ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Endoscopic Frontiers in Inflammatory Bowel Disease

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G&H What is the current gold standard for the diagnosis of inflammatory bowel disease, and how might it be improved?

GK Currently, there is no single blood or stool-based test to diagnose inflammatory bowel disease (IBD). Clinicians rely on a combination of patients' history, physical examination, and blood tests, along with radiologic and endoscopic findings. The most important step remains endoscopic examination with a tissue diagnosis. In a Crohn's disease (CD) patient, for example, the clinician would likely perform a colonoscopy with intubation of the terminal ileum, obtain biopsies from various segments of ileum and colon, and then, hopefully, the pathologist can comment on the pattern and type of injury (chronic vs acute) on the biopsy. All of these findings help make a diagnosis of CD or ulcerative colitis (UC). The endoscopic examination is important not just for tissue diagnosis, but also to note the pattern of inflammation, as that can provide a clue, especially in the first colonoscopy, to help differentiate UC from CD. If the inflammation pattern is continuous from the rectum to either the left side of the colon or the entire colon, then UC is suspected. A pattern of inflammation that appears patchy, meaning there are areas of normal and inflamed mucosa, is usually consistent with CD.

In the recently published American Society for Gastrointestinal Endoscopy guideline, of which I am a coauthor, we discussed how to improve the diagnosis of IBD. I think the most important step remains a high index of suspicion when patients present with certain symptoms. The first colonoscopy or endoscopic examination is very important, as I mentioned, to note the pattern of inflammation in the areas involved, as well as intubating the terminal ileum and obtaining biopsies from the terminal ileum and from the rest of the segments of the colon. Also, using standardized endoscopic scoring systems based on what the clinician suspects, whether it is UC or CD, can help later on in the management of disease. As the field of optical diagnosis in IBD and in gastrointestinal (GI) disease as a whole is evolving, diagnoses are improving. Until there are more advancements in the field, clinicians will continue to rely heavily on endoscopic examination and tissue diagnosis.

G&H What strategies can be used to optimize endoscopic monitoring in IBD?

GK The two most important strategies that can be used in day-to-day practice to optimize endoscopic monitoring in IBD are very simple. First, make sure that patients understand how to do a good bowel preparation because that is still key for a high-quality colonoscopy examination. Second, when evaluating IBD patients endoscopically, clinicians should routinely use standardized endoscopic scoring systems. They should pick at least one of the various scoring systems available for CD and one for UC, based on a person's preference, training level, or type of endoscopy software. All scoring systems have some shortcomings, but it is important to use them to be able to objectively quantify the disease. If an endoscopic scoring system indicates there is no endoscopic remission, then that sometimes entails change in medical therapy. Another important strategy, especially when it comes to surveillance for cancer or dysplasia, is that clinicians should, at the bare minimum, perform all examinations with high-definition white light endoscopy. Certain European guidelines recently have indicated to use chromoendoscopy. The US guidelines have not suggested that for all patients. Obviously, patients who are at higher risk for dysplasia (eg, if they have extensive long-standing colitis,

family history or personal history of dysplasia or primary sclerosing cholangitis) should definitely be considered for chromoendoscopy. However, in routine practice, patients who lack high-risk features should be examined with high-definition white light endoscopy.

G&H Could you discuss when it is appropriate to perform stricture dilation in IBD, which techniques to use, and what the associated risks and outcomes are?

GK For the reader's benefit, a stricture is defined as narrowing in any area of the luminal GI tract. Anytime narrowing is being assessed, the question always is, can we dilate/is it safe to dilate? Endoscopic balloon dilation (EBD) is a safe and effective procedure that has been around for a long time. GI fellowship programs are very robust in training almost every gastroenterology resident in EBD. I encourage fellows to, at least in their 3 years, master this technique. When preprocedure imaging is available, several findings can help in determining which strictures to dilate. Strictures that are short (<4-5 cm) in length are usually more likely to respond to EBD. With each 1-cm increase in stricture length, the response to this therapy decreases. Significant prestenotic dilation (ie, when the lumen above the stricture is dilated up to 5-6 cm in the small intestine) indicates that the stricture is very fibrotic. In this case, EBD may not be helpful, although it may still be performed to buy the patient time for surgery. An associated fistula or an abscess is a contraindication to EBD. If inflammation is present around the stricture, gentle EBD can still be attempted based on patient symptoms. However, this indicates the need to optimize medical therapy to its fullest to help reduce the inflammation, and that will help manage the stricture as well.

There are 2 main types of EBD. In retrograde EBD, the endoscope can be passed with mild resistance across the stricture, and on the way back out, can dilate with the balloon. Although usually a safe technique because it allows the endoscopist to assess the length of the stricture and the mucosa, it is often not possible to advance the endoscope past the stricture, and antegrade EBD is performed. In antegrade EBD, a guide wire is used, and the balloon is passed over the guide wire. Fluoroscopy may or may not be used. This mainly depends on the level of experience of the endoscopist. The next step is to perform graded EBD in sizes of 3's. The balloon is inflated to a certain size based on the endoscopist's initial assessment of what the stricture diameter is. After each inflation, the endoscopist keeps the balloon at least at that size for 30 seconds to 1 minute, then deflates the balloon and examines the mucosa. If there are no big tears, then the balloon can be reinflated to the next higher size. This may be a little subjective, but I usually do not like to perform too much dilation in one procedure, especially if the patient is new, but this is based on the stricture type and length. Another point to keep in mind is that the Global Interventional IBD Group thinks there is not enough evidence to support injecting corticosteroids after EBD in these strictures, so that is not required. EBD should be avoided if the stricture has deep ulcerations because of inflammation, as such strictures are prone to more complications, and when imaging shows fistulas or abscesses.

The biggest risk that endoscopists always tend to worry about is risk of perforation as the balloon is expanding with radial force. The rate of perforation can be anywhere from 2% to 4%, based on various studies. Perforation during EBD of an IBD patient can be challenging to manage endoscopically because of tissue friability and inflammation, and most likely will end up needing surgical resection. There is also a small risk of bleeding, which often can be managed endoscopically. Besides these risks, EBD poses minimal risk other than the inherent risks of undergoing a procedure. Outcomes are generally good. Although up to approximately one-third of patients will require surgical resection at the end of 1 year after EBD, nearly two-thirds of patients may be able to avoid surgery. The patients in the latter group typically have short fibrotic strictures that are not inflamed and do not have significant prestenotic dilatation and thus are most likely to respond to EBD therapy.

G&H What are predictors of success and recurrence of stricture dilation procedures in IBD?

GK EBD has a high rate of technical success, which is 74% to 100% based on various studies. Clinical success is also high, with few complications, as mentioned. In 100 patients who undergo EBD, for instance, nearly 60% will require additional dilation or a surgical intervention over a follow-up period of 20 to 144 months. This is based on how patients respond to the first dilation. Symptom recurrence, which occurs in up to 48% of these patients, is also common. In regard to the predictors of efficacy, there are several factors that influence the success of EBD. Some studies have reported poor prognosis in patients with longer stricture length, Asian ethnicity, elevated body mass index, strictures that are deep in the jejunum, and significant prestenotic dilation (≥5 cm diameter) prior to the stricture. Those patients may not respond well to EBD.

G&H Beyond EBD and enteral stenting, are there any other procedures for managing strictures in IBD patients?

GK One modality that is gaining more traction among gastroenterologists is endoscopic stricturotomy. Basically, when the endoscopist reaches the site of the stricture, an electrosurgical knife is used to cut the stricture or the scar tissue in either a radial, circumferential, or a semi-circumferential fashion. Instead of stretching the scar tissue with a balloon or a stent, the scar tissue is cut out, thereby relieving the obstructive symptoms. The technique has been around for almost a decade but is limited to a few select centers. Initial rates of technical and clinical success with this procedure appear high, and reintervention rates are lower than those for EBD. Endoscopic stricturotomy is also effective in very short strictures (1-3 cm). The same parameters for EBD apply here as well (eg, strictures should not have too much prestenotic dilatation or an associated fistula or abscess), and patients should be able to undergo the incisional therapy. The risk of perforation with this therapy is actually low compared with EBD because the endoscopist can precisely guide the knife to the depth and cut accordingly. With the balloon, once the radial force has been disseminated, damage can happen to the wall. The downside of endoscopic stricturotomy is a higher risk of bleeding, with some studies reporting a 5% to 6% rate of bleeding after the procedure. Again, standard endoscopic interventions are able to control the bleeding. However, this would be an additional procedure, and something for a physician to discuss with the patient before attempting endoscopic stricturotomy.

G&H What is the role of stenting in cases of refractory strictures in IBD patients?

GK The role of stenting in IBD patients is somewhat controversial. Enteral stenting has long been an avenue of research in managing strictures in IBD. Older studies from 15 to 20 years ago had issues such as stent migration, fistulization, and lack of removable stents, and for various reasons (eg, no guidance on what type of stent to use, limited access to stents and stent delivery methods), there was a lack of interest in stenting. Recently, in the past 5 to 7 years, there has been a renewed interest for using stents in IBD patients because now stents can be delivered through a colonoscope, and there is more availability of fully covered, self-expanding metal stents (FCSEMS). However, a recent randomized clinical trial from Europe (ProtDilat study) in which IBD patients with strictures were randomized to either EBD or to FCSEMS showed that EBD had superior outcomes at 1 year and was more cost-effective than enteral stents. The trial led people to think that perhaps stents are not the way of the future. In my opinion, the trial was well conducted; however, we should look at a few details. The FCSEMS used in the trial are currently not designed for IBD patients or for the small intestine; the stents are used in the esophagus and are repurposed for use in IBD patients. This matters because the diameter of the small intestine is much larger than the esophagus diameter. Esophageal stents are also very linear, whereas the small intestine is not always linear. Once a stent is placed, how long to keep it in place is also unclear. Nevertheless, the trial showed that the stents were at least safe. There was a very small rate of proximal migration of a stent, although most of the stents had distally migrated, which may indicate success that the stent had dilated the stricture. The ProtDilat study put into perspective that EBD is still the best approach and is the mainstay for stricture therapy for now. In the future, new stents will likely improve with antimigratory designs. Once stents specifically designed for IBD patients become available, they may be used much more routinely.

G&H How are IBD-associated polyps and dysplasia best managed?

GK The best ways to manage polyps were outlined in the SCENIC international consensus guideline in 2015 and were recently updated in 2021 by the American Gastroenterological Association. The first step according to the guidelines is to classify IBD-associated polyps based on the Paris classification. The next step is to understand the morphology of the polyp (the size, shape, and location of the polyp as well as the polyp's surface pattern) and to make sure there is no deep scarring or any central areas of deferation. Once these features have been identified, the next goal is to select a resection technique. There are 3 main techniques: endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and endoscopic full-thickness resection (EFTR), which is the latest entry with very limited use currently. The SCENIC guideline says that if a lesion is less than 25 mm with clear borders, meaning the polyp can be identified from the surrounding tissue without any difficulty, then endoscopic resection should be attempted, especially if there is no scarring or centralized depression. The goal of polyp management in IBD patients, if possible, most of the time, is to perform en bloc resection (ie, removing the tissue in one piece). This way, the pathologist can assess the lateral and deeper margins.

Based on the size of the polyp, the choice of resection technique, EMR vs ESD, can be made. The size can be a limiting factor. For smaller polyps, EMR can be effective, and en bloc resection can be performed. For a larger polyp (>25 mm), ESD is preferred. Regarding ESD in the United States, there are a few considerations. One is that availability and access to ESD is limited to larger tertiary centers. Although already a highly skilled procedure, ESD can become even more challenging and take longer

to perform in patients with IBD because of underlying fibrosis. However, the good thing is that both safety and efficacy of ESD have improved. In a recent multicenter study from 9 US centers evaluating ESD in IBD patients specifically, en bloc resection was achieved in 96% of 45 colorectal dysplastic lesions, and the median size of the lesions was approximately 30 mm. The study was very encouraging, and there were no major red flags with safety. EFTR is a very new procedure, with limited data, as I mentioned, but the concept remains the same. If a lesion is 25 mm or less, en bloc resection can be performed, and the pathologist can have a good examination of the lesion margins to ensure complete (R0) resection.

The current approach to dysplasia in IBD patients in the United States involves consideration of surgery in certain cases. When an IBD patient has a colonoscopy that shows a polypoid lesion or an area of low-grade dysplasia, EMR, ESD, or EFTR can be performed. However, if a patient is found to have, for instance, multiple areas of low-grade dysplasia or an area of high-grade dysplasia, the tendency is to lean toward surgery, especially if the patient has achieved good inflammation control. Once high-grade dysplasia is found, it is important to consider impending development of colon cancer. A discussion with the patient is necessary to help them understand the need for surgery in this case. Another potential consideration for surgery could be a patient with UC who has extensive pseudopolyposis, in whom effective dysplasia surveillance cannot be done, or if this patient has an area of low-grade dysplasia, even if it is not multifocal. Pseudopolyps can obfuscate the examination, making it extremely difficult to evaluate dysplasia, so clinicians have to be conscious of that.

G&H How has endoscopic treatment of fistulas and perianal disease evolved, and where might it be headed?

GK Fistulas are very challenging to manage in general. In IBD patients, although endoscopic techniques are evolving, they are still not effective as a stand-alone treatment to manage fistulas. Various modalities under the realm of endoscopy can be considered for fistula management. These include endoscopic fistulotomy, endoscopic seton placement, endoscopic ultrasound to drain abscesses, and through-the-scope or over-the-scope clips. Recently, endoscopic vacuum therapy devices, which are not commercially available in the United States, and endoscopic suturing systems have been used to manage fistulas. The biggest challenge is the lack of data on the long-term success with these modalities resulting in fistula repair and healing. Some of these modalities have reported high rates of short-term success based on the location and type (simple vs complex) of fistula. Currently, the clinician may choose one of these therapies or a combination of them in conjunction with optimization of medical and surgical approaches to help the patient.

G&H Is endoscopy-guided drug delivery the future of personalized IBD therapy?

GK The concept of personalized IBD therapy is vast, encompassing medicine, surgery, and endoscopy, along with nutrition. Endoscopic-guided drug delivery is already part of the research being conducted in this area. Currently, a phase 3 clinical trial, which my medical center is participating in, is evaluating the efficacy of a drug-coated balloon for the management of strictures; an antifibrotic drug is released once the balloon is expanded. Other techniques in development include drug-eluting stents for managing strictures and a dissolvable plug–delivered stem cell therapy to treat fistulas. Questions that remain are which agent to use, what concentration of the agent has to be delivered, and which modality should deliver the agent. There have been a few pilot studies evaluating the injection of tumor necrosis factor antagonists into strictures. Use of antifibrotic agents is being considered not just in IBD but across other diseases as well. There is definitely a role in the future for these emerging technologies to help with local drug delivery, especially in severe cases.

Disclosures

Dr Kochhar is an advisory board member for CorEvitas, Eli Lilly, and GIE Medical; a consultant for Boston Scientific, Olympus, PENTAX Medical, Takeda, and Exact Sciences; and a speaker for Eli Lilly. He has stock options in Digbi Health.

Suggested Reading

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