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ECCO Guideline/Consensus Paper

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ECCO Guidelines on Therapeutics in Ulcerative Colitis: Surgical Treatment

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Abstract

This is the second of a series of two articles reporting the European Crohn's and Colitis Organisation [ECCO] evidence-based consensus on the management of adult patients with ulcerative colitis [UC]. The first article is focused on medical management, and the present article addresses medical treatment of acute severe ulcerative colitis [ASUC] and surgical management of medically refractory UC patients, including preoperative optimisation, surgical strategies, and technical issues. The article provides advice for a variety of common clinical and surgical conditions. Together, the articles represent an update of the evidence-based recommendations of the ECCO for UC.

Key Words: Ulcerative colitis [UC]; inflammatory bowel disease [IBD]; surgery

Introduction

Ulcerative colitis [UC] usually presents as a mild condition, but often leads to life-threatening and systemic complications that require urgent interventions.[1–4] Acute severe ulcerative colitis [ASUC] and medically refractory UC represent the main indications for surgery in UC patients.[5,6] The first-line treatment of ASUC consists of intravenous corticosteroid treatment.[7,8] However, up to 30% of patients fail to respond to conservative treatments and require a colectomy.[9] Refractory UC includes steroid dependency and immunomodulator- or biologic-refractory disease. Refractory UC is often accompanied by deteriorated patient condition and is a recognised risk factor of poor postoperative outcomes[10–12]; thus a staged procedure is often preferred, to improve patient status and minimise postoperative complications.[13]

Despite the increasing availability of new pharmacological treatments, multiple attempts at conservative management and consequent therapeutic failures may affect the condition of patients with ASUC and refractory UC and considerably influence postoperative outcomes.[11,12] Accordingly, multidisciplinary [including gastroenterologists and surgeons] management of UC patients is of crucial importance to identify the best therapeutic pathway.

The European Crohn's and Colitis Organisation [ECCO] aims to develop a practical guide for the medical and surgical management of adult patients with UC, based on an interdisciplinary, evidence-based approach. The present article is focused on the first-line treatment of adult ASUC patients and on the surgical management of refractory adult UC patients, including preoperative assessment and technical aspects. The following statements are complementary to the guidelines on medical treatment of adult UC patients, which are presented in a separate article.

Materials and Methods

The present article is part of the ECCO evidence-based consensus on the management of UC and covers the medical treatment of ASUC and the surgical management of medically refractory moderate and severe UC. The current guidelines, together with those on UC medical management, are intended to update the previous ECCO recommendations published in 2017.[14,15] A summary of some of the key changes from previous ECCO UC guidelines is presented in the Supplementary material, available as Supplementary data at *ECCO-JCC* online.

The current guidelines followed the Oxford methodology. A detailed description of the methodology used to develop the guidelines is reported in the Supplementary materials.

General approach to ASUC and surgical management of refractory UC

ASUC usually presents as acute episodes of a chronic disease with a relapsing-remitting pattern. However, ASUC may be the onset feature in up of one-third of UC patients.[16] ASUC is associated with a 30–40% risk of colectomy after one or more severe exacerbations, and 10–20% of patients with ASUC need a surgical intervention at their first admission.[16–19] The definition and classification of ASUC follow the criteria of Truelove and Witts[20] and ECCO, which also include C-reactive protein [CRP] measurement.[15] Patients with ASUC require immediate hospitalisation. The standard initial therapy consists of intravenous corticosteroids.[15] However, approximately 30% of patients fail to respond to conservative treatments.[9] Failure may be predicted using the Travis criterion,[13] which combines the number of stools after 3 days of corticosteroid therapy and the level of serum CRP. In case of failure, different therapeutic strategies may

be considered. However, after 7 days without significant improvements, a surgical intervention is highly recommended to avoid the perioperative complications usually associated with emergent procedures.[21–23] In case of semi-elective surgery, a staged procedure is preferred, including subtotal colectomy with ileostomy during the first operation, followed by ileal pouch-anal anastomosis [IPAA] construction, and then a final operation with ileostomy closure.[24] This standard 'three-step' approach can be replaced by a modified two-step approach, starting also with subtotal colectomy but followed by pouch construction, without temporary stoma, thus avoiding the third operation. A detailed flowchart of the staged procedures is shown in Figure 1. Since early colectomy in ASUC patients is associated with significant improvements in perioperative outcomes and is now widely accepted,[25,26] we will restrict the focus of the ASUC guidelines to the medical therapeutic options for treating ASUC and address surgical management exclusively for medically refractory UC.

The surgical management of moderate-to-severe refractory UC is more varied compared with that of ASUC and there is currently less consensus. Since refractory UC is usually managed in an elective setting, the focus has progressively shifted from sole resolution of symptoms to parallel improvement in functions. Up to 25% of UC patients require a surgical intervention in their lifetime.[27,28] Although total proctocolectomy may provide a definitive resolution of UC symptoms, complete removal of the colon and the associated loss of function may be socially and psychologically unacceptable for the patient.[29] Successful surgical management may provide the resolution of ongoing symptoms and eliminate the need for continuous medical care [including hospitalisations and recurrent transfusions] and immunosuppressive therapies, while protecting the patient from malignancy risk. At the same time, the ideal surgical strategy should ensure acceptable long-term functional outcomes and minimise perioperative complications.[30] In recent decades, the surgical options for the treatment of refractory UC have evolved, combining technical advancements with a more comprehensive management of perioperative pathways. In addition to the medical management of ASUC, the following guidelines also focus on several aspects of the surgical management of medically refractory UC, including indication for surgery, perioperative optimisation, surgical approaches, and related technical strategies.

1. Medical Management of ASUC

1.1.Statement 1.1.

Intravenous corticosteroids as the initial standard treatment for adult patients with ASUC are recommended, as this treatment induces clinical remission and reduces mortality [EL3]

The only randomised controlled trial [RCT] including placebo in the setting of ASUC is the paramount work by Truelove and Witts, who observed that steroids induced clinical remission and decreased mortality without increasing serious adverse events.[20,31] Risk of bias led to downgrading of the evidence level from 2 to 3. No conclusions could be drawn about the need for surgery, as the authors included derivative ostomies and colectomies without distinguishing the type of surgery in the report. Since the results of this pivotal study, placebo-controlled trials to clarify these and other aspects would be unethical.

1.2.Statement 1.2.

Either infliximab or cyclosporine should be used in adult patients with steroid-refractory ASUC. When choosing between these strategies, centre experience and a plan for maintenance therapy after cyclosporine should be considered [EL3]

RCTs and meta-analyses indicate that infliximab is as effective as cyclosporine in inducing clinical response in adult patients with steroid-refractory ASUC (OR [odds ratio]: 1.08; 95% CI [confidence interval]: 0.73–1.60], with no significant differences regarding

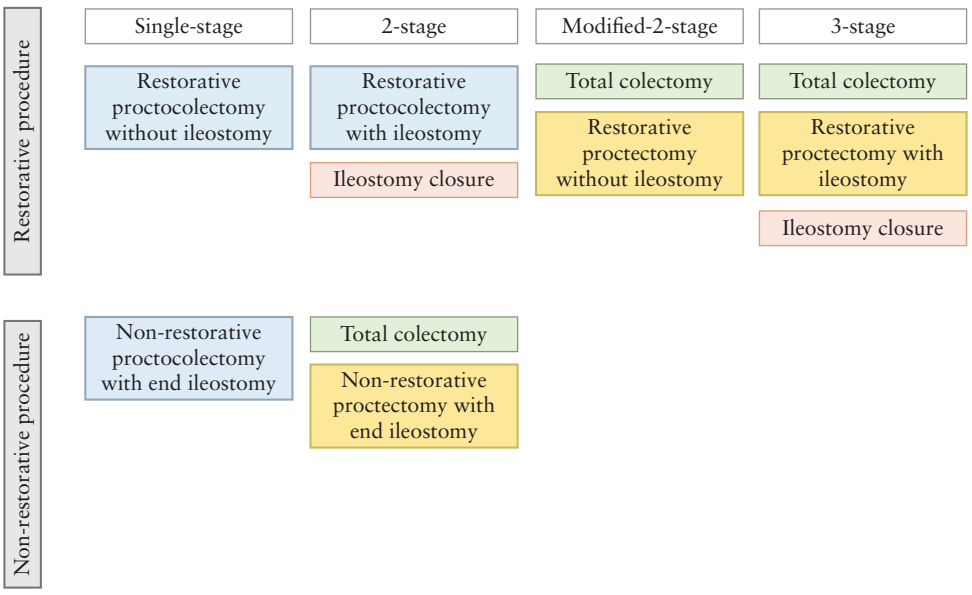

Figure 1. A detailed flowchart of the staged procedures for proctocolectomy. Published with permission from Prof. Antonino Spinelli.!

serious adverse events [OR: 1.78; 95% CI: 0.97–3.27], rate of colectomy at 12 months [OR: 0.76; 95% CI: 0.51–1.14], or in improvement of quality of life [QoL] or mortality [OR: 1.37; 95% CI 0.31–6.10].[32–34] Colectomy-free survival appeared to be similar and also at long-term follow-up [5 years].[35] Length of hospital stay appeared to be shorter with infliximab, although this was only observed in one post-hoc analysis.[36] Quality of evidence was downgraded due to imprecision and publication bias.

1.3.Statement 1.3.

There is currently insufficient evidence to determine the optimal regimen of infliximab rescue therapy in patients with ASUC refractory to corticosteroid therapy [EL4]

A meta-analysis including five RCTs and 30 retrospective and six prospective observational cohort studies reported the colectomy-free survival of ASUC patients after different infliximab induction strategies. Overall, colectomy-free survival following infliximab rescue therapy was 79% [95% CI: 75–84%] at 3 months and 70% [95% CI: 66–74%] at 12 months.[37] We did not find RCTs that compared different induction dosing strategy regimens. A single pilot RCT [that was prematurely terminated] explored the outcomes of different infliximab doses.[38] Colectomy-free survival at 3 months was higher with 5 mg/kg multiple-dose induction compared with 5 mg/kg single dose [OR: 4.24; 95% CI: 2.44–7.36; p <0.001], suggesting that initial treatment with multiple 5 mg/kg infliximab doses may be superior to single-dose salvage.[38,39]

A retrospective cohort study did not reveal differences in short-term [30 days] or long-term [12 months] colectomy rates between ASUC patients treated with accelerated- or standard-dose infliximab.[40]

Patients with ASUC have a high inflammatory burden, with accelerated clearance and faecal loss of infliximab that may lead to low concentrations and immunogenicity. Infliximab concentration is also affected by low albumin levels, which are common among ASUC patients due to malnutrition and protein loss. These considerations may make it reasonable to initiate treatment with intensive dosing regimens of infliximab. However, it is still unclear whether dose intensification will improve clinical outcomes in these circumstances.[41]

Eight observational studies including 736 patients] [9–14] reported that 3-month colectomy rates were comparable between the dose-intensification group [either high-dose or accelerated induction] and the standard induction group [OR: 0.70; 95% CI: 0.39–1.27; p = 0.24], although patients in the dose-intensification group had higher mean CRP and lower albumin levels. However, a recent retrospective propensity score matched cohort study revealed reduced short-term, but not long-term, colectomy rates in patients receiving accelerated infliximab dosing.[42] Recently, the British Society of Gastroenterology guidelines recommended accelerated dosing in patients who have not responded to the standard dose [5 mg/kg] after 3–5 days.[43] Therefore, there is no consensus whether intensive or standard infliximab dosing regimens are recommended. Furthermore, most of the studies were low-quality, uncontrolled, observational cohorts confounded by patient selection bias, heterogeneity, and imprecision. Thus, the optimal regimen for infliximab salvage therapy for ASUC remains unclear. Future RCTs are needed to fill these knowledge gaps and to investigate the role of early therapeutic drug monitoring in IBD patients treated with infliximab and dose optimisation.

1.4.Statement 1.4.

Third-line sequential rescue therapies with calcineurin inhibitors [cyclosporine or tacrolimus] in ASUC refractory to corticosteroid therapy may delay the need for colectomy but are associated with high rates of adverse events and should only be administered in specialised centres [EL2a]

A meta-analysis performed in 2015 found that after sequential treatment with infliximab followed by calcineurin inhibitors [cyclosporine or tacrolimus], 62% [95% CI: 57–68%] and 39% [95% CI: 33–44%] of patients achieved short-term treatment response and remission, respectively. Colectomy rates were 28% [95% CI: 22–34%] at 3 months and 42% [95% CI: 36–49%] at 12 months. Adverse events were experienced by 23% [95% CI: 18–28%] of patients, including serious infections in 7% [95% CI: 4–10%]. Mortality was observed in 1% [95% CI: 0–2%]. However, this meta-analysis was based on low-quality evidence and thus any definite conclusion on appropriate sequence of therapies was not possible.[44] Moreover, sequential third-line therapy is associated with significant adverse events and death.[45] Recent preliminary studies have focused on tofacitinib in ASUC patients refractory to corticosteroid treatment and have shown promising results and a good safety profile, but further investigations are needed to confirm its efficacy.[46,47] In conclusion, third-line therapies with infliximab and calcineurin inhibitors may delay, but not prevent, colectomies and should be carefully balanced with the higher risks of adverse outcomes. Sequential rescue therapy should only be administered at specialised referral centres familiar with the use of calcineurin inhibition.

Venous thromboembolism [VTE]– particularly deep vein thrombosis [DVT] and pulmonary embolism [PE] –is common in UC patients due to multifactorial and disease-related causes,[48–53]and may lead to significant morbidity and mortality.[54–56] The incidence of VTE correlates with disease activity[49,53,57] and increases in hospitalised subjects,[49] making ASUC patients at a high risk of developing VTE among the IBD population. Although several consensus guidelines support the use of anticoagulation prophylaxis in hospitalised UC patients with active disease,[8,58–61] there is still a substantial inconsistency in VTE prophylaxis administration.[62] Prophylaxis with low molecular weight heparin and fondaparinux significantly reduces the risk of VTE in hospitalised IBD patients, with minimal side effects.[61,63,64] However, robust evidence and well-designed clinical trials are lacking on the actual effectiveness of VTE prophylaxis and on the optimal dose regimen for ASUC patients.

2. Medical Versus Surgical Management of Refractory Moderate-to-severe UC

2.1.Statement 2.1.

Reconstructive surgery may be offered to refractory and corticosteroid-dependent patients and improves quality of life despite the risk of early and late complications [EL2b]. Proctocolectomy with end-ileostomy is an alternative for some patients and has lower morbidity and comparable quality of life [EL3a]

Five systematic reviews were performed to define the risk of early and late complications after restorative proctocolectomy with IPAA. Early complications [within 30 days after surgery] occurred in 9–65% of patients, and late complications occurred in 3–55% of patients.[65,66] Systematic reviews indicate that the most frequent complications were pouchitis [2–50%],[30,65–67] wound infection [7–45%],[30,65,66] bowel obstruction [2–33%],[65,66] ileus [14–30%],[66] sepsis [0–20%],[30,65–67] anastomotic leak [0.5–10%],[30,66] and fistula [0–6%].[66] The most common late complications were ileus [3–25%],[66] faecal incontinence [21–22%],[66] pouch loss [0–17%],[30,66] chronic pouchitis [10–16%],[30,67] Crohn's-like disease of the pouch [13%],[67] and fistula [0–8%].[66] The overall mortality rate after surgery was 0.1%.[66]

Despite the rates of early and late complications, most patients were satisfied with the surgical outcomes and more than 50% of patients would have preferred an earlier operation.[68] Delayed surgery may increase morbidity, length of stay, and hospital costs.[69] A recent meta-analysis focused on third-line therapies in severe chronic UC showed that, despite short-term improvements, third-line therapies only delay the need for colectomy and result in higher rates of complications.[68] Moreover, the overall rate of surgery for patients with UC is approximately 30%[30,65,67,68,70] but increases to 53% in steroid-refractory UC patients. The most common reasons to perform surgery are persistent malaise,[68] poor drug compliance,[68] dysplasia or cancer,[30,68] consuming symptoms,[30] and willingness to discontinue constant medical care [e.g., hospitalisations, recurrent transfusions] or immunosuppressive therapy.[30] Three systematic reviews reported that over 90% of patients who had colectomy had a good QoL,[68] with a happiness score of 10/10[30] and a Cleveland global QoL of 9/10.[30] Patients had five to six bowel motions per day[68] and one at night,[30] with a continence over 90%[30,68] and full continence of stool and gas up to 80% at 10 years.[30] Up to 93.3% of patients had a functioning pouch at 30 years, with stable QoL scores.[71]

The studies that compared ileostomy with IPAA were all retrospective and revealed similar results, using a different QoL score. Occasionally the scores obtained in specific domains of health-related QoL differed significantly between the surgical techniques [including body image, travelling, and sexual activity]. Removing the diseased colon offers a good QoL when compared with medical treatment in UC patients, with a morbidity ranging between 20% and 25%.[72]

3. Preoperative Optimisation of Refractory Moderate-to-severe UC

3.1.Statement 3.1.

Correction of altered body composition and nutrition imbalances is advised preoperatively, despite limited evidence [EL5].There is no evidence to support routine enteral or parenteral nutrition to improve the surgical outcomes of patients with UC [EL5]. Iron supplementation is recommended when iron-deficiency anaemia is present [EL1]

Nutritional alterations predict poor postoperative outcomes and mortality and affect QoL.[73,74] Routine perioperative assessment by a nutritionist should be considered in IBD patients in remission, as part of multidisciplinary management.[74] Even if current evidence is limited, it is advisable to correct undernutrition or overnutrition.[73,74] No data support routine perioperative administration of enteral or parenteral nutrition.[73] Delaying surgery by 7–14 days should be considered in patients with malnutrition.[74] High-quality evidence suggests that iron supplementation is recommended when iron deficiency is present, with the goal of normalising haemoglobin [Hb] levels and iron stores.[15,74]

3.2.Statement 3.2.

Patients taking >20 mg prednisolone for >6 weeks are at increased risk of early complications and pouch-specific complications. Steroids should be weaned before restorative proctectomy or proctocolectomy, and if this is not possible, surgery should be postponed [EL4]. Preoperative thiopurines or cyclosporine do not increase the risk of postoperative complications [EL3]. Patients on biologics might be at increased risk of developing early and late pouch-specific complications; three-stage or two-stage modified approaches with deferred pouch construction could be considered under these circumstances [EL4]. Single-stage restorative proctocolectomy should be avoided in patients receiving biologics [EL5]

Low-quality studies reported that patients who have received >20 mg prednisolone for >6 weeks are at 5-fold increased risk of infectious and short-term pouch-specific complications.[15] Steroids should be weaned before surgery; if this is not possible, pouch construction should be postponed.[15] Thiopurines or cyclosporine do not increase the risk of postoperative complications.[15]

Patients on biologics are at increased risk of early and post-ileostomy closure pouch-related complications [OR: 4.12; 95% CI: 2.37–7.15], but study quality is low.[75] Given the conflicting evidence, it would be prudent to avoid single-stage proctocolectomy with ileal pouch construction in patients on anti-tumour necrosis factor [TNF] therapies.[15]

3.3.Statement 3.3.

Prophylactic anticoagulation therapy in adult patients with active UC during hospitalisation is recommended, considering the high risk of venous thromboembolism [VTE] during UC flares [EL4]

One of the extraintestinal manifestations of UC is venous thromboembolism [VTE], which is higher among UC patients who underwent an emergency or elective colectomy [OR: 5.28; 95% CI: 1.93–4.45 and OR: 3.69; 95% CI: 1.30–10.44, respectively] compared with medically responsive UC patients.[76]

Patients with IBD have a 2- to 3-fold increased risk for VTE compared with healthy controls and an up to 8-fold increased risk during a disease flare or hospitalisation.[77,78] An observational study with 439 UC patients revealed a thrombosis prevalence of 5%, and half of the patients developed thrombosis during a UC flare [11% vs. 1%; OR: 8.0].[79]

Among 7078 IBD patients, only 0.6% received post-discharge anticoagulation prophylaxis and 235 patients [3%] developed thromboembolic complications. The strongest predictors of VTE were stoma creation [OR: 1.95; 95% CI: 1.34–2.84] and J-pouch

reconstruction [OR: 2.66; 95% CI: 1.65–4.29].[80] Among 837 IBD patients, 14 VTE events were reported, of which 79% received prophylaxis, but only 36% within 24 h of admission.[81]

A study with 2788 IBD patients reported that pharmacological thromboprophylaxis during IBD-related hospitalisation is associated with reduced risk of post-hospitalisation VTE [hazard ratio: 0.46; 95%CI: 0.22–0.97].[82] Patients who received VTE pharmacological prophylaxis were more likely to be on the surgical service [75% vs. 13%; p <0.001].[63,83]

Several studies suggested that pharmacological prophylaxis does not lead to increased incidence of gastrointestinal bleeding events in UC patients.[63,84–86] A meta-analysis suggested that heparin administration in patients with UC is safe, with no major bleeding events (the average reported dose was Enoxaparin/100 Anti-Xa IU/kg/day subcutaneously [s.c.] for 12 weeks).[87] The Toronto consensus for the management of IBD in pregnancy recommended anticoagulant thromboprophylaxis during hospitalisation over no prophylaxis.[88]

In conclusion, it is essential to emphasise that there are no established RCTs that have evaluated the efficacy of thromboprophylaxis in patients with IBD, due to the incidence of VTE. However, our ECCO consensus group determined that given the higher risk of thrombosis in UC patients with disease flare, VTE prophylaxis should be considered over no prophylaxis.

4. Surgical Strategy of Refractory Moderate-to-severe UC

4.1.Statement 4.1.

After total proctocolectomy for medically refractory UC, IPAA is the procedure of choice, but permanent end-ileostomy is also a reasonable option for some patients. A shared decision-making approach should be used to tailor procedure selection to the patient's preference [EL3]

Although IPAA is the procedure of choice for medically refractory UC patients requiring surgery, both IPAA and total proctocolectomy with end-ileostomy are reasonable options. Total proctocolectomy with end-ileostomy may be offered to patients with contraindications to IPAA. These operations result in similar overall short- and long-term complication rates, QoL, and costs. IPAA is associated with a high risk of pouch-related complications and costs. Total proctocolectomy with end-ileostomy is associated with a high risk for ileostomy-related complications and costs.

Overall, the short-term risks of these procedures appear equivalent and occur in approximately 30% in each group; IPAA is associated with risk of short-term anastomotic leak, fistula, or stricture, and total proctocolectomy is associated with risk of a non-healing perineal wound. The long-term complication profiles for these two procedures are different due to differences in anatomy. IPAA patients are at risk for faecal incontinence, pouchitis, fistula formation, and pouch failure, and total proctocolectomy patients are at risk for parastomal hernia and ileostomy prolapse.[66,89–92] QoL also appears equivalent; in a systematic review of 13 observational studies with 783 IPAA and 820 total proctocolectomy patients, the two procedures were comparable in overall health-related QoL.[72,92] Patients who undergo total proctocolectomy with end-ileostomy have ileostomy supply-related costs, and patients who undergo IPAA have costs related to endoscopic surveillance of the pouch.[91,92]

Although advanced age is a major consideration in procedure selection for patients who are candidates for either procedure, a shared decision-making approach should be used to tailor procedure selection according to the patient's preference.[93]

4.2.Statement 4.2.

IPAA may be performed as a two or three stage procedure. Modified two-stage IPAA may be associated with fewer complications and shorter length of stay than three-stage or two-stage IPAA in patients with medically refractory UC operated in expert centres, but more evidence is needed [EL3]

A modified two-stage IPAA comprises first a total colectomy with end-ileostomy, leaving the rectum in situ, followed by a proctectomy and ileal pouch-anal reconstruction with ileostomy take-down. Patients often undergo total colectomy at a late stage of their disease and present in an exhausted, catabolic state while being heavily medically treated, including with steroids. Hence, the second step is typically performed a few weeks to months after colectomy, allowing time for the patient to recover and for medications to be tapered. Proctectomy and IPAA construction can then be performed together as a modified two-stage approach, thus avoiding a diverting ileostomy which requires a third operative step for reversal and is associated with additional morbidity.[94,95] The modified two-stage IPAA is may become a standard of care, replacing one-stage, two-stage, and three-stage IPAA.[96–99] Clinical results in adults favour a modified two-stage approach, with better anastomotic leak rates,[99,100] fewer postoperative septic complications, and less small-bowel obstruction[101] when compared with two-stage and three-stage IPAA. A modified two-stage IPAA is also associated with less resource consumption and decreased length of hospital stay.[98,99] The IPAA leak rate is approximately 10% with a modified two-stage approach in expert centres. Functional results of IPAA are affected by the occurrence of an anastomotic leak, in particular without a diverting stoma.[102] It is therefore crucial to ensure a diligent postoperative follow-up, including serial CRP measurements and early investigation of any suspicion of leak. Indeed, when detected and addressed early, most leaking IPAAs can be salvaged and long-term pouch function can be preserved.[103]

Pouch-related complications include pouchitis, Crohn's disease of the pouch, cuffitis, and irritable pouch. Among these, pouchitis is the most common complication, occurring in up to 80% of patients after 30 years from the pouch construction.[71,104–106] Pouchitis is commonly diagnosed by endoscopy and histological characterisation. According to the duration and type of symptoms, pouchitis can be classified into acute [symptoms resolving within 4 weeks], chronic [symptoms last >4 weeks], or relapsing [three or more episodes of pouchitis occur in a year]. Treatment for acute pouchitis includes antibiotic administration, mainly consisting of ciprofloxacin and metronidazole.[107–109] However, the evidence of efficacy is low, including only one small RCT demonstrating the superiority of ciprofloxacin over metronidazole in terms of symptoms reduction and endoscopic response.[64] An RCT of rifaximin failed to demonstrate a superiority compared with placebo,[110] and budesonide enemas and metronidazole were equally effective for inducing remission.[111] Patients with chronic pouchitis can develop antibiotic-refractory symptoms. Due to persistent and debilitating symptoms they may ultimately develop pouch failure requiring pouch defunctioning and definitive stoma

construction. Several medications have been investigated to induce remission in chronic antibiotic-refractory pouchitis, including biologic therapy, probiotics, and immunodulators, although the overall quality of evidence is low.[112]

5. Technical Aspects of Surgical Approaches for Refractory Moderate-to-severe UC

5.1.Statement 5.1.

IPAA may be constructed using either a stapled or a handsewn technique, with comparable functional outcomes. Thus, the type of anastomosis should be left to the surgeon's discretion [EL2]

Overall, stapled and handsewn IPAAs seem to result in comparable complication rates, functional outcomes, and QoL. In a meta-analysis of four randomised controlled trials including 184 patients [53% stapled, 43% handsewn], no significant differences were observed in terms of functional outcomes, sphincter resting pressure, or squeeze pressures.[113] Based on low-quality evidence, the stapled technique may be more likely to achieve perfect continence [90% vs. 67%; p <0.0001] compared with the handsewn approach.[114] Despite slightly better functional outcomes after stapled anastomosis, overall QoL appears equivalent between the two groups.[114,115]

Although handsewn IPAA is more commonly performed in patients with dysplasia or cancer, the approach does not reduce the probability of recurrence.[115] In a systematic review of observational studies with 43 rectal cancer patients, most of the cases [70%; 30 patients] occurred after mucosectomy with handsewn anastomosis, and 30% [13 patients] occurred after stapled anastomosis. Of 28 reported cases of dysplasia, 27 [96%] cases occurred after mucosectomy with handsewn anastomosis, and one [4%] occurred after stapled anastomosis. The median time to dysplasia or cancer was 10 years.[116] In a systematic review of 23 observational studies with 2040 patients, the pooled prevalence rate of neoplasia after IPAA was 1.1% and was equally distributed in the pouch, rectal cuff, and anal transition zones. Previous colorectal dysplasia or cancer, but not pouchitis or duration of follow-up, were predictive of rectal cancer or dysplasia,[117] indicating that mucosectomy with handsewn anastomosis does not eliminate the risk of subsequent dysplasia or cancer.

Due to a paucity of high-quality data, no recommendations can be made with regards to sexual function, strictures, and septic complications between stapled and handsewn techniques, although stapled IPAA is likely associated with a higher rate of cuffitis.[118,119]

5.2.Statement 5.2.

Laparoscopic surgery is the preferred approach to patients with medically refractory UC, as it is associated with lower intra- and postoperative morbidity, faster recovery, fewer adhesions and incisional hernias, shorter hospital length of stay, improved female fecundity, and better cosmesis [EL2]

Laparoscopy is the preferred approach to bowel resection for experienced surgeons. Evidence in favour of this recommendation is large, with several meta-analyses in UC reporting benefits in terms of short- and long-term morbidity, functional outcomes, cosmesis, and QoL.[120–125] There is a single RCT including long-term results,[126,127] but nationwide data support minimally invasive approaches,[120] which have long been endorsed by expert centres worldwide. Laparoscopy should be offered for elective and emergent segmental and total colectomy and for reconstructive surgery. Although desirable, laparoscopy is not always possible. Patients with previous abdominal surgery and extensive adhesions or cardiopulmonary instability may require an open procedure. Lack of surgical expertise may also limit access to laparoscopy, particularly in the emergent setting or in remote locations. Operative time tends to be greater when a minimally invasive approach is chosen, and resource consumption may be increased.[123] It is important to note that a previous open procedure does not mandate a second open procedure. For example, a patient who had an open colectomy and end-ileostomy for fulminant colitis should attempt laparoscopic proctectomy and IPAA reconstruction. Beyond functional outcomes, minimally invasive approaches are also associated with better fecundity and pregnancy outcomes.[128–130]

5.3.Statement 5.3.

Although associated with an increased risk of rectal dysplasia, cancer, and dysplasia or cancer recurrence, patients with UC and a minimally affected rectum can be offered the option of an ileo-rectal anastomosis [IRA] [EL4]

IRA is associated with better functional outcomes [number of bowel movements and nocturnal frequency] compared with IPAA.[131–134] Failure rates are similar between IRA and IPAA.[135,136] IRA failure rates were estimated at 27.0% [95% CI: 22–32] and 40.0% [95% CI: 33–47] at 10 and 20 years, respectively, and may be decreased with a two-stage procedure approach [OR: 0.10; 95% CI: 0.03–0.41].[137] Two-thirds of secondary proctectomies were performed for refractory proctitis, and 20% for rectal neoplasia. Acute proctitis occurred in 70% of patients; 76% experienced chronic proctitis.[138] IRA may be associated with an increased risk of rectal cancer development,[135,139] but this was based on limited and low-quality data.

Conclusion

The variability in symptoms and clinical manifestations of UC makes it difficult to establish a unique and predefined therapeutic pathway; the lack of specific protocols may restrict the management of these patients to highly specialised centres, thus limiting accessibility to medical care.

In addition to continuous updates on novel therapeutic strategies and technical trainings, the key to successful management of UC patients is to promote a multidisciplinary approach with close communication between different IBD specialists, who should remember the relevant social and economic burden of UC.

These guidelines were developed using the Oxford methodology, which combines a robust methodological strategy with a multidisciplinary approach. Whereas each statement was drafted by an expert on the topic, identification of the critical questions and discussion on the retrieved evidence involved all members of the committee, which allowed for the identification of aspects that may otherwise have been overlooked.

In addition to the clinical questions addressed in these guidelines, we recognise that many other topics would have been worthy of

discussion. These include early postoperative management of UC patients and the possibility of implementing an enhanced recovery pathway [with related challenges and advantages] and management of pouch-related complications, which are addressed in previous guidelines.[14,15] However, the clinical questions were selected with the aim of providing relevant updates on neglected topics.

The peculiarity of the clinical questions in these guidelines, particularly in the surgical field, often made it difficult to provide specific recommendations. However, the drafting process identified critical needs and revealed gaps in knowledge, thus laying the groundwork for future research.

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Conflict of Interest

ECCO has diligently maintained a disclosure policy of potential conflicts of interests [CoI]. The conflict-of-interest declaration is based on a form used by the International Committee of Medical Journal Editors [ICMJE]. The CoI disclosures are not only stored at the ECCO Office and the editorial office of *JCC*, but are also open to public scrutiny on the ECCO website [https://www.ecco-ibd.eu/about-ecco/ecco-disclosures.html], providing a comprehensive overview of potential conflicts of interest of the authors.

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Supplementary Data

Supplementary data are available at *ECCO-JCC* online.

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