The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Ulcerative Colitis

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The American Society of Colon and Rectal Surgeons (ASCRS) is dedicated to ensuring high-quality patient care by advancing the science, prevention, and management of disorders and diseases of the colon, rectum, and anus. The Clinical Practice Guidelines Committee is composed of society members who are chosen because they have demonstrated expertise in the specialty of colon and rectal surgery. This committee was created to lead international efforts in defining quality care for conditions related to the colon, rectum, and anus and develop clinical practice guidelines based on the best available evidence. While not proscriptive, these guidelines provide information on which decisions can be made and do not dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines.

These guidelines should not be deemed inclusive of all proper methods of care nor exclusive of methods of care reasonably directed toward obtaining the same results. The ultimate judgment regarding the propriety of any specific procedure must be made by the physician considering all the circumstances presented by the individual patient.

STATEMENT OF THE PROBLEM

Ulcerative colitis (UC) is an idiopathic chronic inflammatory condition that affects the mucosa lining the colon and rectum that, for unknown reasons, continues to increase in incidence with nearly 3.1 million people affected in the United States alone.[1] Patients most often present in 2 general age categories, between about ages 15 and 30 or 55 and 65, with rectal bleeding, urgency, and/or tenesmus from proctitis.[2,3] The degree of symptomatology is variable over

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a patient's lifetime, and patients often exhibit a remitting and relapsing phenotype at various points during their course. Although patients can achieve mucosal healing by using an ever-expanding repertoire of immunoregulatory medications, approximately 15% to 20% of patients with UC still require colectomy for medically refractory disease and/or neoplasia of the colon or rectum.[4–8]

Regardless of the indication for surgical intervention, complete removal of all at-risk tissue (ie, the colon and the rectum) is considered curative for the intestinal manifestations of UC. Depending on the clinical scenario, operative strategies for patients with UC may include a total abdominal colectomy with end ileostomy or ileoproctostomy or total proctocolectomy with a permanent end ileostomy, a continent ileostomy, or construction of an IPAA, all of which are increasingly performed using minimally invasive techniques.[7–10] This guideline focuses on the surgical management of medically refractory UC and UC-associated colorectal neoplasia, key technical aspects of operative intervention, postoperative considerations specific to patients with UC, and emerging concepts in UC that warrant further exploration and consideration. Because the optimal management of patients with UC involves a multidisciplinary team approach, including colorectal surgeons, gastroenterologists, radiologists, pathologists, nutritionists, and enterostomal therapists, these guidelines should be viewed in that context and represent only a portion of the treatment paradigm utilized when caring for patients with UC.

METHODOLOGY

This guideline was written as an update to the *ASCRS Practice Parameters for the Surgical Treatment of Ulcerative Colitis* published in 2014.[11] Although bowel preparation, enhanced recovery pathways, ostomy care, and prevention of thromboembolic disease are relevant to the surgical management of patients with UC, these topics are addressed in other ASCRS clinical practice guidelines and are beyond the scope of this guideline.[12–15] An organized search of MEDLINE, PubMed, EMBASE, Scopus, and the Cochrane Database of Collected Reviews limited to the English language was performed between January 1, 1995 and December 18, 2020.[11] The complete search strategy is listed in Supplemental Digital Content http://links.lww.com/DCR/B558. Keyword combinations included "ulcerative colitis," "indeterminate colitis," "inflammatory bowel disease," "Crohn's disease," "surgery," "colectomy," "proctocolectomy," "ileostomy," "laparoscopic," "robotic," "Kock pouch," "mucosectomy," "ileoproctostomy," and "ileal pouch-anal anastomosis." Directed searches using embedded references from primary articles were performed in selected circumstances.

After removal of duplicate references, a total of 8661 unique journal titles were identified. A total of 1232 titles were selected for manuscript review with an emphasis placed on prospective trials, meta-analyses, systematic reviews, and practice guidelines.[16,17] Peer-reviewed observational studies and retrospective studies were included when higher-quality evidence was insufficient. Of the 1232 full-text manuscripts reviewed, 296 references were included in the final manuscript (Fig. 1). The final source material used was evaluated for methodological quality, the evidence base was examined, and a treatment guideline was formulated. The final grade of recommendation was designated using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system (Table 1).[18] When there was disagreement regarding the evidence base or treatment guideline, consensus from the committee chair, vice chair, and 2 assigned reviewers determined the outcome. Members of the ASCRS Clinical Practice Guidelines Committee worked in joint production of these guidelines from inception to final publication. Recommendations formulated by the subcommittee were reviewed by the entire Clinical Practice Guidelines Committee, selected members of the ASCRS Inflammatory Bowel Disease committee, and selected practicing gastroenterologists. Consideration was given to align recommendations with the 2020 ASCRS Clinical Practice Guidelines for the Surgical Management of Crohn's Disease because there was significant overlap in the evidence base supporting these 2 guidelines.[19] The final guideline was approved by the ASCRS Executive Council and peer reviewed by *Diseases of the Colon & Rectum*. In general, each ASCRS Clinical Practice Guideline is updated every 5 years. No funding was received for preparing this guideline and the authors have declared no competing interests related this material. This guideline conforms to the Appraisal of Guidelines Research and Evaluation (AGREE) checklist.

MEDICALLY REFRACTORY ULCERATIVE COLITIS

1. **A multidisciplinary approach including early surgical consultation should be used to guide optimal care in hospitalized patients with moderate-to-severe UC undergoing escalation of medical therapy. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.**

The goal for treating UC is to resolve symptoms and achieve mucosal healing, defined as the resolution of inflammatory changes on endoscopic evaluation. Determining the extent and severity of disease is critical to selecting appropriate medical management. The extent of disease should be characterized anatomically (eg, the Montreal classification designates proctitis as E1, left-sided colitis as E2, and extensive colitis as E3).[20,21] Disease severity is commonly classified according to the Truelove and Witts criteria but may also be classified according to the Seo Index, Rachmilewitz Index, Simple Clinical Colitis Activity Index, or the Mayo Score.[22–28] The 2019 American

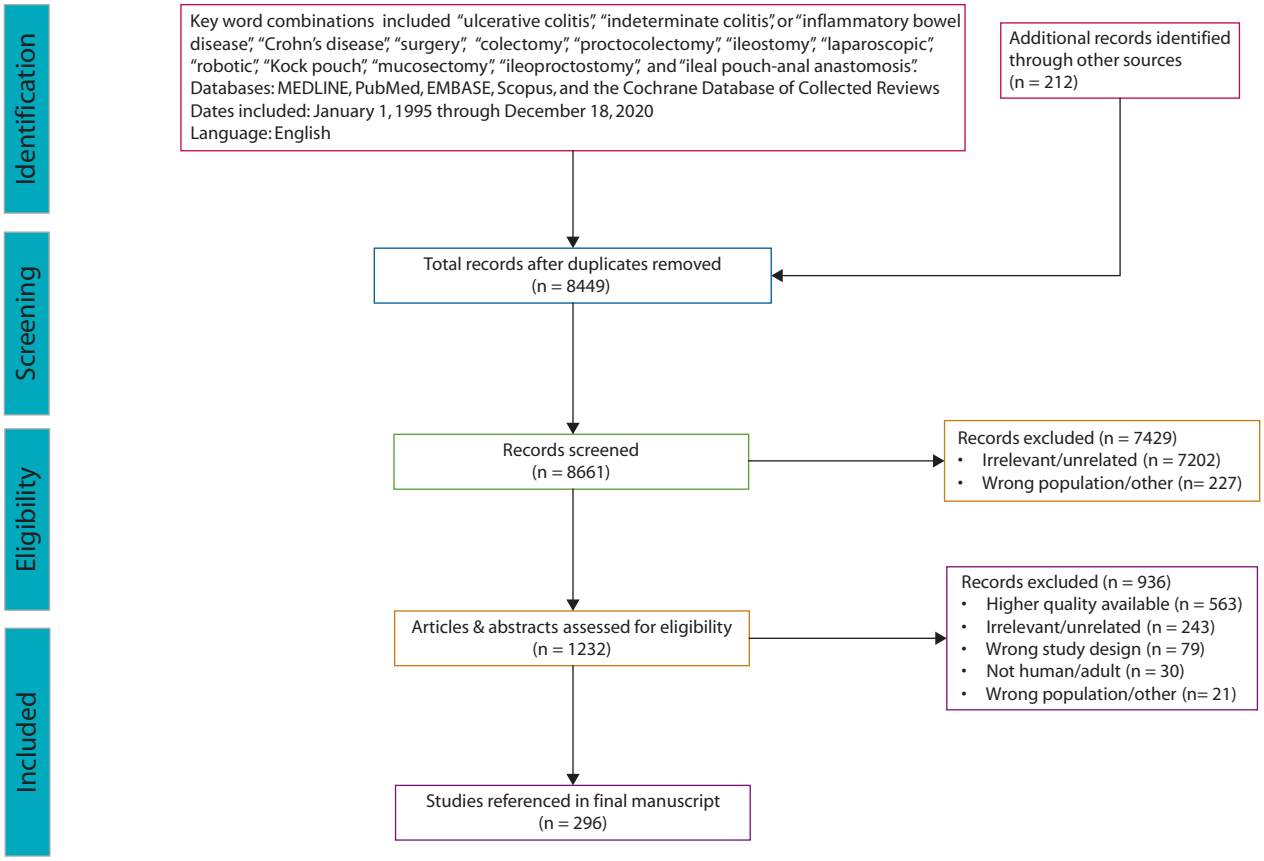

FIGURE 1. PRISMA literature search flow sheet.

College of Gastroenterology guidelines proposed using a modified and more comprehensive version of the Truelove and Witts criteria that incorporated inflammatory markers including fecal calprotectin and endoscopic disease assessment.[1] When patients clinically deteriorate or have increased endoscopic disease severity, escalation of medical therapy may be needed, and utilizing a disease severity index allows for serial evaluations over time and can facilitate evolving treatment approaches. Outpatient management of UC in conjunction with gastroenterology is beyond the scope of this guideline but is reviewed in other guidelines.[1,29]

In the in-patient setting, it can be difficult to predict which patients should continue with escalation of medical therapy and which should undergo surgical intervention. Individualized assessment and decision making under these circumstances should take into account patient-specific preferences, previous medical therapy including exposure to monoclonal antibodies, and concomitant risk factors for requiring a total abdominal colectomy including age at diagnosis of less than 40 years, extensive colitis, severe endoscopic disease with spontaneous bleeding and deep ulcerations, previous hospitalization for colitis, elevated C-reactive protein or erythrocyte sedimentation rate, and low serum albumin.[30–32]

In hospitalized patients with a UC flare, intravenous methylprednisolone 40 to 60 mg daily is typically recommended as first-line therapy.[1] In general, these patients should be continued on a diet, as tolerated, because bowel rest while on intravenous corticosteroids has shown no added benefit in 2 randomized, controlled trials,[33,34] prophylaxis against thromboembolism should be initiated, and plain films should be obtained, as needed, to assess for toxic megacolon. Meanwhile, patients under these circumstances typically undergo endoscopy to assess disease severity and are tested for cytomegalovirus and *Clostridioides difficile*. Patients with UC receiving medical therapy in this setting are monitored for signs of a clinical response, including decreased stool frequency and hematochezia, a downward trend in serum C-reactive protein, and a general improvement in their overall condition.[35,36] More recently, fecal calprotectin has been used to monitor disease activity and has gained acceptance as a surrogate for mucosal healing.[1] If there is insufficient improvement in the 3 to 5 days after initiation of corticosteroids, intravenous infliximab at a dose of 5 to 10 mg/kg or intravenous cyclosporine is typically considered as "rescue therapy."[1] Both infliximab and cyclosporine have a mean response time of approximately 5 to 7 days in randomized, controlled trials; close observation during

TABLE 1. The GRADE System: grading recommendations

	Description	*Benefit versus risk and burdens*	*Methodologic quality of supporting evidence*	*Implications*
1A	Strong recommendation, High-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Strong recommendation, Moderate-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C	Strong recommendation, Low- or very-low-quality evidence	Benefits clearly outweigh risk and burdens or vice versa	Observational studies or case series	Strong recommendation but may change when higher-quality evidence becomes available
2A	Weak recommendation, High-quality evidence	Benefits closely balanced with risks and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B	Weak recommendations, Moderate-quality evidence	Benefits closely balanced with risks and burdens	RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C	Weak recommendation, Low- or very-low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

GRADE = Grades of Recommendation, Assessment, Development, and Evaluation; RCT = randomized controlled trial.
Adapted from Guyatt G, Gutermen D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians Task Force. *Chest*. 2006;129:174–181.[18] Used with permission.

this initial 7-day treatment window is typically recommended with colectomy reserved for patients who do not respond appropriately or clinically worsen during this interval.[27,35–38] A review of standard versus intensive infliximab dosing under these circumstances is beyond the scope of this guideline.

In patients whose condition plateaus after a period of initial improvement, the need and timing for colectomy may be difficult to judge. Second-line infliximab or cyclosporine therapy in corticosteroid nonresponders avoids colectomy in 60% to 80% of patients up to 3 months after the acute episode and in greater than 60% of patients up to 5 years after the acute episode; however, those who avoid a colectomy at their index admission have a high risk of requiring a future colectomy.[37,39–43] In patients treated with a third-line "rescue" therapy (eg, cyclosporine for infliximab nonresponders or infliximab for cyclosporine nonresponders) colectomy-free rates may approach 70% at 3 months and 40% to 60% at 1 year after the acute episode.[44,45] However, the potential risks of using a third-line therapy can be considerable; a systematic review documented that adverse events, serious infection, and death occurred in 23%, 7%, and 1% of patients treated with this approach.[46] In particular, persistent colonic distention under these circumstances characterizes a subgroup of patients who typically respond poorly to further medical therapy and are at increased risk for developing toxic megacolon. Prolonged nonoperative care of these patients can exhaust their physiological reserve and risks increased morbidity including colonic perforation.[45,47] Other biologics (eg, vedolizumab, ustekinumab) and the janus kinase (JAK) inhibitor, tofacitinib, have not yet been adequately evaluated in acute, severe UC requiring hospitalization; however, small case series regarding tofacitinib and ustekinumab support their use under these circumstances.[48,49]

When escalating the medical care of hospitalized patients with UC, early surgical consultation should be considered to optimize patient education and position surgery as a relevant treatment option when there has been an insufficient response to the escalation of medical therapy. This approach also allows for the longitudinal surgical evaluation of a patient's clinical course and ongoing discussion and coordination with the treating gastroenterology team. Consensus statements recommend surgical consultation for hospitalized patients with UC who do not show signs of improvement within 72 hours of initiating intravenous corticosteroids or rescue therapy, because early operative intervention has been associated with decreased postcolectomy complications.[35,36,50–53] Additional considerations include early involvement of an enterostomal therapist to facilitate stoma education, establish perioperative ostomy care, appropriately mark the anticipated stoma location, and alleviate patients' anxiety.[45,54]

2. **Patients with severe medically refractory UC, fulminant colitis, toxic megacolon, or colonic perforation should typically undergo total abdominal colectomy with end ileostomy. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.**

Acutely worsening patients are at risk for developing fulminant colitis or toxic megacolon. Fulminant colitis represents a severe form of acute colitis that may involve more than 10 bloody stools per day, bleeding, a blood transfusion requirement, an erythrocyte sedimentation rate >30 mm/h, fever, tachycardia, and abdominal pain and distension.[36,55] Radiographic findings under these circumstances can include colonic dilation and a thick, edematous colon wall with thumb printing.[36,56] Meanwhile, toxic megacolon, an extreme form of colitis, is usually associated with a thin colon wall and total or segmental colonic dilation (diameter ≥5.5 cm) without a mechanical obstruction but with systemic toxicity.[57]

In practice, in the setting of severe, medically refractory UC, fulminant colitis, or toxic megacolon, clinical deterioration and typical signs of impending or contained (ie, sealed) perforation or peritonitis may be masked by ongoing immunosuppressive medical therapy.[58,59] In a retrospective study of 89 patients who have IBD with fulminant colitis (n = 72; 81%) and toxic colitis (n = 17; 19%) who required colectomy, 14 (16%) had a colon perforation identified either immediately before or during surgery, most often in the cecum or distal third of the transverse colon.[55] Given that mortality rates increase with longer intervals between colonic perforation and surgical intervention, especially in the setting of multisystem organ failure, fulminant colitis or toxic megacolon should prompt urgent total abdominal colectomy with end ileostomy.[58,60–64] A proctectomy is usually avoided under these circumstances,[65,66] and, given the concerns for developing a rectal stump dehiscence, a variety of maneuvers can be utilized, such as implanting the rectal stump in the subcutaneous tissues, creating a mucous fistula instead of a rectal stump, or decompressing the rectal stump transanally via a rectal tube.[67]

3. **A staged approach for an IPAA should typically be considered in patients being treated with high-dose corticosteroids or monoclonal antibodies. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.**

Although the efficacy of corticosteroids for the treatment of acute and refractory UC has been well established, preoperative exposure to corticosteroids is associated with adverse postoperative outcomes.[28,68–71] Preoperative high-dose corticosteroids, defined as >20 mg of prednisone equivalents per day, are associated with significantly increased postoperative infectious complications, although the duration of high-dose corticosteroid use that predisposes to increased risk is not well defined.[72,73] Recognizing this risk, patients maintained on high-dose corticosteroids should typically undergo total abdominal colectomy and end ileostomy as their initial stage rather than a total proctocolectomy with IPAA to reduce the risk of anastomotic leak and pelvic sepsis, the leading causes of pouch failure.[74–77] After a staged total abdominal colectomy, proctectomy with IPAA should typically be delayed until corticosteroids have been weaned because of the increased risk of anastomotic leak and pelvic sepsis related to these medications.[77]

Meanwhile, immunomodulators (eg, 6-mercaptupurine, azathioprine, and methotrexate), originally used as monotherapy for maintenance of remission before the era of biologic therapy and now used in conjunction with biologics to reduce immunogenicity primarily associated with anti-tumor necrosis factor (TNF) agents, have not been associated with increased postoperative complications according to single-center series and systematic reviews.[78–83] The decision to perform a proctocolectomy and IPAA in a staged fashion should not typically be influenced by immunomodulator exposure.

The relationship between monoclonal antibody therapy and adverse postoperative outcomes in the setting of UC remains controversial.[82–89] Most studies show no significant association between the use of preoperative anti-TNF therapy and postoperative complications.[86,87,90–97] However, the 2 largest, single-center series evaluating preoperative exposure to anti-TNF therapy at the time of IPAA showed significantly increased rates of anastomotic leak and pelvic sepsis with anti-TNF exposure.[86,87] Similarly, the largest, relevant meta-analysis of patients with UC showed a significantly increased risk of both early complications after IPAA (OR, 4.12; 95% CI, 2.37–7.15) and late (postileostomy closure) complications (OR, 2.27; 95% CI, 1.27–4.05) in patients exposed to anti-TNF therapy before undergoing IPAA.[98] In addition, a large, retrospective review using data from an insurance claims database found significantly increased rates of postoperative complications following IPAA in the setting of preoperative exposure to anti-TNF therapy.[99] However, in contrast, the largest prospective study to date (the PUCCINI trial presented at Digestive Disease Week, San Diego, CA, in 2019) did not show any association between monoclonal antibodies or their associated drug levels and adverse postoperative outcomes.[100] Likewise, a prospective study of preoperative serum anti-TNF drug levels from 94 consecutive patients with UC found no association between increased serum drug levels and adverse outcomes after surgery.[101]

As with anti-TNF medications, the literature remains controversial regarding whether preoperative exposure to newer classes of monoclonal antibodies or small-molecule inhibitors influences postoperative outcomes. Two single-center, retrospective series reported no significant

increases in post-IPAA complications after preoperative exposure to vedolizumab, but a multicenter, retrospective review including both patients with UC and with Crohn's disease reported significantly increased rates of infectious complications after abdominal operations in patients exposed to vedolizumab compared with patients exposed to anti-TNF medication.[97,102,103] Ustekinumab, an anti-interleukin approved for UC treatment in 2019, has not yet been studied with regard to postoperative outcomes in patients with UC. Tofacitinib, approved for UC treatment in 2018, has also not yet been evaluated regarding postoperative outcomes. Recognizing the ongoing controversy, it is possible that a staged approach to proctocolectomy and IPAA in the setting of monoclonal antibody therapy may mitigate the risk of postoperative pelvic sepsis, especially in patients with additional risk factors such as anemia, poor nutrition, >10% weight loss in the 6 months before the operation, or a BMI <18 kg/m^2.[104]

ULCERATIVE COLITIS-ASSOCIATED COLORECTAL NEOPLASIA

4. **Patients with UC should undergo endoscopic surveillance at regular intervals. Chromoendoscopy or high-definition white-light endoscopy is typically recommended for optimal surveillance. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Compared with age-matched controls, patients with UC are at increased risk for developing colorectal cancer (CRC).[105] Risk factors for CRC in patients with UC include younger age at the time of diagnosis of UC, longer duration of disease, increased extent of disease (pancolitis carries a greater risk than proctitis or left-sided disease), severity of disease and inflammation (quiescent disease carries a lower risk), a family history of CRC especially if diagnosed before the age of 50, and the presence of primary sclerosing cholangitis (PSC).[106] However, recent reports suggest that the risk for developing CRC in the setting of UC has been decreasing over time.[107] Previous reports suggested a 2%, 8%, and 18% cumulative risk of CRC 10, 20, and 30 years after the diagnosis of UC, whereas more recent meta-analyses report a cumulative risk of 1%, 3%, and 7%.[108–110]

Given the risk of neoplasia, surveillance colonoscopy for patients with UC is endorsed by multiple societies; however, controversy persists regarding the optimal timing for initiating screening and recommended surveillance intervals.[111] Regardless of the extent of disease at initial diagnosis, patients should undergo a screening colonoscopy within 8 years of the onset of symptoms. The recommended intervals for subsequent surveillance endoscopic examinations are determined by individualized risk assessment and vary by different societies' guidelines.[112–114] Recognizing their significantly increased risk for neoplasia, patients with PSC should begin screening at the time of diagnosis and undergo surveillance annually. The European Crohn's and Colitis Organization recommends that the highest-risk patients, those with PSC or a history of dysplasia or stricture, undergo annual colonoscopy, that intermediate-risk patients with extensive or long-standing colitis or a family history of CRC undergo colonoscopy every 2 to 3 years, and that low-risk patients utilize a 5-year interval. Surveillance colonoscopy should, ideally, be performed when the colonic disease is in remission.[115] Meanwhile, the American Society for Gastrointestinal Endoscopy recommends that patients with PSC, active inflammation, a history of dysplasia or CRC in a first-degree relative, or an anatomic abnormality such as a stricture have annual surveillance colonoscopy and that average-risk patients undergo surveillance colonoscopy every 1 to 3 years.[116,117] Of note, patients with UC who have had a colectomy but have a rectal stump left in situ are at risk of developing neoplasia and should undergo regular proctoscopic surveillance, as well.[118–120]

Surveillance colonoscopy for patients with UC, according to American Society for Gastrointestinal Endoscopy and American Gastroenterological Association guidelines, is typically recommended using high-definition white-light colonoscopy with nontargeted (ie, random) 4-quadrant biopsies (typically taken at 10-cm intervals with a total of ≥32 biopsies) or using chromoendoscopy with targeted biopsies.[112,113,117,121] Early studies suggested that chromoendoscopy was superior to standard white-light endoscopy for detecting adenomas with or without surrounding dysplasia and resulted in improved dysplasia detection with fewer overall biopsies.[116,122–127] However, endoscopy with high-definition white-light platforms has demonstrated similar dysplasia detection during surveillance colonoscopy compared with chromoendoscopy under these circumstances.[1,128,129] In addition, the infrastructure required for widespread adoption of chromoendoscopy surveillance may be a barrier to implementation given the increased endoscopy time and associated expenses typically related to chromoendoscopy and the relatively limited technical expertise available among endoscopists in practice.[130] For these reasons, high-definition white-light colonoscopy or chromoendoscopy can be used for surveillance examinations depending on availability and local expertise.

Meanwhile, because most dysplasia under these circumstances is visible with high-definition colonoscopy, performing surveillance with random biopsies has been called into question; the decision to perform targeted biopsies only or to also obtain random biopsies may be individualized based on risk factors (eg, PSC, previous dysplasia found on random biopsy).[1] A prospective multicenter study of 1000 patients with IBD undergoing surveillance colonoscopy in France from 2009 to 2011 reported 94 patients with dysplasia. The yield of dysplasia found by random biopsies was 0.2% (68 of 31,865 biopsies), but

only 12 of the 94 patients (13%) with dysplasia were diagnosed by random biopsies. Of note, dysplasia found by random biopsies was associated with a personal history of dysplasia, a colon with loss of compliance and folds, and PSC; therefore, this study recommended random biopsies during surveillance colonoscopies for patients with these risk factors.[131] Finally, a recent randomized, controlled trial of 305 patients with IBD from a single center in Sweden undergoing surveillance colonoscopy with both random and targeted biopsies found that high-definition chromoendoscopy was superior to high-definition white-light endoscopy in terms of detecting neoplasia.[132] In this study, colonoscopies with dye-spray chromoendoscopy took an average of 7 minutes longer than the white-light examinations.

5. **Patients with visible polypoid or nonpolypoid dysplasia that is completely excised endoscopically should undergo endoscopic surveillance. Patients with visible dysplasia not amenable to endoscopic excision, invisible dysplasia in the flat mucosa surrounding a visible dysplastic lesion, or colorectal adenocarcinoma should typically undergo total proctocolectomy with or without IPAA. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

In patients with colitis, endoscopic biopsies may be classified as negative for dysplasia, indefinite for dysplasia, low-grade dysplasia (LGD), or high-grade dysplasia (HGD) based on histopathology assessment. In general, pathology determinations under these circumstances should be confirmed by a second appropriately trained pathologist because of high interobserver variability.[112,133] Indefinite dysplasia is addressed in statement 6.

Regarding the grades of dysplasia, LGD and HGD are differentiated based on the distribution of nuclei within the cells of the mucosa; LGD is characterized by nuclei confined to the basal half of the cells, whereas HGD has nuclei located haphazardly throughout the mucosa.[74,78] The terms dysplasia-associated lesion or mass and adenoma-like mass have been replaced with more simplified descriptors of visible or invisible lesions.[134] Visible lesions are described morphologically by the Paris classification as polypoid (eg, pedunculated or sessile) or nonpolypoid (eg, slightly elevated, flat, or depressed) and borders of lesions are classified as distinct or indistinct.[117] Retrospective studies indicate that 64% to 92% of colorectal dysplasia in patients with UC is visible.[135–137] Other noteworthy descriptors include ulceration and features of potential submucosal invasion such as depression and failure to lift with submucosal injection that may be associated with the inability to resect a lesion endoscopically and raise the suspicion for cancer.[138]

The management of dysplasia in patients with UC depends on whether the dysplasia is invisible or visible and whether a visible lesion is completely excised endoscopically.[113,117] Visible dysplastic lesions with LGD or HGD, in colitic or noncolitic mucosa, that are amenable to complete endoscopic resection (ie, dysplasia-free margins), without invisible dysplasia in the flat mucosa immediately adjacent to the polypectomy site or elsewhere in the colon, should be treated with endoscopic excision when appropriate expertise is available.[113,139–141] En bloc removal is preferred over piecemeal polypectomy to allow for histological evaluation regarding the completeness of resection; this may require referral to a center experienced in advanced polypectomy techniques including endoscopic mucosal resection and endoscopic submucosal dissection. Although the success of endoscopic mucosal resection and endoscopic submucosal dissection in the setting of UC has only been demonstrated in small studies, and the long-term efficacy of these techniques with regard to preventing subsequent neoplasia or influencing the need for surgery is unclear, these advanced approaches may facilitate complete endoscopic excision with negative margins.[142–144] At the time of endoscopic excision, depending on the circumstances, a tattoo can be placed adjacent to the polypectomy site to facilitate future surveillance, and biopsies should typically be obtained of the flat mucosa surrounding the site to evaluate for adjacent invisible dysplasia.[112,145]

The recommendation to pursue ongoing surveillance rather than total proctocolectomy for patients with UC who have had a visible dysplastic lesion excised endoscopically is based on the relatively low risk of developing cancer while undergoing surveillance under these circumstances.[146] In studies reported after 2000, the incidence of HGD or cancer diagnosed at surveillance colonoscopy following the removal of a visible dysplastic lesion in patients with UC was 3% to 18% over surveillance periods of 3 to 7 years.[136,137,147–149] In addition, a study of 30 patients with UC who underwent endoscopic excision of a visible dysplastic lesion reported that 48% had recurrent dysplasia, but none were found to have cancer with a mean 4.1 years of follow-up.[140] However, once dysplasia is identified, patients are at a 10-fold increased risk of developing recurrent dysplasia.[138,150] Thus, close endoscopic surveillance with biopsies taken at the prior excision site is recommended within 1 to 6 months and again at 12 months after removal of the index lesion.[138,150] Treatment recommendations for patients with multifocal, visible, nonpolypoid dysplasia that is completely excised endoscopically warrant a multidisciplinary discussion because there is limited evidence to guide practice and the clinical scenarios are often heterogeneous.

For patients with visible dysplastic lesions not amenable to endoscopic excision, invisible dysplasia in the flat mucosa surrounding visible dysplasia, multifocal dysplastic lesions, or confluent inflammatory pseudopolyposis interfering with the ability to adequately perform surveillance colonoscopy, total proctocolectomy is typically recommended because of the associated increased

risk of having or developing CRC.[112,113,146,147] Patients with UC diagnosed with CRC should undergo staging and be discussed in a multidisciplinary team tumor board and are typically recommended to undergo total proctocolectomy. For patients undergoing total proctocolectomy under these circumstances, an oncological resection with appropriate lymph node harvest should be performed to allow for appropriate oncological staging. Patients with UC diagnosed with rectal adenocarcinoma who undergo neoadjuvant radiotherapy should be appropriately counseled that an IPAA in this setting may have worse functional outcomes; however, external beam radiation therapy is not an absolute contraindication to subsequent pouch formation.[111] Further discussion regarding the management of colon cancer and rectal cancer is beyond the scope of these guidelines.

Although total proctocolectomy is most often recommended to remove all at-risk tissue, selected patients with an increased operative risk or poor functional status may benefit from a segmental colectomy depending on the degree and extent of colitis.[151] In a retrospective study of 59 patients with UC with a median age of 73 years, 24 underwent a segmental colectomy (40% had active colitis at operation) and 35 underwent a total proctocolectomy (77% had active colitis at operation, $p = 0.005$) and, over a median follow-up period of 7 years, no patient undergoing segmental colectomy developed metachronous cancer.[152] In another retrospective Swedish study of 51 patients with UC who underwent segmental colectomy (n = 22) or proctocolectomy (n = 29), none of the patients undergoing segmental colectomy developed metachronous CRC at a mean follow-up of 9.4 years, although 10 patients underwent subsequent proctocolectomy for medically refractory UC.[153] Appropriate ongoing endoscopic surveillance of the retained colon and rectum is necessary when a segmental colectomy is performed in these highly selected patients.[118–120]

6. **Patients with visible indefinite dysplasia not amenable to endoscopic excision or invisible indefinite dysplasia should typically undergo medical treatment to achieve mucosal healing and be referred to an experienced endoscopist for repeat colonoscopy using high-definition colonoscopy with chromoendoscopy with targeted and repeat random biopsies within 3 to 12 months. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.**

The term "indefinite dysplasia" usually applies to situations where the pathologist cannot distinguish between dysplastic and nondysplastic atypia because of the presence of inflamed mucosa that can make histological interpretation difficult. When indefinite dysplasia is identified on nontargeted (ie, random) endoscopic biopsies, up to 28% of patients with UC will have dysplasia on subsequent colonoscopy.[113] A retrospective study of 84 patients with IBD with mucosal biopsies indefinite for dysplasia (92% invisible) who underwent subsequent colonoscopy identified LGD in 13% of patients and HGD/CRC in 2% of patients over a median follow-up period of 28 months.[154] In the setting of nontargeted biopsies indefinite for dysplasia, American Gastroenterological Association guidelines recommend medical optimization to promote mucosal healing followed by repeat endoscopic surveillance within 3 to 12 months using high-definition colonoscopy with chromoendoscopy.[113] Patients with indefinite dysplasia who undergo medical therapy and do not achieve sufficient mucosal healing or who have persistent indefinite dysplasia despite mucosal healing warrant a multidisciplinary discussion, because there is limited evidence to guide practice and the clinical scenarios are often heterogeneous.

7. **Patients with invisible dysplasia should typically be referred to an experienced endoscopist for repeat endoscopy using high-definition colonoscopy with chromoendoscopy with targeted and repeat random biopsies within 3 to 6 months. Patients confirmed to have invisible multifocal, low-grade dysplasia or any invisible high-grade dysplasia should typically be considered for total proctocolectomy. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

When nontargeted biopsies reveal LGD or HGD, patients with UC should typically undergo a high-definition colonoscopy with chromoendoscopy by an experienced endoscopist.[1,155] Patients who undergo repeat nontargeted biopsies in this setting and are found to have no invisible dysplasia or unifocal, invisible LGD warrant a multidisciplinary discussion because there is limited evidence to guide practice and the clinical scenarios are often heterogeneous. If repeat nontargeted biopsies reveal multifocal LGD, total proctocolectomy is typically recommended, although the evidence supporting this is limited. A meta-analysis of 671 patients who have UC with LGD found synchronous CRC in 17% of patients and a 6.1% annual rate of dysplasia progression; risk factors for dysplasia progression included invisible dysplasia and multifocal LGD.[146,156] The largest series of LGD, from the Dutch National Pathology Registry, identified 4284 patients with IBD (3064 with UC) with LGD between 1991 and 2010 and found that the cumulative incidence of subsequent advanced neoplasia was 3.6%, 8.5%, 14.4%, and 21.7% after 1, 5, 10, and 15 years. The median time between the diagnosis of LGD and having advanced neoplasia was 3.6 years. In this study, although there was no stratification based on visibility or focality of lesions, repeat colonoscopy demonstrating LGD was associated with an increased risk of progression to CRC.[157] Further supporting the recommendation for colectomy under these circumstances, a single-center series of 172 patients who have UC with

LGD followed for a median of 48 months revealed that 39% had advanced neoplasia at the time of colectomy.[158] Meanwhile, in a retrospective review of 2130 patients with UC who underwent an abdominal colectomy or total proctocolectomy, of the 141 patients who had a pre-colectomy diagnosis of LGD, cancer was identified in only 3 patients (2%) at the time of resection, and of the 1801 patients without a preoperative diagnosis of dysplasia, only 62 patients (3%) were found to have dysplasia in their colectomy specimen.[159]

As with invisible LGD, the management recommendations for patients with invisible HGD are based on reported rates of developing cancer that are highly variable. Although some series report synchronous cancer in 42% to 67% of patients with invisible HGD, a study of 59 patients who had UC with HGD on preoperative colonoscopy revealed LGD, HGD, or cancer in 20 (34%), 3 (5%), and 1 (2%) patients at the time of proctocolectomy.[159] Furthermore, in a 2019 multicenter, retrospective study of 28 patients with HGD only 4 patients (14%) developed colitis-associated cancer over a median follow-up of 15 years.[135] Regardless of the varying rates of developing CRC, if invisible HGD is confirmed at repeat colonoscopy using high-definition colonoscopy with chromoendoscopy, total proctocolectomy is typically recommended.[112,117,138,141] In practice, one should acknowledge that unaccounted variables including duration, severity, and extent of UC, concomitant PSC, as well as biopsy sampling error and interobserver variability among pathologists influence outcomes among patients who have UC with dysplasia. It is important to counsel patients about the potential risks and benefits of continued endoscopic surveillance versus total proctocolectomy in the setting of dysplasia.[136,160]

8. **Endoscopic surveillance should typically be performed after IPAA. Grade of recommendation: Strong recommendation based on low-quality evidence, 1C.**

Retained rectal mucosa near the anal transition zone (ATZ) following IPAA is at risk for developing dysplasia. A mucosectomy with handsewn anastomosis at the time of IPAA does not eliminate this concern because retained islands of at-risk rectal mucosa can persist following a mucosectomy.[161–163] Although the risk of dysplasia in the rectal remnant/ATZ or ileal pouch is low, periodic endoscopic evaluation should typically be performed.[161,164–166] Recommended surveillance intervals vary based on societal guidelines, but a history of neoplasia in the prior proctocolectomy specimen confers the greatest risk of subsequent dysplasia and warrants increased frequency of surveillance.[113,121,138,167] Although examination intervals are not universally accepted, typically, pouchoscopy is performed 1 year after surgery and then every 3 to 5 years thereafter; for patients who had neoplasia at the time of their proctocolectomy, pouchoscopy every 1 to 3 years should be considered.[168] Pouchoscopy is often performed using a more flexible scope (eg, an upper endoscope) to facilitate retroflexion within the pouch.[169] Treatment of neoplasia diagnosed under these circumstances warrants a multidisciplinary discussion because there is limited evidence to guide practice and the clinical scenarios are often heterogeneous.

TECHNICAL AND POSTOPERATIVE CONSIDERATIONS

9. **For patients with UC undergoing restorative total proctocolectomy with IPAA, a 2-stage, 3-stage, or modified 2-stage approach is preferred for most patients. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

The number of stages involved in pouch surgery is influenced by patient factors and surgeon preference.[69,170] Two-stage, 3-stage, and modified 2-stage approaches to IPAA are the most common pouch operations performed.[171] Despite the popularity of monoclonal antibody therapy and the concern regarding IPAA formation in the setting of these medications, the rates of performing a 2-stage versus 3-stage IPAA have not changed significantly in the past decade; nearly 3 quarters of IPAAs are performed with a 2-stage approach.[172,173] The modified 2-stage IPAA (total abdominal colectomy and end ileostomy followed by completion proctectomy and IPAA without a diverting loop ileostomy), increasingly utilized in recent years, is not associated with increased rates of anastomotic leak, pelvic sepsis, or pouch failure compared with the conventional 2-stage IPAA (total proctocolectomy with IPAA and diverting ileostomy followed by ileostomy closure), but this technique has not been directly compared with the 3-stage approach.[74,174–179]

Meanwhile, a retrospective series of 144 patients with medically refractory UC who underwent a 2-stage IPAA (n = 116) or 3-stage IPAA (n = 28) over an 11-year period suggested an overuse of the 3-stage approach.[172] In this study, perioperative complications were significantly influenced by surgeon experience (high-volume surgeons were defined as having performed ≥50 IPAAs) and not by emergent operative status or preoperative exposure to corticosteroids or anti-TNF therapy. The authors reported that a 2-stage IPAA was not associated with an increased risk of anastomotic leak or pouch failure.[172] Another series of 212 patients with IPAA compared a 2-stage (n = 157) with a 3-stage (n = 55) IPAA and found no differences in postoperative complications, including rates of anastomotic leak, pouchitis, or pouch failure. Of note, there were no differences in the preoperative exposure to corticosteroids or monoclonal antibodies between the 2 groups.[173] On the other hand, 2 multicenter studies found improved postoperative outcomes with a 3-stage approach.[180–183] In practice, it is important to individualize treatment in these cases and consider disease severity, preoperative exposure

to immunomodulators, comorbidities, the presence of anemia, and nutritional status in addition to intraoperative factors such as tension across the pouch anastomosis and surgeon preference.[159] Although the preferred staged approach remains controversial, with the ever-expanding armamentarium of immunomodulatory agents used to treat these patients, a 3-stage IPAA should typically be considered to minimize postoperative morbidity.[180,181]

Regardless of the particular staged approach utilized, laparoscopic or robotic approaches for IPAA are preferred when expertise is available due to reported improved short-term outcomes, including shorter length of hospital stay, reduced intraoperative blood loss, decreased wound infection rates, improved cosmesis, and equivalent long-term functional outcomes and overall pouch failure rates.[184–190] In terms of other minimally invasive techniques, the recently introduced transanal approach to restorative proctectomy has been shown to be safe and feasible in early studies and has demonstrated long-term functional outcomes and quality-of-life scores equivalent to conventional approaches in 2 multicenter comparative series.[191–194]

10. **Total proctocolectomy with IPAA, end ileostomy, or continent ileostomy are acceptable options for patients with UC undergoing elective surgery. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Total proctocolectomy with IPAA has become the most commonly performed operative intervention for patients with UC and is associated with an acceptable morbidity rate (19%–27%), an extremely low mortality rate (<0.5%), and a quality of life that approaches that of the healthy population.[195–203] When appropriate, a minimally invasive approach should typically be considered because of the associated reduced length of hospital stay and improved short-term outcomes, cosmesis, and fertility.[185,187,204–214] Pouch surgery often utilizes a J-type configuration because of its ease of construction and relatively predictable emptying. J pouches are associated with fewer evacuation difficulties compared with S-type pouches (especially an S pouch with a longer spout), but an S-pouch construction may be particularly useful when additional length is needed for a tension-free IPAA.[215,216] In terms of technique, a stapled anastomosis is typically preferred over a mucosectomy with handsewn anastomosis, because the data suggest improved bowel function and symptom-specific quality-of-life metrics with this approach.[217–219]

Although restorative procedures have been popularized, an IPAA may not be suitable for all patients. Advanced age, significant medical comorbidities, underlying bowel dysfunction, and obesity should be considered to optimize IPAA functional outcomes. Appropriately selected older patients without fecal incontinence may safely undergo IPAA because chronological age alone does not significantly affect short-term postoperative outcomes or long-term functional outcomes; however, medical comorbidities and preexisting impaired function should be considered when counseling these patients regarding pouch surgery.[220–225] Of note, older and aging patients with pouch may experience worsening daytime and nighttime bowel frequency and increased rates of fecal incontinence because the sphincter complex weakens with age.[220,222,226–229]

Obesity, in the setting of pouch surgery, is associated with increased operative times, blood loss, and difficulty in achieving sufficient mesenteric length for a tension-free IPAA; however, obesity is not associated with impaired functional outcomes including incontinence, frequency of bowel movements, and pad usage.[230–233] Preoperative weight loss can potentially improve outcomes and performing a 3-stage IPAA to allow time for weight loss and mesenteric lengthening (which typically occurs after creating an end ileostomy) may be a particularly useful strategy in these patients.[234–236]

Total proctocolectomy with an end ileostomy, an alternative to IPAA,[7,8] is considered a safe, effective, and curative operation with quality-of-life outcomes equivalent to IPAA.[237] This nonrestorative approach may be the preferred operative strategy in patients with fecal incontinence, inadequate access to a bathroom, anorectal disease, barriers to surveillance, or limited physiological reserve secondary to comorbid conditions who may be at risk of pouch failure or poor pouch function.[8,238]

A continent ileostomy (eg, Kock pouch) is a potential option for highly selected patients in whom an IPAA is contraindicated or has failed or in those who otherwise prefer a permanent ileostomy over a restorative procedure. However, although continence is achieved in most patients, these reservoirs have high rates of dysfunction and of needing operative revision or excision.[239–244] In a French series of 49 patients undergoing continent ileostomy with a mean follow-up of 20.5 months, 35% experienced early postoperative complications and 45% developed late complications requiring 50 reoperations.[245] Another retrospective series of 330 patients reported 10- and 20-year continent ileostomy survival rates of 87% and 77%. In this study, at a median 11 years of follow-up, patients had, on average, 3.7 complications and 2.9 revisions and had a median revision-free interval of 14 months.[246]

In terms of another potential option for patients who have UC with a failed pouch, redo pouch surgery may be a viable alternative in certain centers. It is important to counsel patients regarding realistic expectations of redo pouch surgery, because these operations can be complicated by higher rates of pelvic sepsis and pouch failure and increased stool frequency and urgency compared with primary pouch surgery.[247–249] Further discussion regarding redo pouch surgery is beyond the scope of these guidelines.

11. **Total abdominal colectomy with ileorectal anastomosis may be considered in selected patients who have UC with relative rectal sparing. Grade of recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

Total abdominal colectomy with an initial or staged ileorectal anastomosis (IRA) is associated with improved functional outcomes and higher quality-adjusted life-years compared with IPAA and avoids a pelvic dissection which may preserve fertility in women.[250–252] Appropriately selected patients for this technique should have a relatively spared, healthy, and compliant rectum. Patients undergoing IRA should be counseled regarding the potential need for future medical therapy to address proctitis, recognizing that at 5, 10, and 20 years post-IRA, 10%, 24% to 27%, and 40% of these patients undergo completion proctectomy for medically refractory disease.[253–255] In addition, surveillance endoscopy of the retained rectum is necessary because dysplasia and adenocarcinoma in the retained rectum occur in 7%, 12% to 14%, and 24% and 0% to 3%, 2% to 7%, and 9% of patients at 10, 20, and 25 years. Prolonged duration of UC or a personal history of colorectal neoplasia or PSC significantly increases the risk for developing neoplasia in this setting.[253–255] For patients with IRA who develop medically refractory proctitis or rectal neoplasia, conversion from an IRA to IPAA results in pouch retention rates similar to primary IPAA surgery with overall pouch survival of 94% and 92% for primary and secondary pouches.[256]

12. **Patients with UC undergoing proctectomy should be counseled regarding possible effects on fertility, pregnancy, sexual function, and urinary function. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Decreased fertility rates following proctectomy with or without IPAA are thought to be related to postoperative pelvic adhesions related to the pelvic dissection that may cause fallopian tube occlusion.[257–260] Given that total abdominal colectomy with an ileorectal anastomosis, and thus no pelvic dissection, is not usually associated with decreased fertility supports this proposed underlying mechanism of infertility.[207,251] Meta-analyses of patients with UC post-IPAA report increased infertility rates of 26% to 63% compared to 12% to 20% in nonoperative controls.[207,257,261] The use of a minimally invasive approach may help reduce infertility rates in this setting because multicenter data demonstrate that a minimally invasive approach to IPAA is associated with significantly lower rates of infertility and reduced time to conceive compared with open IPAA.[204–207] Regardless of the variable natural conception rates following laparoscopic IPAA (31%–73%) or open IPAA (>50%), there are no significant differences in the cumulative live birth rates after in vitro fertilization between patients with UC (with or without IPAA) and patients without UC.[262,263] However, according to a large retrospective review of patients with UC in the Danish National Patient Registry, patients with a failed IPAA had significantly lower in vitro fertilization success rates compared with all other patients with UC.[264]

Pregnancy after IPAA is not associated with an increased rate of maternal or fetal complications including low fetal birth weight, prolonged duration of labor, delivery-related complications, or need for an unplanned cesarean delivery.[257,265,266] Although pouch dysfunction has been reported during the third trimester of pregnancy, this appears to be transient with function returning to pregestational baseline independent of the mode of delivery.[257,266] Meanwhile, the purported benefit of cesarean delivery to preserve function compared with a vaginal delivery remains controversial, but long-term comparative functional studies by colorectal surgeons suggest that vaginal delivery may compromise post-IPAA function.[267–269] When patients who have a pouch plan a cesarean delivery, it is recommended to consider having surgical expertise available to assist, if necessary.[270]

In terms of other quality-of-life outcomes, early studies reported worse sexual function after IPAA, but more recent literature shows no significant effects on sexual desire, ability to achieve orgasm, or sexual satisfaction.[214,265,271–273] One questionnaire-based study even reported an overall improvement in quality of sexual life likely because of improved overall health status after IPAA.[274] Men with IBD, regardless of surgery, have a higher risk of erectile dysfunction than men without IBD, but IPAA surgery does not appear to significantly impair their sexual function; 10 years after IPAA, abnormal ejaculation has been reported in only 3% of men.[214,273–275] In women, studies report worse sexual function after IPAA with increased vaginal dryness and dyspareunia, but affected quality-of-life scores improve within 12 months of IPAA, suggesting that these findings are transient.[271,272] The use of intramesorectal proctectomy, in an effort to avoid pelvic nerve injury, and laparoscopy does not confer an advantage regarding postoperative sexual function.[214,272]

Similarly, urinary function does not appear to be significantly affected in the immediate postoperative period following IPAA.[257,265] However, rates of urinary urgency, frequency, and incontinence may increase over time in women after IPAA.[257,265]

13. **Pouchitis is common after IPAA performed in the setting of UC and is classified according to its responsiveness to antibiotics. Grade of recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Pouchitis is a nonspecific inflammation of the ileal mucosa of the pouch associated with diarrhea, tenesmus, pelvic pain and cramping, blood in the stool, and, occasionally, flu-like symptoms. Pouchitis occurs in up to 40%

of patients with UC post-IPAA and is more common in patients exposed to anti-TNF medications pre-IPAA and in patients with indeterminate colitis or PSC.[276–278] Before treatment, the diagnosis of pouchitis should typically be confirmed by pouchoscopy with biopsies. Endoscopic findings of confluent, erythematous, friable mucosa of the pouch body and histology demonstrating inflammation with a normal afferent limb and ATZ are consistent with a diagnosis of pouchitis.

The most common form of pouchitis is acute, antibiotic-responsive pouchitis that typically responds within 24 hours to oral ciprofloxacin and metronidazole or other alternative antibiotics. Antibiotics are usually prescribed for 10 to 14 days under these circumstances.[279] Chronic pouchitis is less common and is classified as either antibiotic dependent or antibiotic refractory.[280] Antibiotic-dependent pouchitis may be treated with a single agent continuously or with rotating antibiotics.[276] Antibiotic-refractory pouchitis typically necessitates an evaluation for underlying Crohn's disease or other inflammatory disorders of the pouch and referral to gastroenterology for management and treatment (eg, monoclonal antibody therapy). For antibiotic-refractory pouchitis, adalimumab did not demonstrate efficacy when studied in a randomized, controlled trial but infliximab, vedolizumab, and ustekinumab have shown limited efficacy in retrospective analyses and may be considered under these circumstances.[279,281–285] Patients who have recurrent, medically refractory pouchitis may require intestinal diversion or pouch excision to manage their symptoms.[286]

POTENTIAL AREAS FOR FUTURE INVESTIGATION

14. **Appendectomy may decrease the need for proctocolectomy related to medically refractory disease. Grade of recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

The idea that appendectomy may be beneficial in patients with medically refractory UC has been evaluated in a few studies. In a prospective study of 30 patients with medically refractory UC who were referred for proctocolectomy, but who instead underwent laparoscopic appendectomy, 9 patients (30%) had a sustained clinical response and 5 patients (17%) experienced endoscopic remission at 12 months. In this study, the degree of appendiceal inflammation was significantly associated with clinical and endoscopic response.[287] In another prospective, multicenter study of 28 patients with medically refractory UC who underwent a laparoscopic appendectomy rather than proctocolectomy, 13 patients (46%) had a clinical response, 5 patients (18%) had endoscopic remission, and 9 patients (32%) required a colectomy or new experimental medical therapy within 12 months of appendectomy.[288]

15. **A "rescue" diverting loop ileostomy can be considered in the setting of worsening, acute, severe UC to potentially avoid an emergent total abdominal colectomy. Grade of recommendation: Weak recommendation based on low-quality evidence, 2C.**

In the 1980s and 1990s, studies regarding creating a diverting loop ileostomy and blowhole colostomy (eg, Turnbull procedure) rather than performing a colectomy to treat severe or fulminant colitis in pregnancy reported high mortality rates of up to 70%.[289,290] However, a more recent retrospective study done in the era of monoclonal antibody therapy found that a "rescue" diverting loop ileostomy for acute, severe, medically refractory colitis was a potential alternative to colectomy in patients who were severely immunocompromised or malnourished. This study of 33 patients with IBD demonstrated that a "rescue" ileostomy did not increase the rate of colon salvage in patients with UC and Crohn's colitis, but was able to convert an emergent colectomy to an elective colectomy, thereby potentially improving outcomes.[291]

16. **Extended postoperative venous thromboembolism prophylaxis should be considered in patients with UC exposed to tofacitinib. Grade of recommendation: Weak recommendation based on low-quality evidence, 2C.**

Tofacitinib was approved in 2018 by the US Food and Drug Administration for the treatment of moderate to severe UC following the OCTAVE 1 and 2 phase III randomized, controlled trials which demonstrated that study patients had improved induction and maintenance of endoscopic remission compared with controls.[292] With a safety profile similar to anti-TNF therapy, the most commonly reported adverse events in the phase III clinical trials were nasopharyngitis, arthralgia, and headache, and less than 5% of patients experienced a serious, nonopportunistic infection.[293,294] However, the US Food and Drug Administration issued a black box warning in July 2019 detailing increased risks of venous thromboembolism and death from pulmonary embolism related to tofacitinib (10 mg twice daily) in patients with rheumatoid arthritis.[295] Although a retrospective analysis evaluating tofacitinib in the setting of UC did not show a higher rate of thromboembolic events than placebo, patients with UC undergoing major abdominopelvic surgery are already at increased risk of postoperative venous thromboembolism.[13,296] Thus, patients with UC exposed to tofacitinib preoperatively may benefit from extended postoperative thromboprophylaxis.

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