Ask the *expert*

Endoscopy and inflammatory bowel disease

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Ask the expert features questions submitted by members, with answers provided by ASGE physician experts. ASGE's Publications Committee identifies authors and topics for the column. In this issue, Gary R. Lichtenstein, MD, responds to questions on endoscopy and inflammatory bowel disease. Dr. Lichtenstein is a professor of Medicine, Department of Gastroenterology and director of the Inflammatory Bowel Disease Center at the Hospital of the University of Pennsylvania, Philadelphia, Pa.

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ULCERATIVE COLITIS (UC)

1. Q: How long after disease diagnosis do you recommend screening colonoscopy for dysplasia or cancer in a patient with chronic UC?

A: Factors that have been determined to be important risks for the development of colorectal cancer (CRC) include: disease duration, extent of disease, family history of CRC and presence of primary sclerosing cholangitis (PSC).

Annual surveillance colonoscopies with multiple jumbo biopsies should begin at the time of diagnosis of inflammatory bowel disease (IBD) in patients who have concurrent PSC. This recommendation is made because UC can be silent for many years prior to presentation.

Once a patient has had UC that is beyond the extent of proctitis, it is suggested to perform surveillance colonoscopies every one to two years initially, beginning at the eighth year of the disease.

In patients with UC who do not have PSC, it is recommended that surveillance colonoscopy begin at the age of 40 if the patient has a first-degree relative with CRC and that colonoscopy be done at least every three years, and more frequently (every one to two years) when the UC duration reaches the eight- to ten-year mark. A positive family history of sporadic CRC is associated with a two- to three-fold increased risk of CRC in the general population.

2. Q: For screening colonoscopy in UC, do you recommend white-light endoscopy alone or in combination with narrow-band imaging (NBI), chromoendoscopy or another technique?

A: Traditionally, chromoendoscopy has had two main uses. First, it has been shown to improve the detection of subtle colonic lesions, raising the sensitivity of endoscopic examination. This is important for patients who have UC, since flat dysplastic lesions may be difficult to detect with white-light endoscopy.

Additionally, once a lesion is detected endoscopically, the use of chromoendoscopy has been shown to improve the ability to characterize the lesion, thus increasing the specificity of the examination. More recent data have demonstrated, however, that most dysplasia is visible by white-light colonoscopy.[1-3]

The quality of endoscopic instruments' visual ability has improved substantially within the past decade. With the advent of high-resolution endoscopy, we are now able to better visualize abnormal lesions. There has yet to be a prospective randomized study evaluating the detection of dysplasia with high-resolution endoscopy compared with chromoendoscopy.

The American Gastroenterological Association (AGA) Institute guidelines allow the physician to choose either white-light endoscopy or chromoendoscopy. American College of Gastroenterology (ACG) guidelines do not advocate routine use of chromoendoscopy and state that "the recommendation to routinely use chromoendoscopy-enhanced surveillance in low-risk patients awaits additional information regarding longer-term follow-up."

Longitudinal studies of chromoendoscopy will be needed to determine if the incidence of CRC is reduced in patients undergoing surveillance colonoscopy with chromoendoscopy. In addition, NBI has been inadequately evaluated in surveillance of patients with UC.

I performed chromoendoscopy several years ago but have since abandoned its use. The added advantages of chromoendoscopy were unclear to me, given the quality of current high-resolution endoscopes. Additionally, several individuals have noted that use of chromoendoscopy has a potential downside, including: longer procedure times and additional costs of the chromoendoscopy agent; potential staining of undergarments with the chromoendoscopy dye, because of leakage after the procedure; and need to learn how to perform the procedure and interpret the results (i.e., there is a learning curve). It may, however, have a role in select, high-risk subjects, such as those with a personal history of dysplasia.

I currently use high-resolution endoscopy with an appropriate number of biopsies for surveillance.

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3. Q: Do you recommend random biopsies of the colon during screening colonoscopy for UC if no suspicious dysplastic lesions are observed visually? If so, how many biopsies do you recommend?

A: Patients with UC are at increased risk of CRC; the degree of risk is related to the duration of disease, anatomic extent of colitis and the severity of microscopic inflammation over time.[4-13]

Imaging of the colon with computed tomography (CT) colonography, barium enema, magnetic resonance imaging (MRI) scanning or any other radiographic technique is not sensitive for the detection of dysplasia or cancer. As a consequence, colonoscopy with multiple mucosal biopsies represents the current standard in patients with UC of at least eight to ten years in duration when the disease extends proximal to the rectum.

In 1992, a group of investigators from Seattle headed by Cyrus E. Rubin, MD, published a landmark study that estimated that at least 56 non-targeted, jumbo-forceps biopsies are required at each endoscopic surveillance examination to exclude dysplasia in colonic mucosal biopsies with 95 percent confidence. The authors also reported that the 90 percent confidence level for the detection of dysplasia was achieved with 33 jumbo biopsies.[14]

There is clearly a suggestion from these data that fewer biopsies may be associated with the development of interval cancers between surveillance examinations. However, because of the large surface area of the colon, even 33 jumbo forceps biopsies in aggregate constitute only a tiny fraction of the colonic epithelium. It is estimated that the surface area of the colon is 1578.1 + 301.0 cm^2, and the surface area of a biopsy forceps is 2.2-5 mm^2. Given the recommendation to take a minimum of "at least 33 biopsies," the percent surface area of the mucosa that is sampled with this approach is estimated to be only 0.05 to 0.1 percent.

4. Q: Is total colectomy for UC warranted if random biopsies of the colon show low-grade dysplasia (LGD) during screening colonoscopy? What if the same biopsies show high-grade dysplasia (HGD)?

A: Current guidelines from the ACG, the AGA Institute and the Crohn's and Colitis Foundation of America suggest that if a patient has either flat LGD or flat HGD detected during a surveillance colonoscopy and the finding is confirmed by another pathologist, then a total proctocolectomy should be recommended.

In 1994, Charles N. Bernstein, MD, and colleagues published important data noting in a systematic review that 42 percent of patients with flat HGD were found to have CRC at the time of colectomy.[15] A similar finding was noted in a recent study from the St. Mark's Hospital group, reporting a 45 percent rate of CRC in patients who underwent immediate colectomy.[16]

In the systematic review by Dr. Bernstein and colleagues, a crude progression rate of 32 percent was found in patients with HGD who pursued a nonoperative course. They did not report the actuarial rate of progression in this group. Based on aforementioned and related data, performing a total proctocolectomy has been the treatment of choice for patients diagnosed with flat HGD found on a non-targeted biopsy.

Similarly, LGD has been evaluated in patients with UC. In a study by William R. Connell, MD, and colleagues, it was shown that patients with UC and flat LGD have a five-year rate of progression to HGD or CRC of 16 percent to 54 percent.[17] Another study that critically reviewed the surveillance literature reported a 19 percent rate of CRC for patients with LGD who underwent immediate colectomy.[18] A meta-analysis published in 2007 found that the positive predictive value of CRC for patients with flat LGD was 22 percent and that patients with LGD carried a risk for CRC nine times that of patients undergoing surveillance who were dysplasia free.[19] These studies collectively support colectomy as the treatment of choice for patients with flat LGD.

5. Q: How can you differentiate a sporadic colon adenoma from one associated with dysplasia in a patient with UC?

A: The finding of a raised lesion at the time of screening and surveillance colonoscopy is a common occurrence. An adenoma is dysplastic by standard pathologic definition. The issue I suspect you are referring to is the differentiation of a sporadic adenoma in the area of colitis (often referred to as an adenoma-like mass lesion, or ALM) from a dysplasia-associated lesion or mass (DALM).

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The differentiation of ALM from DALM is important. A polyp that has features indicating a malignancy (central umbilication, irregular borders, "spreading," irregularly shaped, associated satellite lesions, not endoscopically resectable, etc.), is more likely to be a DALM than an ALM.

Endoscopic polypectomy is adequate for an ALM in patients with UC. However, for endoscopic polypectomy to be considered sufficient, there can be no associated flat dysplasia, the polypectomy must be complete, additional biopsies of the base of the polyp should reveal no dysplasia and there should be no dysplasia elsewhere in the colon. Additionally, it is important to stress that an ALM looks like a non-IBD related adenoma.

It is important also to stress that the occurrence of a DALM may coincide with synchronous or metachronous neoplasia. Thus, prophylactic proctocolectomy is recommended in all patients with a DALM. In contrast, the term ALM describes a sporadic adenoma that is similar to those observed in non-IBD patients and is treated by standard polypectomy.

It is also important to follow patients who have had an ALM resected to ensure that it is not a DALM. Suggestions have been made that a repeat colonoscopy be done within six months in patients with an ALM.[20]

6. Q: Are pseudopolyps in patients with UC considered dysplastic? When suspected at colonoscopy, do they require biopsy for confirmation of the diagnosis or specific surveillance?

A: Pseudopolyps in themselves are not malignant nor dysplastic. They have been demonstrated to be independent markers of an increased risk of malignancy in patients with UC.[21]

In general, an endoscopist experienced in assessing patients with UC by surveillance colonoscopy should be able to differentiate pseudopolyps from preneoplastic polyps with use of high-resolution endoscopy. Alternatively, chromoendoscopy, when available, may be utilized for this indication.

It is recommended that surveillance biopsies be performed throughout the colon. Any raised lesions should be biopsied, particularly those that have a suspicious appearance. Any lesions that do not have the appearance of typical pseudopolyps should be removed using standard polypectomy techniques, and the mucosa adjacent to the polyp should also be biopsied.

For polyps that are large in size or have an abnormal mucosal pattern, the site should be marked with indelible ink (tattoo) after the polyp is removed. Multiple biopsies should be taken from the areas surrounding the polypoid lesion and elsewhere in the colon to exclude dysplasia. If the endoscopist cannot resect a lesion completely, the site of the polyp should be biopsied and marked with a tattoo, and the patient should be referred to an expert therapeutic endoscopist for polypectomy. Any finding of flat dysplasia in the surrounding tissue or elsewhere in the colon should initiate referral for colectomy.

The endoscopic assessment of multiple pseudopolyps at surveillance colonoscopy can be difficult. The presence of large pseudopolyps, or those with an atypical pit pattern (when viewed with a high-resolution endoscope), should be biopsied or removed endoscopically. When there are coexistent high-risk factors for carcinoma (such as concomitant PSC or a strong family history of colorectal carcinoma), it is important to perform surveillance colonoscopic evaluations.

It should be stressed that colonic surveillance is not "fool proof." A small percentage of patients thought to have pseudopolyps may actually have premalignant lesions. The only true way to eliminate the risk of colorectal carcinoma in those patients with pseudopolyps is by colectomy. There are certainly physicians and patients who would argue that this approach is aggressive.

7. Q: A patient with UC maintained on sulfasalazine for many years undergoes a colonoscopy for worsening hematochezia. Colonoscopy identifies two large mid-sigmoid polyps. The largest polyp is erythematous, has surface erosions and exceeds 4 cm in diameter. Biopsies from the polyps show acute and chronic inflammation compatible with inflammatory polyps. The remaining left colon (including the rectum) shows only mild inflammation, and the right colon, transverse colon and rectum are normal. If these polyps are the presumed cause of the hematochezia, how would you treat them?

A: When large polyps that are endoscopically consistent with large pseudopolyps are found in the colon, it is important to be sure that adequate samples are obtained from the lesions or the polyp is resected in its entirety. On occasion, a carcinoma can have areas of inflammation and can have an appearance similar to that of a pseudopolyp.

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In patients with UC, pseudopolyps represent areas where the mucosa projects above the surface into the lumen of the colon. The size and morphology of pseudopolyps are variable and may be flat, raised, narrow, or on a pedicle (short or long in length). They may or may not possess an inflammatory exudate in part or completely. Pseudopolyps can represent areas of prior inflammation or areas that are currently inflamed.

Assuming that the large pseudopolyp is not malignant (as determined by multiple biopsies or endoscopic resection), I suggest prescribing standard medical therapy for active colitis. Given the size and multiplicity of the polyps, it seems reasonable to resect them endoscopically. If a patient has active inflammation and is already taking oral sulfasalazine, then one can treat the active inflammation by escalating the dose to a maximum of 4 to 6 grams per day and potentially adding topical mesalamine therapy. If this is not advantageous, other agents can be considered: antimetabolite therapy with azathioprine or 6-mercaptopurine (MP), anti-tumor necrosis factor (anti-TNF) therapy or the combination of both agents.

8. **Q: A 40-year old African-American woman with a 20-year history of UC undergoes surveillance colonoscopy. The patient has been compliant on 2.4 grams per day of oral mesalamine for many years. Several months ago, she had six to seven loose, non-bloody stools per day that resolved without further therapy after three weeks. During colonoscopy, the entire left colon appears moderately inflamed and ulcerated, but the remaining colon and terminal ileum appear normal. She is asymptomatic. Do you recommend modification of her current medical therapy? If you do treat to attempt endoscopic remission, when should a colonoscopy be repeated if there are no symptoms to follow?**

A: This case raises an important concept regarding medical therapy of patients with UC. Do patients who are in clinical remission but who have active mucosal disease need to have any modification of their medical therapy?

The individual described is on 2.4 grams per day of mesalamine. There are recent data from the ASCEND I and II trials, suggesting that 4.8 grams per day of oral mesalamine is more effective than 2.4 grams per day for achieving mucosal healing.[22]

In a post-hoc analysis, the published data noted that at Week 3, mucosal healing (endoscopy subscore of 0 or 1) was achieved in 65 percent of patients with moderately active UC on 4.8 grams per day and 58 percent of patients on 2.4 grams per day (P = .219). At Week 6, the rates increased to 80 percent for 4.8 grams per day and 68 percent for 2.4 grams per day (P = .012).

Healing rates with the higher dose of mesalamine were also greater across all extents of disease and in patients with prior glucocorticoid use. At six weeks, the clinical response to therapy and mucosal healing were found to be well correlated (kappa = 0.694). Likewise, the Week 6 change in the IBD questionnaire showed a significant correlation with mucosal healing (P < .0001). In light of the data from this study, the timing that seems most reasonable to check for mucosal healing is six weeks after the initiation of a change in dose.

There have been published data to illustrate that persons who achieve mucosal healing have fewer disease flares over the subsequent year. It was first suggested in 1966 that mucosal healing in patients with UC may be associated with improved long-term remission rates and a lower risk of disease relapse.[23] In the study described above, 40 percent of patients with UC (all different disease severities) who achieved endoscopic remission (defined as a lack of significant inflammation on rectal biopsy) after acute treatment with oral and rectal glucocorticoids, remained asymptomatic during a follow up of one year. On the other hand, only 18 percent of patients who still had endoscopic lesions after treatment remained symptom-free during the same period.

In a subsequent study of 82 patients with UC in clinical remission, histology was evaluated for evidence of mucosal inflammation as manifested by an acute inflammatory cell infiltrate, crypt abscess or mucin depletion. If any of these features were present, those persons had a two- to three-fold greater risk of relapse during a 12-month follow up (regardless of treatment), compared with patients without these abnormalities.[24] This study suggests that in patients who achieve both mucosal healing in addition to the resolution of symptoms and improvement in sigmoidoscopic scores, the risk of symptomatic disease relapse may be substantially reduced.

As a separate issue, the risk of colorectal neoplasia is increased in patients with UC. A subsequent case-control study that evaluated 68 patients and 136 matched controls illustrated that the degree of bowel inflammation is a risk factor for colorectal neoplasia in patients with long-standing extensive UC.[25, 26] Univariate analysis revealed a significant correlation between endoscopic (odds ratio [OR] 2.54; 95 percent confidence interval [CI]: 1.45–4.44; P ¼ 0.001) and histologic (OR 5.13; 95 percent CI: 2.36–11.14; P < 0.001) inflammation scores and the risk of CRC. On multivariate analysis, histologic inflammation scores remained an independent

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predictor of malignancy (OR 4.69; 95 percent CI: 2.10–10.48; P < 0.001). At least two other series have also demonstrated that inflammation is a risk factor for neoplasia.[27, 28]

In light of these data, in the patient described, I suggest first increasing the dose of oral mesalamine from 2.4 to 4.8 grams per day to see if mucosal healing occurs. It should, however, be stressed that there have been no prospective interventional studies to assess the effect of an alteration in the treatment on either mucosal healing or prognosis. Another potential option would be to add topical mesalamine therapy to the oral mesalamine therapy. If this is not beneficial, antimetabolite therapy with azathioprine or 6-MP, anti-TNF therapy or the combination of both agents may be considered.

CROHN'S DISEASE (CD)

9. Q: Should endoscopists repeat a colonoscopy to confirm mucosal healing in a patient with Crohn's ileocolitis who achieves clinical remission after starting an anti-TNF agent?

A: To date, we have not recommended that physicians routinely perform colonoscopy in standard clinical practice to document that clinical remission is accompanied by endoscopic mucosal healing. In other words, if we treat a patient with a specific medication, we do not routinely suggest colonoscopy to document mucosal healing when the patient becomes asymptomatic.

If, however, a patient has active symptoms once a specific therapy (such as an antimetabolite or an anti-TNF agent) has been given, then it is clearly appropriate to determine whether complete mucosal healing has been achieved. If mucosal healing is incomplete, then either dose escalation within class or switching to another class of medications (such as switching from an antimetabolite to anti-TNF therapy) is appropriate.

It seems logical, however, to document mucosal healing in patients with CD even when they achieve clinical remission. As has been seen in the SONIC trial, a reasonably high number of patients who achieve clinical remission have incomplete mucosal healing.[29] Other studies have demonstrated that the presence of complete mucosal healing is associated with lower hospitalization rates and also lower rates of future CD-related surgeries.[30, 31]

In clinical practice, it is reasonable to stratify patients (based on risk if mucosal healing is not achieved) into a high-risk group and a low-risk group. It seems logical to attempt to document mucosal healing in patients classified as high risk. An example might be a high-risk patient who has had several prior operations with resection of a large amount of bowel. If this patient now has active CD in several feet of the remaining small intestine and receives medical therapy, I would attempt to document mucosal healing in this patient. If healing is not achieved initially, I would attempt to optimize therapy with the agent(s) used or switch to another medication after an appropriate trial to achieve mucosal healing.

A prototypic low-risk patient might be one who has had isolated 2-cm long distal ileal disease for 10 years and a recent colonoscopy demonstrating only active ileal inflammation. If treatment in this patient achieves clinical remission, then repeat colonoscopy is not required. There has yet to be a trial that looks at "treat to clinical remission" versus "treat to endoscopic remission." Such a trial is currently being designed.

10. Q: Are there sufficient data for endoscopists to consider using intralesional injection of anti-TNF agents in patients with inflammatory or stenotic CD?

A: The injection of anti-TNF therapy into areas of inflammation has been suggested for the treatment of CD-related inflammatory strictures.[32] The difficulty with the injections is that there has been no standardization of either injection dose or frequency of administration. The published data so far have been an unblinded small series. There have been no randomized double-blind, placebo-controlled trials assessing efficacy and safety of therapy.

In general, the use of medications that are deemed to be effective for the treatment of active inflammation (antimetabolites such as azathioprine, 6-MP or methotrexate, anti-TNF therapy with infliximab, adalimumab or certolizumab pegol and natalizumab) are not meant to be given when fibrosis is present. Although these agents are effective for the treatment of active inflammation, they do not remove scar tissue once it is present. Therefore, their use in patients with fibrotic stenotic CD is not recommended.

Until better data are available and obtained in a blinded fashion, intralesional injection of anti-TNF cannot be recommended for CD.

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MISCELLANEOUS

11. Q: If endoscopy discloses moderate to severe proctitis (with or without ulcers), should there be any additional workup for infectious disease (e.g., *Chlamydia* infection or syphilis) besides routine rectal biopsies?

A: The patients who should be assessed for *Chlamydia* include: sexual partners of patients with *Chlamydia* infection; individuals diagnosed with *Chlamydia* infection in the past 12 months; people with two or more sexual partners in the past two months; all women undergoing termination of pregnancy; people under 25 who are sexually active; and those who receive health care at a sexual health clinic.

In general, all patients who are diagnosed with or suspected of having *Chlamydia* infection and their sexual partners should be advised to abstain from sexual contact until treatment has been completed. Sexual contacts should be notified, and partner notification should be offered to all patients with *Chlamydia* infection, regardless of where they were diagnosed. All contacts should be offered a test for *Chlamydia* and advised to take treatment (1 gram of azithromycin) without waiting for the results. Patients should follow up with their physicians two to four weeks after treatment.

It is important to emphasize that a *Chlamydia* infection is usually asymptomatic. Transmission occurs through vaginal, rectal or oral sex. Early detection and treatment can prevent transmission. Untreated *Chlamydia* infection can result in complications, such as pelvic inflammatory disease, sexually acquired reactive arthritis and epididymo-orchitis.

In assessing a patient for syphilis, it is important to recognize that there may be other sexually transmitted diseases and infections that may have rectal involvement. Agents such as *Chlamydia, Neisseria gonorrhea, Shigella, Campylobacter, Entamoeba* species, herpes simplex virus, adenovirus and syphilis can commonly present with rectal symptoms. Less frequent infections such as lymphogranuloma venereum (LGV) should also be in the differential diagnosis.

It is not necessary to assess for the aforementioned agents in all patients. It is only appropriate to check for these infections in patients who have risk factors for them, such as immunocompromised hosts, persons infected with human immunodeficiency virus (HIV), men who have sex with men, and other patients with known risk factors. Care providers should not be reluctant to ask appropriate questions of patients regarding their sexual practices.

12. Q: Should symptomatic anorectal strictures in patients with IBD be dilated? If so, what do you use to dilate, how do you determine the size of the dilator to use and how often do you perform the procedure?

A: Strictures occur throughout the gastrointestinal tract, most commonly in the ileocecal region, but also in the anorectal region. Stricture dilation of the anorectal region in patients with CD is performed frequently. In recent years, endoscopic through-the-scope (TTS) balloon dilation has offered a valid therapeutic option in patients with intestinal symptomatic strictures.

The use of TTS balloon dilators has made dilation relatively easy and quick to perform. The procedure is minimally invasive, may save intestinal length, and thus avoid short-bowel syndrome and eliminates the risks associated with general anesthesia. Several studies have reported that endoscopic balloon dilation can be a safe alternative to surgical resection or strictureplasty in symptomatic patients, although long-term data on the outcomes and parameters predictive of success are lacking.[33-48]

Two types of dilators are currently available: a fixed-diameter push (bougie) dilator and an expanding radial balloon dilator. Balloons tend to exert a radial vector force against the strictured tissue compared with the longitudinal and shearing force of the bougie-type dilators.

Balloon-dilator systems, with the option for TTS-wire-guided positioning, are commonly used and are easy to position across the stricture. Wire-guided, fixed-diameter push dilators are not commonly used for treatment of colonic strictures. They can, however, be useful for distal colonic strictures. Fluoroscopic guidance is recommended with tight strictures that preclude visualization of the lumen beyond the stricture or when using a guidewire. A recent review described in detail the technique used to perform endoscopic balloon dilation.[49]

It is important to select appropriate candidates for endoscopic balloon dilation of a colonic stricture. Factors that predict a successful outcome include: a relatively narrow stenosis (< 10 mm), a short-segment stricture (< or equal to 4 cm in length) and an anastomotic stricture.[50]

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In older studies, factors that predicted a poor response to dilation were: the presence of numerous strictures, a complete bowel obstruction, fistulas found within the stricture, active inflammation surrounding the stricture, recent surgery, a tight angulation and malignancy.[51]

The frequency of repeat dilation is variable among patients. Different clinical responses dictate that different frequencies be used to repeat dilation if needed. It is not unreasonable to examine the patient by sigmoidoscopy within several weeks after dilation to see if the stricture has recurred.

13. Q: When should an endoscopist consider small bowel stricture dilation in a patient with CD? How should this be performed?

A: There are currently no universally accepted guidelines or a clearly accepted technique for endoscopic treatment of small bowel strictures in patients with CD.

It is difficult to critically analyze the literature pertaining to small bowel stricture dilation. This has been a drawback since different authors have applied different treatment protocols. They have used different balloons with different dilation pressures and different durations of insufflation. Use of intralesional glucocorticoid injections has been variable. Additionally, few authors have reported site-specific recurrence rates. Some authors have reported in detail the number of dilations per patient, whereas others have only reported whether the technique was successful or not.

A recent review of the literature comparing endoscopic balloon dilation to strictureplasty noted that meta-analysis and direct comparison of the two methods was not possible due to differing treatment protocols in the published studies.[52] One can state that there is more literature about strictureplasty than endoscopic balloon dilation, and the median and mean lengths of follow up is longer for those patients. There is no difference between the incidence of major complications after strictureplasty and endoscopic balloon dilation.

The most suitable strictures for endoscopic dilation have been anastomotic strictures. Additionally, it has been suggested that short strictures (< 3 cm) are more likely to do well compared to long strictures when endoscopic balloon dilation is performed in the small intestine.[53]

Additionally, strictures with a predominantly fibrotic component have been reported to fare better with dilation.[54] If possible, and if the patient and physician are willing and able to accept the potential risk, it is reasonable to attempt endoscopic balloon dilation in small intestinal strictures.

It is important to note that small intestinal strictures may leave a patient with persistent symptoms of intestinal obstruction despite endoscopic therapy if adhesions are primarily responsible for the symptoms. It is sometimes difficult to discern if a stricture is the cause of the obstructive symptoms. A cross-sectional imaging study may help to detect another cause of obstructive symptoms such as adhesions. Recently, the use of deep enteroscopy has permitted access and therapy of small bowel strictures.

References

1. Rutter MD, Saunders BP, Wilkinson KH, et al. Most dysplasia in ulcerative colitis is visible at colonoscopy. Gastrointest Endosc 2004; 60:334-9.
2. David T. Rubin, MD, Jami A. Rothe, BS, Jeremy T. Hetzel, AB, Russell D. Cohen, MD, Stephen B. Hanauer, MD. Are dysplasia and colorectal cancer endoscopically visible in patients with ulcerative colitis? Gastrointest Endosc 2007; 65:998-1004.
3. Blonski W, Kundu R, Lewis J, Aberra F, Osterman M, Lichtenstein GR. Is dysplasia visible during surveillance colonoscopy in patients with ulcerative colitis? Scand J Gastroenterol 2008; 43:698-703.
4. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology 2004; 126:451-9.
5. Gupta RB, Harpaz N, Itzkowitz S, et al. Histologic inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: a cohort study. Gastroenterology 2007; 133:1099-105; quiz 1340-1.

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6. Greenstein AJ, Sachar DB, Smith H, et al. Cancer in universal and left-sided ulcerative colitis: factors determining risk. Gastroenterology 1979; 77:290-4.
7. Jess T, Loftus EV Jr., Velayos FS, et al. Risk factors for colorectal neoplasia in inflammatory bowel disease: a nested case—control study from Copenhagen County, Denmark and Olmsted County, Minnesota. Am J Gastroenterol 2007; 102:829-36.
8. Sugita A, Sachar DB, Bodian C, et al. Colorectal cancer in ulcerative colitis. Influence of anatomical extent and age at onset on colitis—cancer interval. Gut 1991; 32:167-9.
9. Sachar DB. Cancer risk in inflammatory bowel disease: myths and metaphors In: Riddell RH (ed). Dysplasia and Cancer in Colitis. Elsevier: New York, 1991; pp. 5-9.
10. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001; 48:526-35.
11. Gilat T, Fireman Z, Grossman A, et al. Colorectal cancer in patients with ulcerative colitis. A population study in central Israel. Gastroenterology 1988; 94:870-7.
12. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 2006; 130:1030-8.
13. Ullman T, Odze R, Farraye FA. Diagnosis and management of dysplasia in patients with ulcerative colitis and Crohn's disease of the colon. Inflamm Bowel Dis 2009; 15: 630-8; 94:870-7.
14. Rubin CE, Haggitt RC, Burmer GC, et al. DNA aneuploidy in colonic biopsies predicts future development of dysplasia in ulcerative colitis. Gastroenterology 1992; 103:1611-20.
15. Bernstein CN, Shanahan F, Weinstein WM. Are we telling patients the truth about surveillance colonoscopy in ulcerative colitis? [see comments]. Lancet 1994; 343:71-4.
16. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 2006; 130:1030-38.
17. Connell WR, Talbot IC, Harpaz N, et al. Clinicopathological characteristics of colorectal carcinoma complicating ulcerative colitis. Gut 1994; 35:1419-23.
18. Bernstein CN, Shanahan F, Weinstein WM. Are we telling patients the truth about surveillance colonoscopy in ulcerative colitis? [see comments]. Lancet 1994; 343:71-4.
19. Thomas T, Abrams KA, Robinson RJ, et al. Meta-analysis: cancer risk of low-grade dysplasia in chronic ulcerative colitis. Aliment Pharmacol Ther 2007; 25:657-68.
20. Helmut Neumann, Michael Vieth, Cord Langner, Markus F Neurath and Jonas Mudter. Cancer risk in IBD: How to diagnose and how to manage DALM and ALM. World J Gastroenterol 2011 July 21; 17:3184-91.
21. Velayos FS, Loftus EV Jr., Jess T, Harmsen WS, Bida J, Zinsmeister AR, Tremaine WJ, Sandborn WJ. Predictive and protective factors associated with colorectal cancer in ulcerative colitis: A case-control study. Gastroenterology 2006 Jun; 130:1941-9.
22. Lichtenstein GR, Ramsey D and Rubin DT. Delayed-Release Oral Mesalamine 4.8g/day versus 2.4g/day in Endoscopic Mucosal Healing: ASCEND I & II Combined Analysis. Alimentary Pharmacology and Therapeutics 2011 Mar; 33:672-8. doi: 10.1111/j.1365-2036.2010.04575.x. Epub 2011 Jan 23.
23. Wright R, Truelove SR. Serial rectal biopsy in ulcerative colitis during the course of a controlled therapeutic trial of various diets. Am J Dig Dis 1966; 11:847-57.
24. Riley SA, Mani V, Goodman MJ, et al. Microscopic activity in ulcerative colitis: what does it mean? Gut 1991; 32:174-78.
25. Loftus EV Jr. Epidemiology and risk factors for colorectal dysplasia and cancer in ulcerative colitis. Gastroenterol Clin North Am 2006; 35:517-31.
26. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology 2004; 126:451-9.
27. Rutter MD, Saunders BP, Wilkinson KH, et al. Cancer surveillance in longstanding ulcerative colitis: endoscopic appearances help predict cancer risk. Gut 2004; 53:1813-16.
28. Rubin DT, Huo D, Rothe JA. Increased inflammatory activity is an independent risk factor for dysplasia and colorectal cancer in ulcerative colitis: a case-control analysis with blinded prospective pathology review. Gastroenterology 2006; 130:A – 2 Abstract 14.
29. Colombel JF, Rutgeerts P, Reinisch W, et al. SONIC study group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med 2010; 362:1383-95.

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30. Baert F, Moortgat L, Van Asche G, Caenepeel P, Vergauwe P, De VOs M, Stokkers P, Hommes D, Rutgeerts P, Vermiere S and D'Haens G. Mucosal Healing Predicts Sustained Clinical Remission in Patients with Early-Stage Crohn's Disease. Gastroenterology 2010; 138:463-8.

31. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomized trial. Lancet 2002; 359:541-49.

32. Arun Swaminath, MD, Simon Lichtiger. Dilation of Colonic Strictures by Intralesional Injection of Infliximab in Patients with Crohn's Colitis. Inflamm Bowel Dis 2008;14:213-16S.

33. Williams AJ, Palmer KR. Endoscopic balloon dilatation as a therapeutic option in the management of intestinal strictures resulting from Crohn's disease. Br J Surg 1991; 78:453-4.

34. Blomberg B, Rolny P, Järnerot G. Endoscopic treatment of anastomotic strictures in Crohn's disease. Endoscopy 1991; 23:195-8.

35. Couckuyt H, Gevers AM, Coremans G, et al. Efficacy and safety of hydrostatic balloon dilatation of ileocolonic Crohn's strictures: a prospective long term analysis. Gut 1995; 36:577-80.

36. Ramboer C, Verhamme M, Dhondt E, et al. Endoscopic treatment of stenosis in recurrent Crohn's disease with balloon dilation combined with local corticosteroid injection. Gastrointest Endosc 1995; 42:252-5.

37. Matsui T, Hatakeyama S, Ikeda K, et al. Long-term outcome of endoscopic balloon dilation in obstructive gastroduodenal Crohn's disease. Endoscopy 1997; 29:640-5.

38. Dear KL, Hunter JO. Colonoscopic hydrostatic balloon dilatation of Crohn's strictures. J Clin Gastroenterol 2001; 33:315-8.

39. Sabaté JM, Villarejo J, Bouhnik Y, et al. Hydrostatic balloon dilatation of Crohn's strictures. Aliment Pharmacol Ther 2003; 18:409-13.

40. Brooker JC, Beckett CG, Saunders BP, et al. Long-acting steroid injection after endoscopic dilation of anastomotic Crohn's strictures may improve the outcome: a retrospective case series. Endoscopy 2003; 35:333-7.

41. Thomas-Gibson S, Brooker JC, Hayward CM, et al. Colonoscopic balloon dilation of Crohn's strictures: a review of long-term outcomes. Eur J Gastroenterol Hepatol 2003; 15:485-8.

42. Morini S, Hassan C, Lorenzetti R, et al. Long-term outcome of endoscopic pneumatic dilatation in Crohn's disease. Dig Liver Dis 2003; 35:893-7.

43. Singh VV, Draganov P, Valentine J. Efficacy and safety of endoscopic balloon dilation of symptomatic upper and lower gastrointestinal Crohn's disease strictures. J Clin Gastroenterol 2005; 39:284-90.

44. Ferlitsch A, ReinischW, Püspök A, et al. Safety and efficacy of endoscopic balloon dilation for treatment of Crohn's disease strictures. Endoscopy 2006; 38:483-7.

45. Ajlouni Y, Iser JH, Gibson PR. Endoscopic balloon dilatation of intestinal strictures in Crohn's disease: safe alternative to surgery. J Gastroenterol Hepatol 2007; 22:486-90.

46. Van Assche G, Vermeire S, Rutgeerts P. Endoscopic therapy of strictures in Crohn's disease. Inflamm Bowel Dis 2007; 13:356-8.

47. Foster EN, Quiros JA, Prindiville TP. Long-term follow-up of the endoscopic treatment of strictures in pediatric and adult patients with inflammatory bowel disease. J Clin Gastroenterol 2008; 42:880-5.

48. Hoffmann JC, Heller F, Faiss S, et al. Through the endoscope balloon dilation of ileocolonic strictures: prognostic factors, complications, and effectiveness. Int J Colorectal Dis 2008; 23:689-96.

49. Lemberg B and Vargo JJ. The Expert Corner: Balloon Dilation of Colonic Strictures. Am J Gastroenterol 2007; 102:2123-25.

50. Hassan C, Zullo A, De Francesco V, Ierardi E, Giustini M, Pitidis A, Taggi F, Winn S, Morini S. Systematic review: Endoscopic dilatation in Crohn's disease. Aliment Pharmacol Ther 2007 Dec; 26:1457-64. Epub 2007 Sep 28.

51. Kozarek RA. Endoscopic management of small bowel, anastomotic, and colonic strictures in Crohn's disease. In: Bayless TM, Hanauer SB, eds. Advanced therapy of inflammatory bowel disease. Hamilton, Canada: B.C. Decker Inc., 2001:509-13.

52. Wibmer AG, Kroesen AJ, Gröne J, Buhr H-J and Ritz J-P. Comparison of strictureplasty and endoscopic balloon dilatation for stricturing Crohn's disease—review of the literature. Int J Colorectal Dis 2010; 25:1149-57.

53. Hirai F, Beppu T, Sou S, Seki T, Yao K, Matsui T. Endoscopic balloon dilatation using double-balloon endoscopy is a useful and safe treatment for small intestinal strictures in Crohn's disease. Dig Endosc 2010 Jul; 22:200-4.

54. Saunders BP, Brown GJ, Lemann M, et al. Balloon dilation of ileocolonic strictures in Crohn's disease. Endoscopy 2004; 36:001-7.