

# Practice Parameters for the Surgical Treatment of Ulcerative Colitis

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## STATEMENT OF THE PROBLEM

Ulcerative colitis (UC) is characterized by a chronic inflammatory condition that affects the rectum and extends proximally into the colon for varying distances. Although many patients are treated effectively by a wide variety of medications, approximately 15% to 30% of patients will require or elect operative intervention. Surgical indications vary from acute colitis to malignancy and often have a dramatic impact on morbidity, mortality, and quality of life.<sup>1,2</sup> Failure to respond to medical therapy (ie, intractability) remains

the most common surgical indication for UC. Whether it is secondary to an inability to control symptoms, poor quality of life, risks/side effects of chronic medical therapy (especially long-term corticosteroids), noncompliance, or growth failure, patients may opt for surgery in the elective or semielective setting.<sup>3</sup> Complete removal of all the potential disease-bearing tissue is theoretically curative in UC. Operative options include an abdominal colectomy or total proctocolectomy with either a permanent end ileostomy or surgical construction of a “new” rectum through an IPAA that restores GI continuity.<sup>4,5</sup> All these procedures may be performed by using open or minimally invasive techniques.<sup>6,7</sup> Although various treatment options are available for UC, this parameter will focus on the surgical management for the patient with UC.

## METHODOLOGY

These guidelines are built on the last set of the American Society of Colon and Rectal Surgeons Practice Parameters for treatment of UC published in 2005.<sup>8</sup> An organized search of Medline, PubMed, and the Cochrane Database of Collected Reviews was performed through July 2013. Keyword combinations included inflammatory bowel disease, ulcerative colitis, ileal pouch-anal anastomosis, ileostomy, proctocolectomy, colorectal neoplasm, surgery, colectomy, ileoproctostomy, immunomodulator, infliximab, steroids, and related articles. Directed searches of the embedded references from the primary articles also were accomplished. The final grade of recommendation was performed using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system (Table 1).<sup>9</sup>

## INDICATIONS FOR SURGERY

### Acute Colitis

1. Patients with clinical evidence of actual or impending perforation should undergo urgent surgery. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

**TABLE 1.** The GRADE system-grading recommendations

|    | Description                                              | Benefit vs risk and burdens                                                                                   | Methodological 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, methodological 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, methodological 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, Guterma 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. Used with permission.

The diagnosis of *severe* colitis is based on the criteria of Truelove and Witts<sup>10</sup> and is defined as colitis with more than 6 bloody stools per day, fever (temperature, >37.5°C), tachycardia (heart rate, >90 beats per minute), anemia (hemoglobin, <75% of normal), and elevated sedimentation rate (>30 mm/h).<sup>11</sup> *Toxic or fulminant* colitis is characterized by more than 10 bloody stools per day, fever (>37.5°C), tachycardia (>90 beats per minute), anemia requiring transfusion, elevated sedimentation rate (>30 mm), colonic dilation on radiography, and abdominal distention with tenderness.<sup>11</sup> When the colonic distention of the transverse colon exceeds 6 cm, the diagnosis becomes *toxic megacolon*.<sup>12,13</sup> Surgery is required in 20% to 30% of patients with toxic colitis, and typically consists of a subtotal colectomy with end ileostomy.<sup>14,15</sup>

Perforation in patients with toxic colitis is associated with a high mortality rate (27%–57%), regardless of whether the perforation is contained or free.<sup>16,17</sup> The mortality rate also increases as the time interval between perforation and surgery increases.<sup>16,18</sup> Signs of impending perforation may be masked by ongoing medical therapy. Persistent or increasing colonic dilation, pneumatosis coli, worsening local peritonitis, and the development of multiple organ failure can be signs of impending or ac-

tual perforation.<sup>17,19,20</sup> Likewise, localized peritonitis may reflect local inflammation or may be a sign of impending perforation.<sup>21</sup> Perforation may also occur without dilation; these patients often do not exhibit classic signs of peritonitis.<sup>16</sup>

The development of multisystem organ failure (MSOF) is an ominous sign. In a series of 180 patients with toxic colitis, 11 (6%) developed MSOF. The overall mortality in the entire group was 6.7%; however, of the 12 patient deaths, 8 occurred in patients with MSOF.<sup>22</sup>

**2. For patients with moderate to severe colitis, early surgical consultation should be obtained. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Although most physicians agree that an urgent surgical consultation should be obtained in patients with sepsis or fulminant/toxic colitis, there is no high-quality literature depicting the appropriate timing for surgical consultation in patients with a lesser degree of disease. Recent consensus statements from surgical and gastroenterology experts have suggested that a failure of primary therapy or those patients being considered for monoclonal antibody or cyclosporine therapy warrant surgical consultation.<sup>23</sup> It

is important to keep in mind that, even in those patients who have a good initial response to medical therapy, the eventual need for colectomy ranges from 20% to 80%.<sup>24–27</sup> Early involvement of the surgeon is important to not only follow the patient's clinical course, but also to provide information and answer questions should the need for surgical therapy eventually arise. This is best performed in an elective setting rather than urgently in a patient who has perforated or is clinically deteriorating. Concomitant involvement of an enterostomal therapist is also valuable in providing education and perioperative ostomy marking should the need arise.<sup>28,29</sup>

**3. Patients whose condition worsens on medical therapy or who do not make significant improvement after a period of 48 to 96 hours of appropriate medical therapy should be considered for either a second-line agent or surgery. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Medical therapy is considered to have failed in patients if their condition worsens while on medical therapy, or if they do not improve after a period of initial stabilization. Monoclonal antibody therapy (eg, infliximab, adalimumab) has demonstrated effectiveness for rescue therapy for hospitalized patients.<sup>30–32</sup> The short-term response rate, defined as avoidance of colectomy *and* cessation of corticosteroids, is ~25% (range, 20%–90%). The ability to avoid colectomy following an acute episode in the short term for patients refractory to steroids has been reported in up to 90%,<sup>33</sup> although the impact of infliximab for rescue therapy is still evolving. Concerns about using biological agents are related to the large percentage of patients who ultimately require colectomy, and safety issues that are primarily infectious complications.<sup>33–38</sup> Limited evidence suggests that intravenous cyclosporine is more effective than standard steroid-based treatment for severe colitis<sup>39–41</sup> and has been advocated as a second-line agent before colectomy, in part, secondary to its rapid onset of action and short half-life.<sup>42</sup> Sequential “rescue” therapy with either monoclonal antibody therapy or cyclosporine following failure of the other has been associated with poor outcomes and is generally not recommended.<sup>43–45</sup>

The need for and timing of surgery in patients whose condition seems to “plateau” after a period of initial improvement often is difficult to judge. Patients with more than 8 stools per day, or 3 to 8 stools and a C-reactive protein > 45 mg/mL after 3 days of therapy, have an 85% chance of requiring colectomy during the same hospitalization, regardless of whether corticosteroid or cyclosporine treatment is used.<sup>46</sup> Patients who have a contraindication to (or do not desire) monoclonal antibody or cyclosporine therapy, or when steroids fail, should be considered for surgery. Furthermore, persistent colonic distention seems to characterize a subgroup of patients who respond

poorly to medical therapy and are at increased risk for the development of megacolon.<sup>47</sup> Prolonged observation of these patients may risk exhaustion of their physiological reserve, but does not necessarily increase perioperative morbidity outside of a perforation.<sup>15</sup> Most series define a period of 48 to 96 hours after which surgery is indicated if the patient does not improve or worsens,<sup>14,18,19</sup> although evidence specifying the most appropriate time period for a trial of medical therapy, especially with “second-line” agents, is lacking.

**4. A decision regarding the response to second-line or “rescue” therapy should be made within 5 to 7 days after initiation. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Both cyclosporine and monoclonal antibody therapy have been shown to have mean response times of 5 to 7 days in controlled trials.<sup>31,39,40</sup> Population-based data evaluating timing of colectomy in UC have also demonstrated that mortality rates increase as operative timing progresses from within 3 to 6 days (OR, 2.12; 95% CI, 1.13–3.97) and 11 days (OR, 2.89; 95% CI, 1.41–5.91).<sup>48</sup> Longer waiting times may result in worsening physiological reserve, further depletion in nutrition stores, and an inappropriate delay in surgery with no apparent gain.<sup>49</sup>

### Intractability

**1. Surgery is indicated in chronic UC when medical therapy is ineffective. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Intractability is one of the most common surgical indications for UC. Symptoms may be insufficiently controlled, despite an intensive medical regimen, and the patient is unable to achieve an acceptable quality of life. Alternatively, the response to treatment may be adequate, but the risks of chronic medical therapy may be excessive. Additionally, patients who are unable to tolerate the deleterious side effects of medical therapy and those patients who are noncompliant with treatment regimens may be candidates for surgical management.

Disabling extraintestinal manifestations of UC may prompt resection. Typically, episcleritis, erythema nodosum, aphthous ulcerations, and large joint arthropathy are more likely to be responsive to colectomy. Hepatic, vascular, hematologic, cardiopulmonary, and neurological comorbidities typically are not. Finally, growth failure in children is another form of intractability that may require colectomy. Surgery should be considered if growth failure persists despite maximal nutritional and medical therapy, with data reporting that surgical resection is at least as effective as immunosuppressants for allowing “catch-up” in growth status.<sup>50–52</sup>

## Cancer Risk and Surveillance

1. **Patients with long-standing UC should undergo endoscopic surveillance. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Surveillance recommendations in UC are based on patient risk factors, current literature, and expert panel consensus with the goal of early detection of premalignant and malignant lesions, along with decreasing mortality. Risk factors associated with the development of malignancy include the extent of colonic disease, pancolitis (proximal to the splenic flexure) greater than left-sided colitis, and prolonged disease duration (>8 years with pancolitis).<sup>53,54</sup> Consensus evidence also remains that a diagnosis of UC at a younger age is associated with an increased risk of colorectal cancer.<sup>53</sup> Additional risk factors include family history of IBD<sup>55</sup> and concomitant primary sclerosing cholangitis.<sup>56–58</sup> Although a meta-analysis demonstrated the cumulative risk of colorectal cancer for UC patients to be 2.1% at 10 years, 8.5% at 20 years, and 17.8% at 30 years,<sup>59</sup> population-based series have reported lower annual incidence rates of 0.06% to 0.2%.<sup>60,61</sup> Despite this, it is generally accepted that chronic UC is associated with an increased risk of malignancy.

Surveillance colonoscopy is recommended for these patients, even though data supporting a survival benefit are lacking. A Cochrane update reported that there is “no clear evidence” that surveillance colonoscopy is associated with longer survival in patients with extensive colitis (relative risk, 0.81; 95% CI, 0.17–3.83).<sup>62</sup> The authors did note that cancers are generally detected at an earlier stage in those undergoing regular surveillance endoscopy, with a corresponding associated overall better prognosis.

Patients with extensive colitis (disease proximal to the splenic flexure) should be advised to undergo endoscopy after 8 years of disease and should have a surveillance colonoscopy performed every 1 to 2 years. This interval will depend on the presence or absence of dysplasia in biopsy specimens (see below). Previous recommendations based on expert opinion suggest that, for patients with left-sided disease (disease distal to the splenic flexure yet proximal to the rectum), the same surveillance programs may begin after 15 years of the disease;<sup>63–66</sup> however, recent American Gastroenterological Association guidelines suggest that the evidence is not strong enough to recommend different surveillance intervals.<sup>67</sup> Patients with 2 successive negative surveillance colonoscopies may undergo surveillance colonoscopy at 1 to 3 years, although this should be tailored to the patient.<sup>63</sup> There are additional data to indicate that patients with concomitant primary sclerosing cholangitis are at an even higher risk for malignancy, with a cumulative risk of cancer or dysplasia approaching 50% at 25 years of disease.<sup>58</sup> Therefore, it is recommended that these patients adhere to annual surveillance endoscopy regardless of previous normal findings.

2. **Endoscopic surveillance should involve 2 sets of 4-quadrant random biopsies at ~10-cm intervals throughout the colon and rectum, along with directed biopsies of suspicious lesions. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Recommendations vary slightly based on society and expert opinion.<sup>66–69</sup> The recommended surveillance endoscopy technique normally involves 2 sets of 4-quadrant biopsies in each colon segment (right, transverse, left, rectosigmoid), producing ~32 random biopsies divided into 4 specimen cups. A minimum of 32 random biopsies has been shown to result in an 80% to 90% sensitivity for detecting dysplasia.<sup>70,71</sup> Directed biopsies of polypoid lesions, masses, strictures, or irregular mucosa distinct from surrounding inflammation should also be performed.<sup>72,73</sup> Additionally, adjacent “normal”-appearing tissue, when present, should be sent for comparison. Polyps that appear potentially dysplastic can be removed by polypectomy, and the adjacent flat mucosa also should be biopsied to exclude dysplasia.

In an attempt to aid in identifying more subtle, flat, dysplastic lesions, targeted biopsies with the use of magnification chromoendoscopy have been described. In this technique, a stain/dye such as indigo carmine or methylene blue is applied throughout the entire colon and rectum to enhance mucosal changes that are less well visualized by standard techniques.<sup>74</sup> This may be combined with advanced imaging capabilities including narrow-band imaging and confocal laser endomicroscopy to further augment visualization of dysplastic areas.<sup>75</sup> A small number of prospective studies have demonstrated significant improvement in intraepithelial neoplasia detection over conventional light endoscopy.<sup>76–78</sup> Although this promising development may be considered, further widespread availability and collective experience outside of select centers is required before generalized recommendations.

3. **Total proctocolectomy, with or without IPAA, is recommended for patients with carcinoma, non-adenoma-like dysplasia-associated lesion or mass, or high-grade dysplasia. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Malignancy in UC patients is felt to be secondary to similar genetic mutations responsible for sporadic colon cancer in the general population, as well as persistent inflammation resulting in cell proliferation, oxidative stress, and, ultimately, dysplasia.<sup>79,80</sup> Unlike sporadic cases, cancer in UC patients may not always follow a progression from normal epithelium to low-grade dysplasia, high-grade dysplasia, and finally invasive malignancy. Nevertheless, dysplasia detection by conventional histopathologic assessment of colonoscopic biopsies remains the criterion standard to identify patients at highest risk of developing cancer in UC.<sup>81</sup> Consideration should be made for all biopsies con-

cerning for high-grade dysplasia to be confirmed by 2 independent GI pathologists when possible.

Findings of colorectal cancer, a *nonadenoma* dysplasia-associated lesion or mass (DALM), or high-grade dysplasia are almost uniformly accepted as indications for proctocolectomy<sup>82</sup> with or without IPAA, because approximately 43% to 50% will have concomitant malignancy at the time of colectomy.<sup>82–85</sup> In a classic study evaluating 10 prospective cohorts including 1225 patients undergoing surveillance colonoscopy, 10 of 24 patients (42%) found to have high-grade dysplasia who underwent immediate colectomy were found to have a synchronous cancer.<sup>82</sup>

*Adenoma-like* DALM may occur in areas outside of colitis and may be successfully treated via endoscopic polypectomy similar to sporadic adenomas.<sup>86–89</sup> Recent studies suggest that adenoma-like DALM located within regions of active inflammation may also be removed endoscopically with the avoidance of colectomy, given a complete resection and no evidence of adjacent flat dysplasia or adenocarcinoma.<sup>90</sup> However, when the polypectomy base or surrounding mucosa does contain dysplasia, patients should undergo surgical resection.<sup>91</sup>

**4. Total proctocolectomy, or surveillance endoscopy, is recommended for patients with UC and low-grade dysplasia. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1C.**

The management of unifocal, flat, low-grade dysplasia in the setting of UC remains controversial. Reported progression rates to high-grade dysplasia range widely from 0% to 53%.<sup>92–95</sup> A recent meta-analysis including 20 colonoscopic surveillance studies and 508 patients with flat low-grade dysplasia with DALM, reported a 9-fold risk of developing cancer (OR, 9.0; 95% CI, 4–20.5) and 12-fold risk of developing any advanced lesion (OR, 11.9; 95% CI, 5.2–27).<sup>96</sup> Bernstein et al<sup>82</sup> confirmed the risk of cancer in the setting of low-grade dysplasia as 19%; however, in up to 29% of the patients they followed, untreated low-grade dysplasia went on to develop a DALM, high-grade dysplasia, or cancer, prompting the authors to recommend immediate colectomy for these patients.

In a conflicting study, 60 patients with low-grade dysplasia in flat mucosa identified during endoscopy were followed for an average of 10 years; low-grade dysplasia was seen at several locations and, during repeated colonoscopies, in 73% of cases. However, progression to high-grade dysplasia or a dysplasia-associated lesion/mass occurred in only 11 patients (18%).<sup>92</sup> Although high rates of interobserver variation between histopathologists confound the findings and recommendations,<sup>94,97–99</sup> it is important that patients are counseled about the potential risks and benefits of continued endoscopic surveillance versus surgical therapy.<sup>100</sup>

Patients may benefit from chemoprevention with 5-aminosalicylate (5-ASA), but there are few prospective

data evaluating this topic. A recent meta-analysis of 9 observational studies reported a reduced risk of developing colorectal carcinoma or dysplasia with 5-ASA use (OR, 0.51; 95% CI, 0.38–0.69).<sup>101</sup> Case-control series have demonstrated a significant risk reduction (OR range, 0.19–0.60, all  $p < 0.05$ ) for both dysplasia and colorectal cancer in patients using 5-ASA compounds.<sup>97,102,103</sup> Other large population-based and case-control studies have not found a protective effect with regular 5-ASA exposure.<sup>104,105</sup> Nevertheless, the side effects of these medications should be compared with the potential for reducing malignancy when counseling patients.

**5. Patients with UC who develop a stricture, especially with long-standing disease, should typically undergo resection. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Among the most common manifestations of colorectal carcinoma in chronic UC are colonic strictures, which develop in 5% to 10% of patients with UC. Although the majority of strictures are benign, as many as 25% will be malignant, and malignant strictures account for up to 30% of cancers occurring in UC patients. Although biopsy may reveal dysplasia or malignancy,<sup>106</sup> a negative biopsy may not be reliable because of the risk of sampling error and the more infiltrative nature of colitis-associated malignancies. Therefore, in general, all patients with strictures should undergo an oncological resection.<sup>107,108</sup>

## SURGICAL OPTIONS

### Emergency

**1. The procedure of choice for emergency surgery in UC is total or subtotal abdominal colectomy with end ileostomy. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

The surgical goals in the acute setting are designed to remove the bulk of the diseased bowel, restore patient health with the greatest reliability and least risk, and preserve reconstructive options after the patient has recovered and medications are withdrawn.<sup>5</sup> Subtotal colectomy with end ileostomy and Hartmann closure of the distal bowel or creation of a mucous fistula is a safe and effective approach.<sup>15,109,110</sup> Although, historically, this has been performed via a laparotomy, multiple reports have confirmed the feasibility and safety of a minimally invasive approach in this setting.<sup>111–113</sup> Extrafascial placement of a closed rectosigmoid stump may be associated with fewer pelvic septic complications and facilitates subsequent pelvic dissection.<sup>114</sup> Transanal drainage of the distal stump may further decrease the risk of pelvic sepsis.<sup>115</sup> The resected colon specimen should be examined microscopically for confirmation of UC or Crohn's disease, because the likelihood

of an altered diagnosis is appreciable after colectomy.<sup>15,113</sup> In patients with confirmed UC, a completion proctectomy and IPAA can often be safely performed at a later date to remove the remaining disease and restore intestinal continuity. Although there are reports of successful outcomes following total proctocolectomy with IPAA in select patients with a “moderate” form of fulminant colitis, in general, this should be avoided.<sup>116,117</sup>

### Elective Surgery

#### 1. Total proctocolectomy with ileostomy is an acceptable surgical option for patients with UC. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Total proctocolectomy with ileostomy has been the conventional operative approach for patients with UC and may be considered a benchmark procedure with which all other operations are compared.<sup>6,7</sup> It is a safe, effective, and curative operation that permits most patients to live a full, active lifestyle.<sup>118</sup> Although restorative proctocolectomy with IPAA has become increasingly popular during the past 3 decades, proctocolectomy with ileostomy can still be considered the first-line procedure for patients who choose not to undergo a restorative proctocolectomy and for those at significant risk for pouch failure, such as patients with impaired anal sphincter muscles, previous anoperineal disease, or limited physiological reserve secondary to comorbid conditions.<sup>119,120</sup> When the expertise is available, minimally invasive surgery can be considered.<sup>121</sup>

Regardless of technique, the operation does have recognized complications. Although stoma-associated problems, such as stenosis and prolapse, are probably the most frequent,<sup>122</sup> other complications that are common to any abdominal/pelvic procedure also have been recognized following this operation.<sup>122,123</sup> These include small-bowel obstruction, infection/fistula, persistent pain, unhealed perineal wound, sexual and bladder dysfunction, and infertility.<sup>124,125</sup> In 1 study of 44 patients, the long-term complication rate of proctocolectomy with permanent ileostomy was significantly lower than restorative proctocolectomy (26% vs 52%).<sup>123</sup> There have also been several recent case reports of carcinoma arising at the ileostomy site, similar to that of the rectal stump, highlighting the need for continued surveillance.<sup>126–129</sup>

#### 2. Total proctocolectomy with IPAA is an appropriate operation for selected patients with UC. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

Total proctocolectomy with IPAA has become the most commonly performed procedure for patients with UC who require elective surgery. The operation, whether performed through an open procedure or, when expertise is

available, by the use of minimally invasive techniques, is relatively safe and durable.<sup>130–135</sup> Ileal pouch-anal anastomosis is associated with an acceptable morbidity rate (19%–27%),<sup>136,137</sup> an extremely low mortality rate (0.2%–0.4%),<sup>136–142</sup> and a quality of life that approaches that of the healthy population.<sup>143–153</sup> When deciding on IPAA, patient selection should consider factors such as baseline continence, ability to undergo major pelvic surgery and its complications, and medical comorbidities.

The complications of the procedure are similar to those of any major abdominal operation, but they also include risks arising from the pelvic dissection, such as infertility or sexual dysfunction, and pouch-specific complications, such as pouchitis. Additionally, anastomotic leak with pelvic sepsis, fistula, stricture, and cuff inflammation may occur. Medical therapies, such as antibiotics, immunomodulators, and biologics, as well as surgery, may be attempted to salvage pouch function and are successful in more than 50% of cases.<sup>154–156</sup>

When comparing the open versus a laparoscopic approach, a 2009 Cochrane review consisting of 11 trials and more than 600 patients found similar length of stay, morbidity, reoperation, readmission, and mortality rates between the 2 approaches.<sup>157</sup> Laparoscopy was associated with improved cosmesis, smaller total incision length, and longer operative times. Comparing 2-stage procedures, retrospective data have demonstrated that laparoscopy is associated with a shorter time to ileostomy closure and restoration of intestinal continuity, likely secondary to decreased adhesion formation.<sup>158</sup> Studies using diagnostic laparoscopy at the time of ileostomy closure have confirmed lower adhesion formation with a minimally invasive approach, whether in the incisional, abdominal, or adnexal location,<sup>159</sup> including >70% with no adnexal adhesions.<sup>160</sup>

The impact of moderate- to high-dose steroids on the incidence of postoperative complications after IPAA is well described.<sup>161</sup> However, the impact of infliximab in this setting is less clear. There is a larger experience with these agents and surgery for Crohn's disease that has not clearly demonstrated a relationship between  $\alpha$ -tumor necrosis factor agents and postoperative complications.<sup>162</sup> Unfortunately, the literature on the impact of these agents in patients with chronic UC undergoing IPAA is limited to retrospective single-institution studies with varying patient numbers with differing procedure mixes and variable definitions of complications.<sup>143,163–168</sup>

Currently, reports regarding the impact of  $\alpha$ -tumor necrosis factor therapy before IPAA on postoperative complications are limited to observational studies, have different patient populations, and lack a consistent definition of complications. Further larger studies, ideally multi-institutional, using standardized procedures and complication definitions will be required to identify any

association with the preoperative use of these agents and poor outcomes after IPAA.

**3. Patients with UC considering pelvic operations should be counseled regarding the potential negative effects on sexual function and fertility. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

Although many studies have shown no difference in fertility in women with UC compared with healthy controls,<sup>169,170</sup> those who undergo surgical treatment for UC have a lower rate of conception compared with their non-surgical counterparts.<sup>144–147,170–172</sup> The results of a meta-analysis indicate a 3-fold increase in infertility in women with UC undergoing surgical therapy, particularly IPAA, compared with either healthy controls or those with UC who do not have surgery.<sup>172</sup> Overall, infertility rates after IPAA range from 38% to 64% compared with only 10% to 38% for nonoperative patients or controls.<sup>144–147,170–172</sup> Furthermore, a greater percentage of women after IPAA require fertility treatments (18% vs 6%).<sup>145,170</sup> Pelvic adhesions and occlusion of the fallopian tubes are the proposed reasons for this difference. This seems to be associated with the rectal resection component and not pouch placement itself, because ileorectal anastomosis in UC has not been associated with decreased fertility.<sup>173</sup>

Rates of postoperative fertility problems are similar between proctocolectomy with IPAA and with end ileostomy following other types of rectal resection such as familial adenomatous polyposis.<sup>174</sup> Yet, in the UC population, the literature has focused more on fertility following IPAA than after total proctocolectomy with end ileostomy. Multicenter data have demonstrated that a minimally invasive approach is associated with significantly lower rates of infertility in comparison with traditional open surgery, citing conception rates of 31% to 73% following a straight laparoscopic IPAA.<sup>175,176</sup> Pregnancy after IPAA is also not associated with an increase in maternal or fetal complications,<sup>144,177</sup> although an increase in stool frequency and pad usage has been reported in the third trimester.<sup>144</sup> Vaginal delivery appears to be safe after IPAA, although this is based on small retrospective series.<sup>144,177–179</sup> Anterior sphincter defects have been reported in up to 50% of women undergoing vaginal delivery, although this does not seem to significantly influence pouch function.<sup>180,181</sup> After delivery, transient anal dysfunction normally resolves<sup>177,182</sup> and pouch function returns to pregestational function within 6 months,<sup>144</sup> independent of the mode of delivery.<sup>183</sup>

Sexual function for both men and women after proctectomy for UC has been variable following surgery, with some reports demonstrating improvement and others deterioration. Several early studies in women noted increased frequency of sexual function, with normal sexual desire, ability to achieve orgasm and minimal sexual dissatisfaction; however, these studies were retrospective and

did not use validated measures.<sup>184–186</sup> There was a clear increase in dyspareunia after surgery ranging from 11% to 22%.<sup>144,185,186</sup> Rates of retrograde ejaculation and erectile dysfunction in men range from 2% to 19% and 0% to 15%.<sup>185–187</sup> The largest retrospective review of sexual function in 1454 men and women after IPAA reported no change in 56%, better function in 25%, and worse function in 19%.<sup>188</sup> More recent studies using validated measures<sup>189,190</sup> have demonstrated that, although men may have improved sexual function, women may have no improvement or even worsening sexual function, especially with IPAA at an early age.<sup>191</sup> Further prospective studies are needed to confirm these findings.

**4. Total proctocolectomy with IPAA may be offered to selected UC patients with concomitant colorectal cancer. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Ulcerative colitis patients with a concomitant carcinoma have postoperative complications and functional results comparable to colitis patients without cancer.<sup>192–198</sup> Nearly 20% of UC patients with cancer who underwent an IPAA subsequently die of metastatic disease.<sup>197</sup> A more conservative management approach has been advocated by some who recommend an abdominal colectomy with ileostomy followed by a restorative proctectomy after an observation period of at least 12 months to better ensure that no recurrent or distant disease develops.<sup>198</sup>

Metastatic disease is generally considered a contraindication to IPAA. These patients are ideally managed with segmental colectomy or abdominal colectomy with anastomosis to facilitate early discharge and allow them to pursue chemotherapy and spend the rest of their lives relatively free of complications relating to extensive surgery. Another group of patients who may not be eligible for IPAA are those with cancer of the mid or low rectum. Performing a standard oncological resection with total mesorectal excision, ensuring adequate margins and sphincter preservation, may allow IPAA construction after completion of adjuvant therapy. Importantly, adjuvant radiotherapy, if indicated, should be performed *preoperatively* whenever possible, because postoperative radiotherapy is associated with a high incidence of pouch loss secondary to radiation enteritis and poor pouch function.<sup>192,194</sup> Ulcerative colitis patients with cecal cancers represent another unique subgroup of patients. If a long segment of adjacent distal ileum with its mesenteric vessels must be sacrificed, difficulties with positioning of the reservoir into the pelvis may ensue, and an ileostomy may be necessary if a tension-free anastomosis cannot be attained.

**5. Total proctocolectomy with IPAA may be offered to selected elderly patients with UC. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Ileal pouch-anal anastomosis in select elderly patients is safe and feasible.<sup>199–203</sup> Chronologic age should not by itself be used as an exclusion criterion. However, careful consideration should be given to underlying comorbidities, as well as the patient's mental status and anal sphincter function. Pouch procedures are feasible in suitably motivated elderly individuals who understand the risks and potential functional difficulties that often accompany this procedure. Although some series have found that bowel frequency remains constant in the first decade after the surgical procedure,<sup>204</sup> others have found that the number of daytime and nighttime stools increases, as does the likelihood of fecal incontinence.<sup>130</sup>

**6. Mucosectomy and double-stapled procedures are both acceptable techniques in most circumstances. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

The potential advantages of the double-stapled approach include enhanced technical ease, because this approach avoids mucosectomy and the perineal phase of the operation, less tension on the anastomotic suture line, and possibly improved functional results.<sup>205</sup> Sphincter injury is minimized<sup>206</sup> and the anal transition zone, with its abundant supply of sensory nerve endings, is preserved. Three prospective, randomized trials and 1 comparative study have demonstrated no significant difference in perioperative complications or functional results for patients in whom a mucosectomy was performed versus those patients in whom the proximal anal canal mucosa was preserved with a double-stapled procedure.<sup>207–210</sup> Whereas the majority of patients undergo a double-stapled procedure, it is important that the surgeon performing an IPAA be familiar with both techniques in the event of failure or the inability to use a surgical stapler.<sup>211</sup>

**7. Pouch configuration may be chosen based on individual surgeon preference. Grade of Recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

Several ileal pouch configurations have been devised in an attempt to reduce pouch complications and improve functional outcome. These include the double-loop J-pouch, the lateral isoperistaltic H-pouch, the triple-loop S-pouch, and the quadruple-loop W-pouch.<sup>212–214</sup> Two randomized trials comparing the J-pouch and W-pouch did not substantiate an improvement in functional outcomes with a larger reservoir.<sup>215,216</sup> In 1 study, the median number of stools per day was the same in patients with a J-pouch or a W-pouch, and there was no difference between the 2 reservoirs in the rates of incontinence, urgency, soiling, and the use of antidiarrheal agents.<sup>215</sup> An S-pouch can provide additional length (2–4 cm) compared with the J-pouch, and may help to minimize anastomotic tension.<sup>217</sup> However, the 2-cm exit conduit of the S-pouch may elongate with time, and obstructed defecation may develop.

**8. In carefully selected patients, a 1-stage IPAA can be considered. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Numerous centers have published series supporting the omission of a protective ileostomy at the time of restorative proctocolectomy in patients who meet certain criteria.<sup>218–223</sup> Although they report similar anastomotic leak rates and pelvic sepsis-related complications for both diverted and nondiverted groups, in all of these studies, the use of protective ileostomy was left to the discretion of the surgeon—a potential source of bias. In general, those patients undergoing 1-stage procedures have been younger, healthier, less obese, without anemia or hypoalbuminemia, and on either no immunosuppressive medications or lower dosages.<sup>224</sup> Furthermore, all technical aspects of the surgery were straightforward, with no excess blood loss, good blood supply to the ileal pouch, no anastomotic tension, and a visibly intact anastomosis. A few studies have strongly encouraged the abandonment of this practice owing to higher anastomotic leak rates, more life-threatening septic complications, and the need for subsequent emergent operation.<sup>225–227</sup> The nondiverted patients also appear to have a higher incidence of postoperative ileus, although the overall number of hospital days is less than for those with an ileostomy.<sup>223,228,229</sup> Although it is clear that the use of a protective ileostomy does not alter the incidence of anastomotic leak, the milder pelvic sepsis related to fecal diversion may have a favorable impact on subsequent pouch function or retention.<sup>230</sup> This advantage must be weighed against the significant complications associated with both creation and takedown the ileostomy, including dehydration, wound infection, ileostomy closure leak and fistula, ileoanal anastomotic stricture, and small-bowel obstruction.<sup>220,223,228,229,231–234</sup> As in any operation, proper patient counseling regarding risks and benefits, along with informed consent, are imperative.

**9. Continent ileostomy is an alternative for patients with UC who are not eligible for or have had a failed restorative proctocolectomy. Grade of Recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

The present role of the continent ileostomy, also known as the Kock pouch, is primarily confined to patients with poor sphincter function or a failed IPAA, or to those who are dissatisfied with a conventional Brooke ileostomy.<sup>235,236</sup> This reduced role is the result of the success of the IPAA and the high rate of early and late complications associated with the continent ileostomy.<sup>237</sup>

Early complications, most commonly sepsis (secondary to suture line leaks, fistulas, and stomal necrosis) and obstruction, are seen in approximately one-fourth to one-third of patients.<sup>235,238,239</sup> Late complications occur in up to 60% of patients and include incontinence and ob-

struction secondary to disruption or dysfunction of the valve.<sup>235</sup> Valve revision is required in up to 60% of patients.<sup>237</sup> Although valve prolapse has been reduced with stapling techniques,<sup>240,241</sup> the overall pouch failure rate has not decreased.<sup>242</sup>

Initial pouch retention rates have been reported in up to 96% after 1 year,<sup>235, 237</sup> with a 71% cumulative success rate at 29 years in 1 study.<sup>237</sup> The failure rate is greater after a previously failed IPAA (46%) than after primary construction (23%),<sup>242</sup> as well as being higher after conversion from conventional ileostomy than when created primarily.<sup>243</sup> For the two-thirds of patients with a functional continent ileostomy, the reported quality of life is similar to that described for patients with IPAA.<sup>235,237,244</sup> Largely, this procedure has been relegated to surgeons with the expertise and experience of not only pouch construction, but also the aftercare of these patients as well.

**10. Total abdominal colectomy with ileoproctostomy may be considered only in a highly selected group of patients with UC. Grade of Recommendation: Weak recommendation based on moderate-quality evidence, 2B.**

Total abdominal colectomy with ileoproctostomy requires a relatively normal rectum to create a safe anastomosis; severe rectal inflammation and marked decrease in rectal compliance are contraindications to the procedure.<sup>245,246</sup> Severe anoperineal disease, although unusual in UC, also precludes an ileorectal anastomosis.<sup>247</sup> Caution should be exercised with this procedure in the setting of colonic dysplasia, or carcinoma in a potentially curative situation.<sup>248</sup>

The benefits of total abdominal colectomy with ileoproctostomy are its relative simplicity and predictability compared with IPAA. Preliminary results from a recent study also suggest that ileorectal anastomosis preserves female fertility.<sup>249</sup> The disadvantages are related to the long-term durability of the procedure. Studies demonstrate a 12% to 53% failure rate with follow-up of at least 3.5 years.<sup>250–253</sup> In addition, the theoretical risk of developing cancer in the remaining rectum should be considered when counseling the patient about surgical options. Although the incidence of developing cancer seems low (0%–8% with long-term follow-up),<sup>253–256</sup> patients undergoing total abdominal colectomy with ileorectal anastomosis must be willing to undergo annual endoscopic screening.<sup>246–248,251–254</sup>

## POSTOPERATIVE CONSIDERATIONS

**1. Routine surveillance of ileal pouches for dysplasia in the ileal mucosa is not warranted. Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.**

Dysplastic and neoplastic transformation within the pouch performed in UC seems to be extremely rare, unlike the low, although slightly higher, rate seen in familial ade-

nomatous polyposis.<sup>257–263</sup> A decrease in villous height and increase in concentration of crypts have been observed in most ileal pouches.<sup>264</sup> These metaplastic changes of the ileal mucosa to a colonic type mucosa are considered adaptations to the reservoir function of the pouch. Outside of symptoms, routine surveillance of the pouch does not appear to be beneficial or warranted.

**2. Surveillance of the residual rectal cuff or the anal transition zone following restorative proctocolectomy may detect malignant degeneration. Grade of Recommendation: Strong recommendation based on weak-quality evidence, 1C.**

Although little evidence supports routine surveillance of the ileal pouch itself,<sup>257,265</sup> short-segment inflammation (ie, “cuffitis”)<sup>266–268</sup> and perianastomotic zone carcinoma<sup>269–273</sup> are infrequent, but more legitimate concerns. Rare instances of adenocarcinoma in the pouch outlet, or anal transition zone, have been reported following both mucosectomy and stapled anastomoses—in some cases, more than 10 years following the initial operation.<sup>274–276</sup> Although the optimal surveillance interval remains largely anecdotal, patients should be counseled about the risk of malignant degeneration in or near the anal transition zone, and can be offered periodic surveillance by endoscopic or anoscopic means every few years, or when symptomatic.<sup>274,277,278</sup>

**3. Pouchitis is common after IPAA and is managed with antibiotics in most circumstances. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.**

The most frequent long-term complication after IPAA for UC is a nonspecific inflammation of the ileal pouch known as pouchitis.<sup>137,143,279,280</sup> The presence of extraintestinal manifestations of UC before colectomy, especially primary sclerosing cholangitis, has been associated with an increased incidence of pouchitis.<sup>281,282</sup> It is unclear whether the presence of backwash ileitis or the extent of disease predicts the likelihood of ultimately developing pouchitis,<sup>283–285</sup> although a recent study found the presence of backwash ileitis to be an independent risk factor for chronic pouchitis.<sup>282</sup> The origin of this nonspecific inflammation is unclear, but it may be the result of an overgrowth of anaerobic bacteria.<sup>286,287</sup> Presenting symptoms usually include abdominal cramps, fever, pelvic pain, and an increase in stool frequency. Clinical diagnosis may require confirmation by endoscopy and pouch mucosal biopsy.<sup>288,289</sup> However, it seems that histologic evaluation may be omitted without compromising diagnostic accuracy, and therapy can be successful based on the appearance of the pouch and the appropriate clinical picture.<sup>290</sup>

Treatment of pouchitis relies primarily on antibiotics, such as metronidazole and ciprofloxacin.<sup>291–293</sup> Probiotics have been used successfully in pouch patients to provide

prophylaxis against pouchitis and to maintain remission in chronic pouchitis.<sup>294,295</sup> In a recent Cochrane review, probiotics were found to be more effective than placebo in the treatment of chronic pouchitis as well as the prevention of its onset.<sup>296</sup> In antibiotic-refractory cases, budesonide enemas or other medical treatments may be useful.<sup>297</sup> Patients who have chronic pouchitis should be assessed for Crohn's disease. Uncommonly, an ileostomy with or without pouch excision is required for severe refractory pouchitis.<sup>292</sup>

Ileal inflammation extending proximal to the pouch in the neoterminal ileum has been recently described and termed prepouch ileitis. This nonspecific inflammation may extend up to 50 cm, and biopsies have shown histology similar to pouchitis.<sup>298</sup> In a recent study, the incidence of prepouch ileitis was 5.7%.<sup>299</sup> All patients had concurrent pouchitis, but less than one-fourth (23.5%) were symptomatic. Early data show no evidence for Crohn's disease in these patients.

## APPENDIX A: CONTRIBUTING MEMBERS OF THE ASCRS STANDARDS COMMITTEE

Janice Rafferty, Chair; Scott Steele, Co-Chair; Jose Guillem, Council Representative; W. Donald Buie, Advisor; Andreas Kaiser; George Chang; Dan Feingold; Dan Herzig; John Monson; Scott Strong; Kirsten Wilkins; Marty Weiser; Samantha Hendron; Ian Paquette.

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