnosis was associated with a 70% higher discontinuation rate.

"The reason for this [latter finding about aminosalicylates] is not clear but may be an indicator of insurance-related or other barriers to care," the investigators wrote.

Dr. Ali and colleagues concluded by noting how concerning, and commonplace, biologic discontinuation is in this patient population.

"This poses a serious problem for pediatric patients who will require treatment for decades to come," they wrote. "Thoughtful strategies are needed to preserve treatment longevity and minimize the loss of treatment options."

This work was supported by the Gary and Rachel Glick Charitable Fund. The investigators disclosed relationships with Janssen, Eli Lilly, AbbVie, and others. ■

Five Key Measures to Ensure a Quality Colonoscopy

BY MEGAN BROOKS

A task force established by the American College of Gastroenterology (ACG) and the American Society for Gastrointestinal Endoscopy (ASGE) issued updated recommendations highlighting what they consider to be the highest priority quality indicators for colonoscopy, a list that, for the first time, includes adequate bowel preparation and sessile serrated lesion detection rate (SSLDR).

"Endoscopy teams now have an updated set of guidelines which can be used to enhance the quality of their colonoscopies and should certainly use these current quality measures to 'raise the bar' on behalf of their patients," task force member Nicholas J. Shaheen, MD, MPH, Division of Gastroenterology and Hepatology, The University of North Carolina at Chapel Hill, said in a statement.


Dr. Shaheen

The task force published the recommendations online August 21 in *The American Journal of Gastroenterology* and in *Gastrointestinal Endoscopy*. It represents the third iteration of the ACG/ASGE quality indicators on colonoscopy recommendations and incorporates new evidence published since 2015.

"The last set of quality indicators from this group was 9 years ago. Since then, there has been a tremendous amount of new data published in colonoscopy quality," Ziad F. Gellad, MD, MPH, AGAF, professor of medicine, Duke University Medical Center, Durham, North Carolina, said in an interview.

"Keeping up with that data is a challenge, and so guidelines such as these are important in helping clinicians synthesize data on quality of care and implement best practices," said Dr. Gellad, who was not involved with the task force.

Two New Priority Indicators

The task force identified 15 quality indicators, divided into preprocedure, intraprocedure, and postprocedure. It includes five "priority" indicators — two of which are new.

One is the rate of adequate bowel preparation, preferably defined as a Boston Bowel Preparation Scale score ≥ 2 in each of three colon segments or by description of the preparation as excellent, good, or adequate. It has a performance target > 90%.

"Inadequate bowel preparation substantially increases the cost of colonoscopy delivery and creates risk and inconvenience for patients, thus warranting a ranking as a priority indicator," the task force wrote.

Dr. Gellad explained that the addition of this priority indicator is "notable because it highlights the importance of bowel prep in high-quality colonoscopy. It also shifts more of the responsibility of bowel prep from the patient to the practice."


Dr. Gellad

The second new quality indicator is the SSLDR, which was selected because of its ability to contribute to cancer prevention.

Based on available evidence, the task force recommends a current minimum threshold for the SSLDR of 6%. "This is expected to be revised upward as evidence of increasing detection occurs," they wrote.

Dr. Gellad said the addition of SSLDR is "an important advance in these recommendations. We know that serrated adenomas are a precursor for colorectal cancer and that the detection of these subtle lesions is variable.

"Providing a benchmark encourages practices to measure the detection of serrated adenomas and intervene when rates are below benchmarks. Prior to these benchmarks, it was difficult to know where to peg our expectations," Dr. Gellad added.

Changes to the Adenoma Detection Rate (ADR)

The ADR remains a priority indicator in the update, albeit with changes.

To keep the ADR measurement consistent with current screening guidelines, the task force now recommends that the ADR be measured starting at age 45 rather than 50 years.

"ADR plays a critical role in evaluating the performance of the colonoscopists," task force lead Douglas K. Rex, MD, AGAF, a gastroenterologist at Indiana University School of Medicine in Indianapolis, said in the statement.

"It is recommended that ADR calculations include screening, surveillance, and diagnostic colonoscopy but exclude indications of a positive noncolonoscopy screening test and therapeutic procedures for resection or treatment of known neoplasia, genetic cancer syndromes, and inflammatory bowel disease," Dr. Rex explained.

The task force recommends a minimum ADR threshold of 35% (40% in men and 30% in women) and that colonoscopists with ADRs below 35% "undertake remedial measures to improve and to achieve acceptable performance."

Additional Priorities

The cecal intubation rate (CIR) — the percentage of patients undergoing colonoscopy with intact colons who have full intubation of the cecum with photo documentation of cecal landmarks — remains a priority quality indicator and has a performance target ≥ 95%.


Dr. Rex

"A trained colonoscopist should achieve a high CIR with a very high level of safety," the task force wrote. "Low CIRs have been associated with higher PCCRC [postcolonoscopy colorectal cancer] rates."

The final priority indicator is the rate of using recommended screening and surveillance intervals, which carries a performance target ≥ 90%.

"We recommend that quality improvement efforts initially focus on high-priority indicators and then progress to other indicators once it is ascertained that endoscopists are performing above recommended thresholds, either at baseline or after corrective interventions," the task force wrote.

"The priority indicators are absolutely important for practices to implement," Dr. Gellad said.

"There is compelling evidence that these measures are correlated with clinically important outcomes, particularly ADR," he added. "Many practices already capture this data, and the changes in ADR calculation make measurement less burdensome. Hopefully, this will encourage more practices to collect and report these measures."

Dr. Rex is a consultant for Olympus, Boston Scientific, Braintree Laboratories, Norgine, GI Supply, Medtronic, and Acacia Pharmaceuticals; receives research support from Olympus, Medivators, Erbe USA, and Braintree Laboratories; and is a shareholder in Satisfai Health. Dr. Shaheen had no relevant disclosures. Dr. Gellad has consulted for Merck and Novo Nordisk and is a cofounder of Higgs Boson. ■

Continued from previous page

improvements were sustained through 12 months.

Improvements on the 5-D Itch Scale in both the moderate- to severe-pruritis population and the overall population also favored Livdelzi over placebo for itch relief, which had a positive impact on sleep.

"The availability of a new treatment option that can help reduce [the] intense itching while also improving biomarkers of active liver disease is a milestone for our community," Carol Roberts, president, The PBCers Organization, said in a news release announcing the approval.

Significantly more patients taking Livdelzi than placebo had normalization of the alkaline phosphatase level (25% vs 0%). The average decrease in ALP from baseline was 42.4% in the Livdelzi group vs 4.3% in the placebo group.

The most common adverse reactions with Livdelzi were headache, abdominal pain, nausea, abdominal distension, and dizziness.

The company noted that the FDA granted accelerated approval for Livdelzi based on a reduction of ALP. Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval of Livdelzi for PBC may be contingent on verification and description of clinical benefit in confirmatory trial(s). ■

Member SPOTLIGHT

GI Doc Is a 'Creative at Heart'

Tennessee *from page 1*

and downs in stride," she added.

In an interview, Dr. Pointer spoke more about her work in IBD and the ways in which she's given back to the community through music and mentoring.

Q: Why did you choose GI?

I knew from a very young age that I was going to be a physician. I had always been interested in science. When I got into medical school and became exposed to the different areas, I really liked the cognitive skills where you had to think through a problem or an issue. But I also liked the procedural things as well.

During my internal medicine residency training, I felt that I had a knack for it. As I was looking at different options, I decided on gastroenterology because it combined both cognitive thinking through issues, but also taking it to the next step and intervening through procedures.

Q: During fellowship, your focus was inflammatory bowel disease. What drew your interest to this condition?

There are a lot of different areas within gastroenterology that one can subspecialize in, as we see the full gamut of gastrointestinal and hepatic disorders. But treating some conditions, like functional disorders, means taking more of a "trial and error" approach, and you may not always get the patient 100% better. That's not to say that we can't improve a patient's quality of life, but it's not always a guarantee.

But inflammatory bowel disease is a little bit different. Because I can point to an exact spot in the intestines that's causing the problem, it's very fulfilling for me as a physician to take a patient who is having 10-12 bloody bowel movements a day, to normal form stools and no abdominal pain. They're able to gain weight and go on about their lives and about their day. So that was why I picked inflammatory bowel disease as my subspecialty.

Q: Tell me about the gastroenterology elective you developed for family medicine residents and undergraduate students. What's the status of the program now?

I've always been interested in teaching and giving back to the next generations. I feel like I had great mentor opportunities and people who helped me along the way. In my previous hospital position, I was able to work with the family medicine department and create an elective through which residents and even undergraduate students could come and shadow and work with me in the clinic and see me performing procedures.

That elective ended once I left that position, at least as far as I'm aware. But in the private practice that I co-own now, we have numerous shadowing opportunities. I was able to give a lecture at Middle Tennessee State University for some students. And through that lecture, many students have reached out to me to shadow. I have allowed them to come shadow and do clinic work as a medical assistant and watch me perform procedures. I have multiple students working with me weekly.

Q: Years ago, you founded the nonprofit Enchanted Fingers Piano Lessons, which gave free piano lessons to underserved youth. What was that experience like?

Piano was one of my first loves. In some parallel universe, there's a Dr. Pointer who is a classical, concert pianist. I started taking piano lessons when I was in early middle school, and I took to it very quickly. I was able to excel. I just loved it. I enjoyed practicing, and I still play.

The impetus for starting Enchanted Fingers Piano lessons was because I wanted to give back again to the community. I came from an underserved community. Oftentimes children and young adults in those communities don't get exposed to extracurricular activities and they don't even know what they could potentially have a passion for. And I definitely had a passion for piano. I partnered with a church organization and they allowed me to use their church to host these piano lessons, and it was a phenomenal and rewarding experience. I would definitely like to start it up again one day in the future. It was an amazing experience.

It's actually how I met my husband. He was one of the young adult students who signed up to take lessons. We both still enjoy playing the piano together.

Q: When you're not being a GI, how do you spend your free weekend afternoons?

I'm a creative at heart. I really enjoy sewing and I'm working on a few sewing projects. I just got a serger. It is a machine that helps you finish a seam. It can also be used to sew entire garments. That has been fun, learning how to thread that machine. When I'm not doing that or just relaxing with my family, I do enjoy curling up with a good book. Stephen King is one of my favorite authors. ■

LIGHTNING ROUND

Texting or talking?
Talking

Favorite junk food?
Chocolate chip cookies

Cat or dog person?
Cat

Favorite vacation?
Hawaii

Number of cups of coffee you drink per day?
I don't drink coffee

Favorite ice cream?
Butter pecan

Favorite sport?
I don't watch sports

Optimist or pessimist?
Optimist

➤IBD & INTESTINAL DISORDERS

New Associations Identified Between IBD and Extraintestinal Manifestations

BY CAROLYN CRIST

FROM GASTROENTEROLOGY

Certain extraintestinal manifestations (EIMs) in inflammatory bowel disease (IBD) have distinct clinical, serologic, and genetic associations that reveal underlying mechanisms and indicate targets for new or existing drugs, according to a recent study.

For instance, antinuclear cytoplastic antibody is associated with primary sclerosing cholangitis (PSC) in Crohn's disease, and *CPEB4* genetic variation is associated with skin manifestations.

"Up to 40% of people with IBD suffer with symptoms from inflammation that occurs outside the gut, particularly affecting the liver, skin, and joints. These symptoms can often have a bigger impact on quality of life than the gut inflammation itself and can actually be life-threatening," said senior author Dermot McGovern, MD, PhD, AGAF, director of translational medicine at the F. Widjaja Foundation Inflammatory Bowel Disease and Immunobiology Research Institute at Cedars-Sinai Medical Center, Los Angeles.

"With the advances in therapies for IBD, including availability of gut-selective agents, treatment choices often incorporate whether a patient has one of these manifestations or not," he said. "We need to understand who is at increased risk of these and why."

The study was published in *Gastroenterology* (2024 July. doi: 10.1053/j.gastro.2024.02.026).

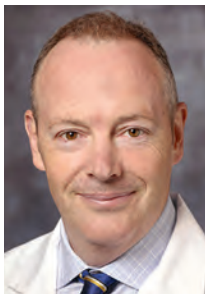
Analyzing Associations

Dr. McGovern and colleagues analyzed data for 12,083 unrelated European ancestry IBD cases with presence or absence of EIMs across four cohorts in the Cedars-Sinai Medical Center IBD Research

Continued on following page

Continued from previous page

Repository, National Institute for Diabetes and Digestive and Kidney Diseases IBD Genetics Consortium, Sinai Helmsley Alliance for Research Excellence Consortium, and Risk Stratification and Identification of Immunogenetic and Microbial Markers of Rapid Disease Progression in Children with Crohn's Disease.



Dr. McGovern

'Up to 40% of people with IBD suffer with symptoms from inflammation that occurs outside the gut. ... These symptoms can often have a bigger impact on quality of life than the gut inflammation itself.'

In particular, the researchers looked at EIM phenotypes such as ankylosing spondylitis and sacroiliitis, PSC, peripheral arthritis, and skin and ocular manifestations. They analyzed clinical and serologic parameters through regression analyses using a mixed-effects model, as well as within-case logistic regression for genetic associations.

Overall, 14% of patients had at least one EIM. Contrary to previous reports, only 2% had multiple EIMs, and most co-occurrences were negatively correlated. Nearly all EIMs were more common in Crohn's disease, except for PSC, which was more common in ulcerative colitis.

In general, EIMs occurred more often in women, particularly with Crohn's disease and colonic disease location, and in patients who required surgery. Jewish ancestry was associated with psoriasis and overall skin manifestations.

Smoking increased the risk for multiple EIMs, except for PSC, where there appeared to be a "protective" effect. Older age at diagnosis and a family history of IBD were associated with increased risk for certain EIMs as well.

In addition, the research team noted multiple serologic associations, such as immunoglobulin (Ig) G and IgA, perinuclear antinuclear cytoplastic antibodies, and anti–*Pseudomonas fluorescens*–associated sequences with any EIM, as well as particular associations with PSC, such as anti-*Saccharomyces cerevisiae* antibodies and anti-flagellin.

There were also genome-wide significant associations within the major histocompatibility complex and *CPEB4*. Genetic associations implicated tumor necrosis factor, Janus kinase–signal transducer and activator of transcription, and interleukin 6 as potential targets for EIMs.

"We are working with colleagues across the world to increase the sample size, as we believe there is more to find," Dr. McGovern said. "Importantly, this includes non-European ancestry subjects, as there is an urgent need to increase the diversity of populations we study so advances in clinical care are available to all communities."

Considering Therapies

As medicine becomes more specialized, physicians should remember to consider the whole patient while choosing treatment strategies.

"Sometimes doctors wear blinders to the whole person, and it's important to be aware of a holistic approach, where a gastroenterologist also asks about potential joint inflammation or a rheumatologist asks about bowel inflammation," said David Rubin, MD, AGAF, chief of the Section of Gastroenterology, Hepatology and Nutrition at the University of Chicago Medicine, Chicago.

Dr. Rubin, who wasn't involved with this study, has researched and published on EIMs in IBD. He and colleagues analyzed the prevalence, pathophysiology, and clinical presentation of EIMs to better understand possibilities for disease management.

"As we've gotten a better understanding of the immune system, we've learned that an EIM can sometimes provide a clue to the treatment we might use," he said. "Given a similar amount of bowel inflammation, if one patient also has joint pain and another doesn't, we might choose different treatments based on the immune pathway that might be involved."

Dr. Rubin

'Sometimes doctors wear blinders to the whole person, and it's important to be aware of a holistic approach, where a gastroenterologist also asks about potential joint inflammation.'

In future studies, researchers may consider whether these genetic or serologic markers could predict EIM manifestation before it occurs clinically, Dr. Rubin said. He and colleagues are also studying the links between IBD and mental health associations.

"So far, we don't have a blood test or biopsy test that tells you which treatment is more or less likely to work, so we need to think carefully as clinicians and look to other organ systems for clues," he said. "It's not only more efficient to pick a single therapy to treat both the skin and bowel, but it may actually be more effective if both have a particular dominant pathway."

The study was supported by internal funds from the F. Widjaja Foundation Inflammatory Bowel and Immunobiology Research Institute. Several authors reported consultant roles or other associations with pharmaceutical companies. Dr. Rubin reported no relevant disclosures. ■

Navigating Ethical and Clinical Considerations Relating to Percutaneous Gastrostomy (PEG) Tubes

BY EMILY SELTZER, DO, MS;
ANTOINETTE PUSATERI, MD;
ANH D. NGUYEN, MD;
ELLEN STEIN, MD, AGAF

Cases

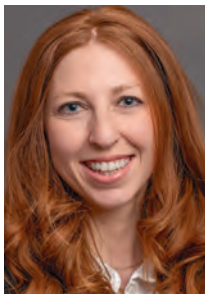
Consults for percutaneous endoscopic gastrostomy (PEG) tube placement for a patient ...

1 *With dysphagia after stroke:* A 70-year-old female with a history of hypertension presented to the hospital with altered mental status and left-sided weakness. She was previously active and independently living. MRI of the brain revealed a right basal ganglia infarct. As a result, she developed dysphagia. She was evaluated by speech and language pathology and underwent a modified barium swallow. Given concerns for aspiration, the recommendation was made for gastroenterology (GI) consultation to place a PEG tube for nutrition and medication administration.

If the gastroenterologist encounters more contentious consultations, there are ways to build consensus to both alleviate patient and family suffering as well as elevate the discussions between teams.

2 *With advanced dementia:* An 85-year-old male with an extensive medical history including advanced dementia was admitted from his nursing home for decreased oral intake. His baseline mental status is awake and alert, but he is nonverbal and does not follow commands. Upon 72-hour calorie count, the nutrition consultants determined that he cannot independently meet his nutrition goals. His family wants "everything done" and are asking about a "feeding tube." The primary team has now consulted GI for PEG tube placement.

3 *Who is being discharged to a long-term care facility:* A 45-year-old male was admitted to the ICU after a heroin overdose. CPR was initiated in the field and return of spontaneous circulation was obtained after 25 minutes. The patient has minimal brainstem reflexes. He is ventilator dependent. He has no family, and now is status-post tracheostomy placement by two-physician consent. The patient is ready for discharge to a long-term care facility that will not accept patients with nasogastric tubes. GI is consulted for PEG tube placement.


Dr. Seltzer


Dr. Pusateri


Dr. Nguyen


Dr. Stein

Discussion

Gastroenterologists are often consulted for PEG tube placement. However, the circumstances surrounding and the implications of PEG tube placement are often complicated for reasons beyond nutritional or technical considerations. This is rooted in the fact that, as one expert wrote, "feeding, unlike any other medical treatment, has a moral and emotional significance derived from culture."[1] Understanding the evidence, ethical considerations, and team dynamic behind PEG tube placement is critical for every gastroenterologist. Herein we review these topics and offer guidelines for having patient-centered conversations involving these fundamental concepts.

First, the gastroenterologist should understand the evidence to debunk myths and clarify truths surrounding PEG tube placement. While PEG tubes may help patients with amyotrophic lateral sclerosis stabilize their weight and can even be prophylactically placed in select patients with head and neck cancer,[2,3] they are not always appropriate in patients in early recovery from stroke and have not been shown to improve outcomes in patients with advanced dementia. At least 50% of stroke-related dysphagia resolves within 1-2 weeks, and so the American Heart Association Stroke Council recommends continuing nasogastric tube feeding for 2-3 weeks in patients such as the one presented in case 1 before considering PEG tube placement.[4]

In situations of advanced dementia such as in case 2, several studies demonstrate that PEG tubes do not reduce or prevent aspiration pneumonia, prevent consequences of malnutrition, prolong life, reduce pressure ulcers, reduce urinary or gastrointestinal tract infections, lead to functional improvement, mitigate decline, or even improve comfort or quality of life for patients or their caregivers.[5-7] Despite this evidence, as demonstrated in case 3, it is true that many American skilled nursing facilities will not accept a patient without a PEG if enteral feeding is needed. This restriction may vary by state: One study found that skilled nursing facilities in New York City are much less likely to accept patients with nasogastric feeding tubes than randomly selected skilled nursing facilities throughout the country.[6]

Nonetheless, gastroenterologists should look to the literature to understand the outcomes of populations of patients after PEG tube placement and use that data to guide decision-making.

Secondly, the five ethical principles that inform all medical decision making — autonomy, beneficence, nonmaleficence, justice, and futility — should also inform the gastroenterologist's rationale in offering PEG placement.[8]

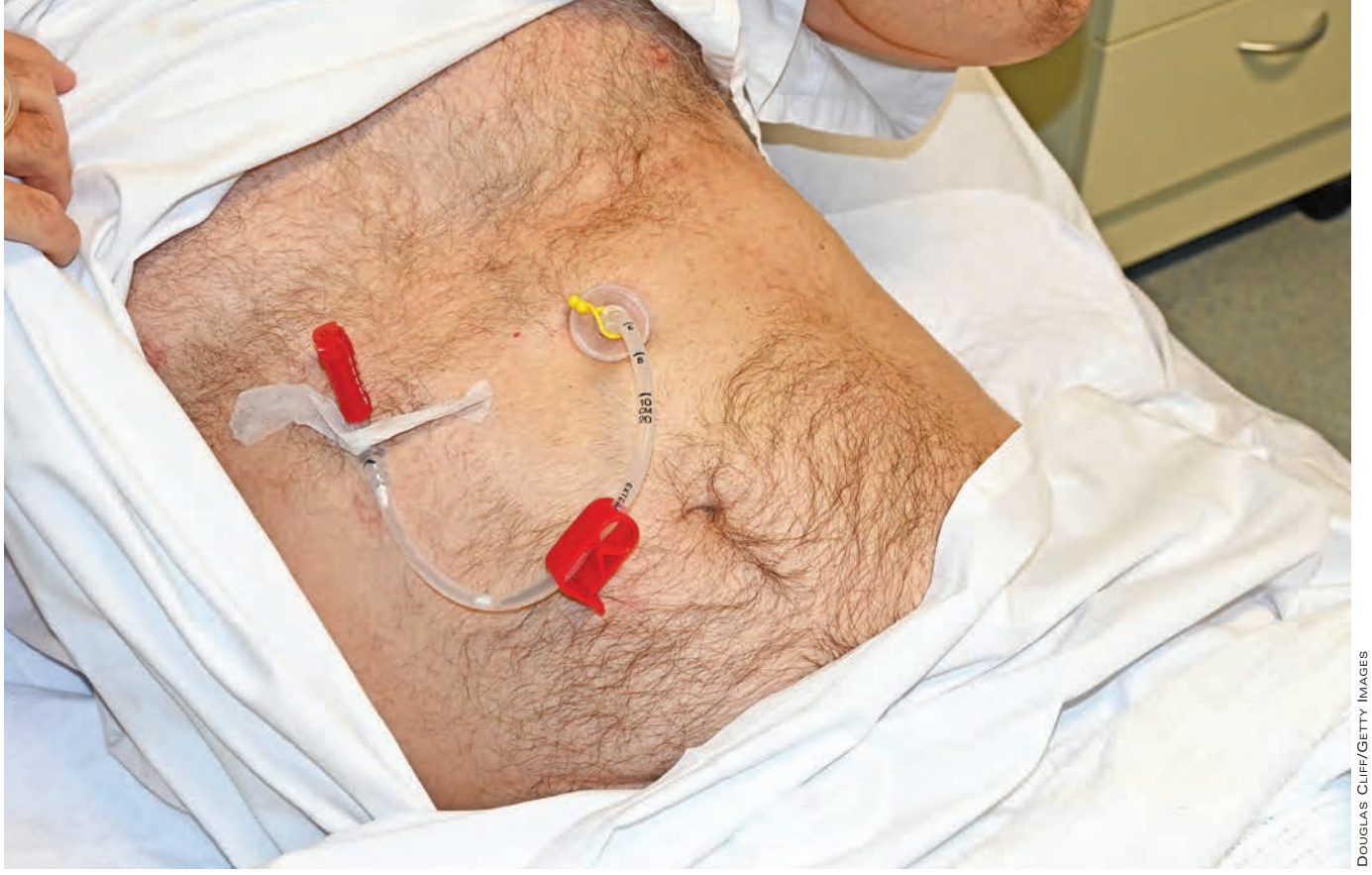
Autonomy implies that the medical team has determined who is able to make the decision regarding PEG tube placement for the patient. Beneficence connects the patient's medical diagnosis and technical parameters of PEG tube placement with his or her goals of care. Nonmaleficence ensures the decision-making party understands the benefits and risks of the procedure, including anticipatory guidance on possible PEG tube management, complications, risks, and need for replacement. Justice incorporates the context of the patient's life, including family dynamics and religious, cultural, and financial factors. Futility connects the patient's prognosis with practical aspects of having a PEG tube.

The complexity of PEG placement lies in the fact that these ethical principles are often at odds with each other. For example, case 2 highlights the conflicting principles of autonomy and futility for elderly dementia patients: While PEG tube placements do not improve comfort or quality of life in advanced dementia (futility), the family representing the patient has stated they want everything done for his care, including PEG tube placement (autonomy). Navigating these ethical principles can be difficult, but having a framework to organize the different factors offers sound guidance for the gastroenterologist.

Finally, the gastroenterologist should recognize the roles of the multidisciplinary team members, including the patient and their representatives, regarding PEG tube placement consults. While gastroenterologists can be viewed as the technicians consulted to simply "place the tube," they must seek to understand the members of the team representing the patient to be stewards of their skill set.

Consulting team physicians carry great responsibility in organizing the medical and psychosocial aspects of each patient's care, and their proper goals to relieve suffering and prevent death may color their judgment regarding who they believe is a candidate for a PEG tube. Nutritionists, speech therapists, and case managers can help provide objective data on the practicality and feasibility of a PEG tube in their patients. The healthcare system may influence the decision to consult heavily, as seen in the rules of the long-term care facility in case.[3] While it is the job of the multidisciplinary medical team to explain the evidence and ethical considerations of PEG tube placement in a patient-centered manner, ultimately the decision belongs to the patient and their family or representatives.

The moral burden of not pursuing



Douglas Cliff/Getty Images

PEG placement may supersede the medical advice in many situations. There is an emotionally taxing perception that withholding nutrition via PEG is "starving the patient," despite literature showing many terminally ill patients do not experience thirst or hunger, and those who do have alleviation of these symptoms with small amounts of food or liquid, not with PEG placement.[5] As every patient is unique, PEG tube consultation guidelines created with input from all stakeholders have been utilized to ensure that patients are medically optimized for PEG tube placement and that evidence and ethics-based considerations are evaluated by the multidisciplinary team.

While gastroenterologists can be viewed as the technicians consulted to simply 'place the tube,' they must seek to understand the members of the team representing the patient to be stewards of their skill set.

If the gastroenterologist encounters more contentious consultations, there are ways to build consensus to both alleviate patient and family suffering as well as elevate the discussions between teams.

First, identify the type of consult that is repeatedly bringing differing viewpoints and differing ethical principles into play. Second, get representatives from teams together in a neutral environment to understand stakeholders needs. New data suggest, in stroke cases like case 1, there may be dramatic benefit in long-term ability to recover if patients can get early intensive rehabilitation.[9] This intense daily rehabilitation is not available within the hospital setting at many locations, and facilitation of discharge may be requested earlier than usually advised tube placement. Third, build a common language for requests and responses between teams. For instance, neurologists can identify and document which patients have *less likelihood of early spontaneous recovery*, and this can allow gastroenterologists to understand that those patients with little potential for early swallowing recovery can safely be targeted for PEG earlier during the hospital course. Other patients described as having a *potential for spontaneous improvement* should be given time to recover before an intervention is considered.[10] Having a common understanding of goals and a better-informed decision pathway helps each team member feel fulfilled and rewarded, which will ultimately help reduce compassion fatigue and moral burden on providers.

In conclusion, PEG tube placement can be a challenging consultation for gastroenterologists because of the clinical, social, and ethical ramifications at stake for the patient. Even when PEG tube placement is technically feasible, the gastroenterologist should feel empowered to address the evidence-based outcomes of PEG tube placement, discuss the ethical principles of the decision-making process, and communicate with a multidisciplinary team using guidelines as set forth by this paper to best serve the patient. ■

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Top-Down Treatment Better for Crohn's Patients

BY CAROLYN CRIST
MDedge News

Top-down treatment with a combination of infliximab and an immunomodulator should be adopted as the standard of care for most patients with newly diagnosed active Crohn's disease, according to a recent study.

Top-down treatment achieved substantially better outcomes at 1 year after diagnosis than step-up treatment, with nearly 80% of those receiving top-down therapy having both symptoms and inflammatory markers controlled, as compared with only 15% of those receiving accelerated step-up therapy.

"Up until now, the view has been: 'Why would you use a more expensive treatment strategy and potentially overtreat people if there's a chance they might do fine anyway?' " asked senior author Miles Parkes, MBBS, professor of translational gastroenterology at the University of Cambridge in England.

"As we've shown, and as previous studies have demonstrated, there's actually a pretty high risk that an individual with Crohn's disease will experience disease flares and complications even in the first year after diagnosis," he said. "We now know we can prevent the majority of adverse outcomes, including need for urgent surgery, by providing a treatment strategy that is safe and becoming increasingly affordable."

The study was published in *The Lancet Gastroenterology & Hepatology* (2024 May. doi: 10.1016/S2468-1253[24]00034-7).

Comparing Treatments

Dr. Parkes and colleagues conducted a multicenter, open-label, biomarker-stratified randomized controlled trial among adults with newly diagnosed active Crohn's disease. Participants were tested for a prognostic biomarker derived from T-cell transcriptional signatures and randomly assigned to a top-down or accelerated step-up treatment based on biomarker subgroup, endoscopic inflammation (mild, moderate, or severe), and extent (colonic or other).


Dr. Parkes


Dr. Narula

The primary endpoint was sustained steroid-free and surgery-free remission after completing a steroid induction (maximum 8-week course) to week 48. Remission was defined by a composite of symptoms and inflammatory markers at all visits, with a Harvey-Bradshaw Index (HBI) score of less than 5 or resolved inflammatory markers or both, while a flare was defined as active symptoms (HBI ≥ 5) and raised inflammatory markers.

Across 40 UK hospitals, 386 patients (mean age, 33.6 years; 54% male) were randomized, with 193 receiving a top-down therapy of combination intravenous infliximab plus immunomodulator (azathioprine, low-dose mercaptopurine with allopurinol, or methotrexate) and 193 receiving an accelerated step-up therapy of an immunomodulator and then infliximab if further flares occurred after the steroid course. In the step-up group, 85% required escalation to an immunomodulator, and 41% required infliximab by week 48.

Overall, sustained steroid-free and surgery-free remission was significantly more frequent in the top-down group than in the accelerated step-up group (among 149 of 189 patients vs 29 of 190 patients), at 79% vs 15%, marking an absolute difference of 64 percentage points.

Top-down treatment also showed greater efficacy in achieving endoscopic remission (67% vs 44%), improved quality of life, lower need for steroids, and reduced number of flares requiring treatment escalation.

In addition, there were fewer adverse events (168 vs 315) and fewer serious adverse events (15 vs 42) in the top-down group than in the step-up group. There were also fewer complications that required urgent abdominal surgery, with one in the top-down group for gallstone ileus and nine in the step-up group requiring intestinal resection for structuring or fistulating complications.

However, the biomarker showed no clinical utility, and none of the baseline measurements predicted which patients were at risk of adverse outcomes with the step-up approach, Dr. Parkes said.

"The key message is that Crohn's is unpredictable; hence you are better off treating everyone who has significant disease at diagnosis with combo therapy (anti-TNF [tumor necrosis factor] plus immunomodulator) rather than 'wait and see,' as bad things happen to people with uncontrolled inflammation during that 'wait and see' stage," he said.

In the PROFILE trial, the need for a prognostic biomarker was based on the lack of an effective, safe, and affordable treatment strategy for newly diagnosed patients, the study authors wrote, but effective top-down management could reduce the need for a biomarker.

"In one sense, this is a negative study as the blood-based CD8+ T-cell transcriptomic biomarker that was being studied was not predictive of outcomes at all. But PROFILE makes it very clear that early effective therapy leads to better outcomes than accelerated step-up therapy," said Neeraj Narula, MD, of McMaster University, Hamilton, Ontario, Canada, and staff gastroenterologist focused on inflammatory bowel disease at Hamilton Health Sciences.

"There does remain a concern that using this strategy for all patients may lead to overtreatment of some, but perhaps any harm done by overtreatment of a minority may be offset by the harm resulting from undertreatment of the majority," he said.

The study was funded by Wellcome and PredictImmune and jointly sponsored by the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust. Dr. Parkes and several authors declared fees and grants from numerous companies outside of this study. Dr. Narula reported no relevant disclosures. ■

Cold Snare Underused in US

Polyps *from page 1*

when safety concerns are paramount," Dr. Steinbrück said in an interview. "Cold snare resection is standard of care in our center in these cases, but our data show no superiority over hot snare in terms of resection speed."


Dr. Steinbrück

'Our study suggests that sessile serrated lesions larger than 2 cm should be resected with the cold snare. Selected cases of lateral spreading tumors may also be good candidates for cold snare resection ...'

Despite recommendations for its use, the cold snare method appears to be underused in the United States.

The Study

From June 2021 to July 2023, the 19-center intention-to-treat analysis enrolled 363 patients (48.2% women) with a total of 396 polyps and randomly assigned those with polyps of ≥ 20 mm to cold (n = 193) or hot EMR (n = 203). The primary outcome was major AEs such as perforation or postendoscopic bleeding.

Major AEs occurred in 1.0% of the cold group and in 7.9% of the hot group (P = .001, odds ratio [OR], 0.12; 95% CI, 0.03-0.54).

Rates for perforation and postendoscopic bleeding were significantly lower in the cold group, with 0 vs 8 (0% vs 3.9%, P = .007) perforations in the two groups, respectively, as well as 1.0% vs 4.4% (P = .040) for postprocedural bleeding.

Somewhat surprisingly, intraprocedural bleeding was also less common in the cold EMR group at 14% vs 23%.

Residual adenoma, however, was found more frequently in the cold group at 23.7% vs 13.8% (OR, 1.94; 95% CI,1.12-3.38; P = .020).

Commenting on the study but not involved in it, Seth Crockett, MD, MPH, AGAF, a professor of medicine in the Division of Gastroenterology and Hepatology at Oregon Health & Science University in Portland, Oregon, called the CHRONICLE findings very important.

"Interestingly, near identical results were found in a recent report from a multicenter US trial presented at DDW [Digestive Disease Week] earlier this year by Pohl et al, which adds credence to their findings," he said. "While this study helps move the needle toward using cold EMR for large polyps, it also highlights an Achilles heel of this approach, a higher risk of residual polyps during follow-up."

In other study findings, postpolypectomy syndrome occurred with similar frequency in both groups (3.1% vs 4.4%, P = .490).

As to the size factor, multivariable analysis revealed that a lesion diameter of at least 4 cm was an independent predictor of major AEs (OR, 3.37), residual adenoma (OR, 2.47), and high-grade dysplasia/cancer for residual adenoma (OR, 2.92).

In the case of suspected sessile serrated lesions, the rate of residual neoplasia was 8.3% (n = 4 of 48; 95% CI, 3.3-19.5) in the cold group and 4.8% (n = 2 of 42; 95% CI, 1.3-15.8) in the hot group (P = .681).

As for laterally spreading tumors (LSTs), Dr. Steinbrück said, "The higher recurrence rate after cold snare resection of LST nodular mixed types is unacceptable, and therefore, hot snare EMR with margin coagulation should be the treatment of choice.

"For LST granular type homogeneous and LST nongranular type without suspicion of malignancy, cold snare EMR with additional measures such as margin coagulation may be an option in selected cases — for example, when the risk of delayed bleeding is high," he said.


Dr. Crockett

'Interestingly, near identical results were found in a recent report from a multicenter US trial presented at DDW earlier this year by Pohl et al, which adds credence to their findings.'

Implications

This study has several implications, Dr. Crockett said. First, more research and innovation are needed to develop techniques to maximize complete resection during cold EMR and minimize residual polyp rates. "Ideally, this would involve other cold techniques so as not to offset the safety benefits of cold EMR," he noted.

Second, patient selection is important, as cold EMR is likely more suitable for those with serrated lesions and for those in whom follow-up can be ensured, he added. "For patients who have the largest polyps, particularly lesions of the laterally spreading tumor, nodular mixed type, and those who do not wish to participate in surveillance, hot EMR may be preferable, at least at this point."

The authors agreed that new technical development that improves the outcomes and cost-effectiveness of cold snare polypectomy and combines its demonstrated safety with recurrence reduction is necessary, as are studies to identify optimal candidate lesions.

"The next step is to evaluate whether cold snare EMR with additional measures leads to a recurrence rate comparable to hot snare EMR with margin coagulation," Dr. Steinbrück said. "If this is the case, cold snare resection may be the future treatment of choice for all large nonpedunculated polyps without suspected malignancy in the colorectum."

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