REVIEW

Inflammatory bowel disease position statement of the Italian Society of Colorectal Surgery (SICCR): ulcerative colitis

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Abstract

The Italian Society of Colorectal Surgery (SICCR) promoted the project reported here, which consists of a Position Statement of Italian colorectal surgeons to address the surgical aspects of ulcerative colitis management. Members of the society were invited to express their opinions on several items proposed by the writing committee, based on evidence available in the literature. The results are presented, focusing on relevant points. The present paper is not an alternative to available guidelines; rather, it offers a snapshot of the attitudes of SICCR surgeons about the surgical treatment of ulcerative colitis. The committee was able to identify some points of major disagreement and suggested strategies to improve the quality of available data and acceptance of guidelines.

Keywords Inflammatory bowel disease · IBD · Ulcerative colitis · UC · IPAA · Pouch

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Introduction

Several surgical societies have developed authoritative guidelines on the management of inflammatory bowel disease (IBD) [1–6]. Following the Delphi think tank project in 2015 [7, 8], the Italian Society of Colorectal Surgery (SICCR) has developed a Position Statement on the surgical treatment of IBD. This manuscript will deal specifically with ulcerative colitis (UC). As reported in the first manuscript from the 2019 SICCR project [9], the current manuscript is not intended to replace the available guidelines—rather, the goals are to stimulate discussion about the surgical issues of IBD among experts at a national level, aiming at standard treatment practices—and to focus attention on the importance of applying standard management pathways in everyday practice nationwide. A patient representative was involved in the entire process.

This is not intended to be a strict rules of conduct, but should be considered a decisional aid, to be adapted for each individual patient.

Methods

The methods have been thoroughly described in the manuscript on the Position Statement for the surgical treatment of CD [9].

Briefly, a steering committee, including a patient representative (SL), an external advisor (DSK), and an external expert supervisor (SD), identified experts who were invited to participate in the project. Each collaborator contributed with a specific section, and drafted the statements with evidence levels (EL) graded according to "The Oxford Levels of Evidence 2″ from the Oxford Centre for Evidence-Based Medicine OCEBM (https://www.cebm.net/index.aspx?o=5653), along with a brief supporting text. Contributions were circulated via SurveyMonkey (SurveyMonkey Inc., San Mateo, CA, USA, https://www.surveymonkey.com). Answers were reviewed by the steering committee, and statements and supporting text about which there was less than 80% agreement needed to be changed. A second round of voting of the statements was performed and the manuscript was finalized. Statements about which there was less than 80% agreement were either deleted or moved to the supporting text. Some statements with > 80% agreement were revised to include the comments received.

Acute colitis

Salvage medical treatment

> *Item 1*
> *First line treatment for patients with acute severe ulcerative colitis is intravenous (IV) corticosteroids*

(EL1). In case of corticosteroid-refractoriness, a second line salvage medical treatment should be considered. Medical treatment options should be cyclosporin (CYS) (EL1), infliximab (IFX) (EL1), or tacrolimus (EL2).
[Agreement: "Agree" 83.3%, "Neutral" 16.7%, round II]
Item 2
Multiple 5 mg/kg infliximab doses are superior to single-dose treatment (EL1). Alternative induction strategies such as dose-intensification or dose-acceleration have outcomes similar to standard induction (EL1).
[Agreement: "Agree" 94.4%, "Neutral" 5.6%, round I]
Item 3
Cyclosporin and infliximab have demonstrated equal efficacy and are associated with comparable colectomy rates (EL1). Patients with intolerance or inadequate response to thiopurine should not be considered for treatment with cyclosporin (EL4).
[Agreement: "Agree" 88.9%, "Partially agree" 5.6%, "Neutral" 5.6%, round I]

IV corticosteroids are the first choice for treatment of acute severe colitis about 30% of patients show corticosteroid refractoriness and should be considered for second-line "rescue" medical therapy [10]. CYS, IFX and tacrolimus have demonstrated efficacy in randomized controlled trials (RCTs) and observational studies. CYS is a calcineurin inhibitor. Its short-term efficacy was first demonstrated in an RCT by Lichtiger et al. [11]. Van Assche et al. [12] compared 4 mg/kg with 2 mg/kg IV CYS and showed equal efficacy with similar response rates (82% and 83%, respectively) and no difference in short-term colectomy rates (13% vs 9%). As regards long-term outcomes, colectomy rates of 58% and 88% over 7 years of maintenance therapy with azathioprine were reported [13]. As regards safety and toxicity, studies reported about 5% of serious infections and 1–3% of mortality [14, 15]. IFX, a monoclonal antibody against tumor necrosis factor-alpha (TNF-alpha), was first used in an RCT including patients with steroid-refractory acute severe colitis which reported a 3-month colectomy rate lower than that of the placebo group (29% vs 67%) [16]. In the long term, the same cohort had lower colectomy rates compared to controls (50% vs 76%) [17]. A retrospective multicenter analysis on 211 patients showed colectomy rates of 36%, 41% and 47% after 1, 3 and 5 years, respectively [18]. Other studies reported colectomy rates ranging from 20 to 75% [19–22]. Safety and mortality rates were similar to those related to CYS treatment [23, 24]. New studies about pharmacokinetics of IFX showed how increased drug clearance, low serum levels or fecal loss could lead to worse outcomes [25–27]. Alternative strategies such as dose intensification or accelerated induction protocols for induction were assessed

leading to conflicting results [28–31]. A review of observational studies showed a benefit for IFX optimization with a 80% reduction in colectomy rates, while a multicenter study with meta-analysis comparing accelerated vs standard IFX found no significant differences in outcomes [32]. A recent meta-analysis on 2158 patients showed overall colectomy-free rates of 79.7% and 69.8% at 3 and 12 months, respectively. Patients treated according to alternative protocols did not show significantly improved outcomes when compared to patients receiving a standard induction [33]. Tacrolimus (FK506) is another calcineurin inhibitor. In trials, there was a better response to tacrolimus than to placebo (67% vs 18%, 68% vs 10%) [34]. In a systematic review with meta-analysis tacrolimus was associated with colectomy-free rates of 86%, 84%, 78% and 69% at 1, 3, 6 and 12 months, respectively [35]. Similar rates were reported in a recent retrospective study (90.9%, 86%, 77.3% and 68.2% at 1, 3, 6 and 12 months, respectively) [36]. IFX has been compared to CYS. In the CySIF trial, there was no statistically significant difference between the IFX and CYS groups in terms of treatment failure (54% in the IFX group vs 60% in the CYS group, $p = 0.49$) and colectomy rates (21% vs 18%; $p = 0.66$). [23]. Similarly, the CONSTRUCT trial showed no differences between IFX- and CYS-treated groups in terms of quality-adjusted survival, colectomy rates, time to colectomy and serious adverse events [37]. Comparable remission rates in patients treated with IFX and CYS were also confirmed in a meta-analysis [38] and in the recent study by Ordás et al. (26.2% vs 25.4%) [39]. An advantage of IFX could be that if a good response is achieved, the same therapy can be used as maintenance treatment.

Indications for surgery and outcomes

Item 4
Confirmed diagnosis of Acute Severe Colitis requires surgery in case of failure of first and second level rescue therapy. Prolonged ineffective medical therapy with delayed surgery increases the risk of overall morbidity and mortality (EL4). Surgery is a valid alternative to protracted medical therapy in patients partially responding to rescue therapy (EL5).
[Agreement: "Agree" 100%, round I]

Acute severe colitis, diagnosed with the Truelove and Witts' criteria, occurs in 12–25% of patients with UC and is a life-threatening condition. Intensive medical treatment (rescue therapy) associated with timely surgery has reduced acute mortality from 24 to 1% in referral centers [40]. Centralized care in high volume hospitals is recommended and multidisciplinary management including surgeons and gastroenterologists is highly desirable [41]. Initial treatment for acute severe colitis is high-dose IV corticosteroids. After

3 days of IV corticosteroids without benefit, patients should be considered for second-level rescue therapy (IV CYS, IFX or tacrolimus). Improvement after second-level therapy must be identified by day 7 of treatment. In case of failure, surgery is indicated. Delayed surgery in patients refractory to medical therapy is associated with higher morbidity and mortality [42].

Clinical, biochemical, endoscopic and radiological tests have been suggested as early predictors of failure of corticosteroid therapy with consequent need for second-level rescue therapy or colectomy [43].

Identifying the appropriate therapeutic procedure for patients with partial improvement after rescue therapy is difficult; there is no clear scientific evidence in the literature. However, considering the high number of patients that underwent surgery after rescue therapy (43% by 12 months in a pooled randomized trial [38, 44], the surgical option can be proposed to partially responder patients with potential advantages in terms of quality of life (QoL), symptom relief and avoidance of ongoing need for medication [3] It can also be offered to patients with recurrent acute episodes.

Item 5
A staged surgical procedure with initial subtotal colectomy, closure of the rectal stump and end ileostomy is the treatment of choice in an acute setting because of the poor general and local conditions of patients due to disease and drug' effects (EL4). A laparoscopic approach is to be preferred when performed by experienced surgeons (EL3).
[Agreement: "Agree" 94.4%, "Disagree" 5.6%, round I]

A staged procedure with subtotal colectomy and end ileostomy with rectal preservation is the procedure of choice for patients with acute severe colitis [16]. Restorative surgery [completion proctectomy with ileal pouch anal anastomosis (IPAA)] should be postponed to allow improvement of patients' health and nutritional status. A staged procedure makes it possible to rule out other causes of colitis (e.g., Crohn's disease, indeterminate, ischemic, infectious and toxic colitis) by histological examination [1].

A systematic review and meta-analysis reported a favorable effect of laparoscopic (performed by experienced surgeons) vs open colectomy in terms of the risk of infections and shorter hospital stay with no significant differences in rates of reoperation, ileus, gastrointestinal bleeding or mortality [45]. Laparoscopy is associated with only minor postoperative adhesions and this could be a major advantage for restorative surgery [46].

An open procedure is indicated in cases of toxic dilatation, perforation and severe hemorrhage [3, 47].

Item 6

Toxic megacolon, free perforation and massive lower gastrointestinal hemorrhage require emergency surgery (EL4).
[Agreement: "Agree" 100%, round II]

Five percent of patients with acute severe colitis will progress to a severe toxic colitis, defined as more than ten stools per day, daily continuous bleeding, fever (> 38.6 °C), tachycardia (> 100 bpm), anemia (hemoglobin level < 10 g/dl), leukocytosis (> 10,500/mm^3), elevated C-reactive protein (CRP) (> 30 mg/l), abdominal tenderness and distension. When dilatation of the transverse colon exceeds 6 cm, the condition becomes toxic megacolon and risk of perforation ranges from 16 to 36% [48].

Toxic colitis requires first-level steroid therapy, empirical treatment with oral vancomycin until stool is confirmed negative for C. difficile toxin and a plain abdominal X-ray 24 h after the start of therapy. If the patient's general condition improves with no clinical/radiological signs of colic perforation or dilatation, medical therapy can be continued [49].

Worsening of the clinical condition or an increase in colonic dilation and CRP levels mandates immediate surgery [50]. Perforation during toxic colitis or toxic megacolon is associated with a high mortality rate that increases if surgery is delayed [51].

In immunosuppressed patients, colonic perforation can occur without clinical signs of peritonitis or colonic dilatation [52]. Computed tomography (CT) scans may help with decision-making [53].

Severe lower gastrointestinal hemorrhage due to IBD is a rare but serious complication which, however, accounts for about 5% of indications for colectomy. After resuscitation and exclusion of other sources, massive bleeding during acute severe colitis requires urgent colectomy [3].

Restorative proctocolectomy

Indications for restorative proctocolectomy

Item 7
Restorative proctocolectomy is undertaken as an elective procedure (EL2). It has become the standard surgical procedure for patients with UC who have no sphincter disorders and no risk factors for postoperative complications (EL1).
[Agreement: "Agree" 94.4%, "Partially agree" 5.6%, round I]

Restorative proctocolectomy (RP) is considered the standard treatment in elective surgery [54, 55] for those who have no sphincter disorders and no risk factors for postoperative complications related to rectal dissection—RP is the only surgery that can avoid permanent ileostomy, remove the disease and be potentially curative [56] with excellent long-term results in terms of both functionality and QoL [57, 58]. Surgery in an elective setting is often performed in two-stages, with fashioning of an ileostomy, to minimize the risk of pelvic sepsis [59, 60]. It can also be performed as a single-stage procedure to avoid ileostomy and its complications in selected patients [60–62], although the risk of IPAA-related complications might be higher. Indications for elective surgery in UC include patients with inadequate response to medical management, steroid dependency or those who have developed relevant side effects of medical therapy [56, 59, 63], and patients with dysplasia or carcinoma found during screening colonoscopy [64]. The finding of high-grade dysplasia in a flat mucosa is an indication for proctocolectomy, since it is linked to a 40% risk of underlying malignancy. There is little debate about the need for proctocolectomy when single or multifocal locoregional colorectal cancer, high-grade dysplasia or multifocal low-grade dysplasia is found and confirmed by an expert pathologist. On the contrary, management of non-adenoma-like low-grade dysplasia remains controversial [56]. Colorectal cancer is not a contraindication to IPAA [65], but oncologic lymphadenectomy is mandatory, which could make IPAA formation difficult (e.g., oncologic ligation of ileocolic vessels might prevent the pouch from reaching the anal canal without tension). Tumor location in the left colon, presence of strictures and younger age strongly correlate with a higher risk of N+ cancer [66], suggesting that such features should be considered when dealing with UC patients. Patients with rectal cancer might be candidates for IPAA [65, 67]. If radiotherapy is required, this should be performed preoperatively [5, 68]. These cases need to be discussed by a multidisciplinary team. Absolute contraindications to reconstructive surgery are sphincter incompetence, lower rectal cancer requiring a total excision of the anus–rectum and an acute setting, due to the high risk of pelvic bleeding, sepsis and injury to pelvic nerves [59, 64]. Surgery needs to be performed in centers with surgeons who achieve an adequate volume of procedures in order to optimise long-term results and reduce the failure rate [58], which is 4.3% (95% CI 3.5–6.3) at 5 years [69, 70]. Elderly patients can be selectively offered IPAA [71]; they should be offered the procedures, and potential complications and expected functional results should be clearly explained. The final decision will be made by the patient.

Item 8
Colectomy and subsequent RP should be considered in children or adolescents with growth retardation (EL2)

[Agreement: "Agree" 83.3%, "Partially agree" 16.7%, round II]

Pediatric UC is known to have a different clinical course than adult onset UC and it is typically more aggressive and extensive at the time of diagnosis [72]. Colectomy and subsequent RP should be considered if growth failure persists despite maximal nutritional and medical therapy [4, 73–75]. RP is indicated in patients with UC in developmental age with diminished growth or signs of delayed puberty. The goal of the treatment in younger patients is to induce as well as maintain remission, improve quality of life, ensure normal growth and prevent colonic neoplastic degeneration. IPAA can be safely performed in childhood by experienced surgeons; in this case, functional results are comparable to those of patients undergoing the pelvic pouch procedure in adulthood. In the Mayo Clinic's systematic review (2412 UC/268 FAP), < 30-day short-term IPAA postoperative complication rates were low and long-term functional outcomes were good, with an overall pouch failure rate of 8% (95% CI 6–12%-median follow-up 109 months), highlighting the safety of this operation in pediatric patients [76]. Although pouchitis is more likely to occur in the pediatric population (related to a younger age at diagnosis), the majority has good long-term functional outcomes with regard to stool frequency [77, 78].

Timing of surgery

Item 9
RP or completion proctectomy with pouch construction (second stage operation) should be performed when steroids are tapered to a minimum or stopped. Prednisolone 20 mg daily or the equivalent for more than 6 weeks before surgery increases surgical complications (EL3); thus, the impossibility to wean from prednisolone 20 mg daily for more than 6 weeks before surgery should prompt a staged procedure, delaying pouch formation (EL5).
[Agreement: "Agree" 88.8%, "Partially agree" 5.6%, "Neutral" 5.6%, round II]

Prolonged preoperative steroid use is associated with an increased risk of complications after surgery and this has been demonstrated in both prospective and retrospective studies, showing a significant increase of infectious complications, which is not further worsened by the concomitant use of immunosuppressants (6-mercaptopurine/azathioprine) [79–81]. This result has also been confirmed by a meta-analysis of seven observational studies including 1532 patients, showing how patients who received higher doses of perioperative steroids (> 40 mg) had a higher risk of total complications [82]. A Belgian cohort study has also demonstrated that perioperative moderate–high doses of

corticosteroids (at least 20 mg of metilprednisolone daily) is associated with short-term pouch-specific complications (OR 10.20, $p = 0.001$), surgical site infections (OR 7.96, $p = 0.002$) and infectious complications overall (OR 5.19, $p = 0.003$), suggesting that patients on corticosteroids are better candidates for subtotal colectomy first, with pouch construction as a second-stage surgery [83]. A recent multicenter, retrospective study including 640 patients from three referral centers has also shown how the combination therapy of anti-TNF alpha and steroids is a risk factor for anastomotic leakage after restorative proctocolectomy [84].

Item 10
Patient optimization with improvement of nutritional status should also be considered prior to elective RP, and timing should be discussed among surgeons and gastroenterologists (EL5).
[Agreement: "Agree" 100%, round II]

Optimization of nutritional status is another key factor influencing surgical outcomes and should be taken into account when deciding the timing for RP or completion proctectomy and pouch. In fact, malnutrition is a known factor associated with increased surgical morbidity and mortality, as well as with a higher infection rate and longer hospital stay. It is defined as a weight loss > 10–15% in the previous 6 months, body mass index (BMI) < 18.5 kg/m^2 and serum albumin < 30 g/l [85, 86]. Thus, in elective situations, such as chronic refractory colitis despite optimal treatment, surgeons and gastroenterologists should discuss both the timing and surgical strategy, to find the balance between the need to treat disease activity and the optimization of the patient's general condition prior to surgery [87, 88].

A delay in a restorative procedure may be also considered in women desiring a pregnancy, considering the risk for tubal adhesions after pelvic surgery and its impact on fertility [89–91].

Item 11
In patients with refractory UC, biologic medications (anti-TNF alpha and anti-integrins) should be discontinued in order to reduce postoperative pouch-related septic complications before any planned elective RP (EL3). A suspension period of at least 4 weeks is advisable (EL 5).
[Agreement: "Agree" 77.7%, "Partially agree" 16.7%, "Neutral" 5.6%, v round II]

Data regarding the use of biological therapy in the preoperative period and its impact on surgical outcomes is quite conflicting, and the quality of available studies is generally low [92, 93]. A case-matched study from the Cleveland Clinic, on IFXvs no IFX in patients subsequently undergoing two-stage restorative proctocolectomy, demonstrated how the odds of early complication of patients on IFX was 3.54

times that of controls ($p = 0.004$) and the odds of sepsis was 13.8 times greater ($p = 0.08$) [94]. Nevertheless, it should be kept in mind that the use of biologics is often associated with disease severity which might account itself for the higher complication rate. On the other hand, several reports exist, mainly based on retrospective series, with opposite results, showing how biologics seem not to significantly increase morbidity in UC patients having restorative proctocolectomy [95, 96]. A meta-analysis reporting the prevalence of postoperative complications in IBD patients, who underwent surgery while receiving IFX, reported a complication rate of 35%; results from the pooled analysis reported an increase of overall and infectious complications in patients with CD, but this was not significant in UC [97]. A meta-analysis by Yang et al. [98] included five observational studies and 706 patients to address the role of preoperative IFX in determining postoperative complications in UC patients, demonstrating an increase of short-term overall postoperative morbidity and a trend toward increased postoperative infections. A more recent systematic review and meta-analysis comparing the outcomes of patients undergoing IPAA surgery for UC, with or without previous exposure to IFX, found that patients treated with biological therapy were more likely to develop early (OR 4.12, $p < 0.001$) and post-ileostomy closure pouch-specific complications (OR 2.27, $p = 0.005$) [93]. An interesting report based on insurance claims data from a large national US database also revealed how IFX use within 90 days prior to surgery was associated with higher postoperative complications [99]. Data regarding the use of vedolizumab in the preoperative period and its effect on surgical outcomes are scarce and even conflicting and no definitive conclusions can be drawn [100, 101]. Given the currently available evidence, considering a half-life for IFX of 7–18 days, a wash-out period of at least 4 weeks prior to surgery seems to be reasonable or, if clinical circumstances do not allow this, it might be better to opt for a three-stage procedure, delaying pouch formation.

Surgical approach

Item 12
Laparoscopic RP is feasible and may lead to better short term outcomes (EL2).
[Agreement: "Agree" 94.1%, "Disagree" 5.9%, round I]

A significant reduction of postoperative complications has been reported for the minimally invasive technique as well as reduced intraoperative blood loss and earlier recovery [102]. Furthermore, significantly better preservation of female fertility after laparoscopic RP has been reported [46, 102, 103].

Colectomy could be performed with single-port laparoscopic surgery (SILS), placing the port at the site of ileostomy. According to an international, multicenter study, placing the rectosigmoid stump at the same site as the ileostomy at the time of subtotal colectomy is a feasible approach and facilitates subsequent completion proctectomy and IPAA formation [104].

Reports from referral units have described the feasibility of a robotic approach to completion proctectomy and IPAA, with some advantages over laparoscopy, including multiple degrees of freedom [105] and similar short-term postoperative morbidity [106]. However, results are too preliminary to draw conclusions, and the costs associated with the procedure are considerable.

Minimally invasive transanal surgery for proctectomy and IPAA can be used if the operating surgeon has adequate expertise in the procedure [107, 108].The procedure requires careful planning [109] and dedicated training, but functional results are promising [110].

Item 13
Due to the simple construction technique and the recognized long- term functional outcomes, the J-pouch is the standard of care (EL2). A stapled anastomosis is preferred and a long rectal cuff (> 2 cm) should be avoided in order to reduce the risk of subsequent inflammation or dysplasia (EL3). Mucosectomy may result in a reduction of continence along with hand-sewn anastomosis (EL3).
[Agreement: "Agree" 94.1%, "Partially agree" 5.9%, round I]

The final pouch function is affected by pre-existing sphincter function, pouch volume and pouch compliance [111]. A J-pouch is the most common form, but alternative pouch designs have been proposed (e.g., S-, or W-pouch). Surgical complications, failure rate and mortality are similar when the different pouch designs are compared [112]. Even though J-pouches are easier and faster to perform, they are characterized by a higher number of bowel movements than W-pouches because of the intrinsic lower volume [113]. However, a randomized trial comparing J- with W-pouches found that the difference disappeared after 6 months of follow-up [114]. On the other hand, S-pouches may present difficulty in emptying due to a long efferent limb, with the necessity of intubation [115, 116], and require manual anastomosis. S-pouches can still be useful, as they reach lower than J-pouches [117, 118]. A modification of the S-pouch with a shorter efferent limb has been described [119]. To reduce the risk of cuffitis and dysplasia, the rectal remnant should be minimal (> 2 cm). A retained rectal cuff of 2 cm may require abdominal advancement of the pouch for persistent disease [120–122]. Mucosectomy and hand-sewn anastomosis may reduce continence [123].

In the event of a staged procedure, it is common practice to perform a pouchogram before loop-ileostomy closure in patients with IPAA, although recent studies question the utility of routine use of a radiological examination in asymptomatic patients with negative EUA [124, 125].

Management of short-term and long-term complications

Item 14
Early RP complications occur within 30 days post-operatively. Recognition and early treatment of early compliucations are necessary in order to preserve the long-term functioning of the pouch (EL2). Preoperative exposure to IFX increases the risk of pouch-related postoperative septic complications in the short term (EL3).
[Agreement: "Agree" 88.2%, "Partially agree" 5.9%, "Disagree" 5.9%, roundI]

IPAA is associated with a low operative mortality rate (0.4%), but it is associated with an early morbidity rate of approximately 30% [126]. Complications include anastomotic leak (discussed in "Management of a pouch leak"), pelvic sepsis that can lead to pouch failure and pouch bleeding [57, 70, 122]. In a systematic review with meta-analysis, pooled rates of pouch failure and pelvic sepsis were 4.3% (95% CI 3.5–6.3) and 7.5% (95% CI 6.1–9.1), respectively [69]. Pelvic sepsis is a serious postoperative complication and it can be defined as an abscess developing close to the anastomosis or to the blind limb, with or without a detectable defect in the pouch–anal anastomosis, and with or without a fistula [127–129]. Early-onset sepsis is linked to worse results and a delay in its treatment is responsible for pouch failure in 40% of patients [130]. An intra-abdominal abscess requires percutaneous ultrasound (US)- or CT-guided drainage and antibiotic therapy. If it is not reachable this way, EUA and drainage through the anastomosis are necessary. Relaparotomy or relaparoscopy is reserved for those cases in which CT-guided drainage or minor surgery has failed to control sepsis [64, 131]. The rate of successful salvage ranges between 75 and 85% [132]. Bleeding of the staple line is rare (1.5%) [133] and it can be controlled in 80% of patients by EUA and local irrigation with 1:200,000 adrenaline solution injected through a Foley catheter. Hemostasis can be obtained via diathermy or transanal sutures. In case of failure, revision laparotomy is required [3, 128, 134].

Item 15
Late RP complications occur after 30 days postoperatively. They include small bowel obstruction, strictures, pouch related-fistula, female infertility, pouchitis and neoplastic transformation (EL2).

[Agreement: "Agree" 88.9%, "Disagree" 11.1%, round II]

The incidence of late complications after IPAA ranges between 17 and 55% [63]. Pooled incidence rates for late complications are: small bowel obstruction 11.4 (95% CI 9.1–14.1), stricture 10.7 (95% CI 8.2–13.8) and fistula 4.5 (95% CI 3.5–5.7) [69]. Female fertility is discussed in "Functional outcome, fertility, and Qoç". Small bowel obstruction is a common complication, which is found more frequently in long-term follow-up. In a large proportion of patients, small bowel was adherent to the pelvis or to a previous stoma site. It usually resolves when treated with bowel rest, nasogastric tube and hydration, but 25% of patients require surgery [3, 128]. More often, a stricture at the IPAA level is a consequence of a previous anastomotic complication and can occur after both stapled and hand-sewn anastomosis (12.5 vs 18.2 $p = 0.20$) [135]. It is self-limiting, and can be dilated with Hegar dilators during the closure of the ileostomy with 95% pouch retention for non-fibrotic strictures [3, 128, 136]. Pouch inlet and mid-pouch strictures are less common. Pouch inlet strictures can be safely managed using a combined medical and endoscopic approach. Mid-pouch strictures should raise suspicion of CD of the pouch; they are not well studied, with both medical, endoscopic and surgical management reported as successful [136]. Operative trauma, postoperative pelvic sepsis and undiagnosed CD can result in a pouch–vaginal fistula, one of the most common causes of pouch failure. Its management includes long-term seton placement and fecal diversion, to achieve a local control of sepsis. The definitive treatment, in case of high fistula (originating > 2 cm from the dentate line), equires a transabdominal advancement of the ileoanal anastomosis, with a success rate of 80%, which drops to 60% in case of low fistula, which requires a perineal approach [64]. Pouch prolapse and torsion are rarer complications, which might require further surgery [122]. A decrease in fecal continence can occur over time [137]. Preliminary data have suggested that sacral nerve stimulation (SNS) treatment could be proposed in these patients [138]. Sexual dysfunctions can be reduced by a close rectal dissection of the rectum or with a "bad" total mesorectal excision [139]. However, it has been suggested that age at surgery might be more important than the plane of rectal dissection in predicting postoperative impotence [140].

Item 16
Neoplastic transformation in patients with UC and IPAA is very rare (EL1). Therefore, routine endoscopic surveillance is not necessary in asymptomatic patients with no primary sclerosing cholangitis and no risk factors for neoplasia, provided that the rectal cuff is < 2 cm (EL 2).

A systematic review of cuff and pouch cancer has reported a pooled cumulative incidence of pouch-related adenocarcinoma of 0.33% (95% CI 0.31–0.34) at 50 years from the diagnosis and of 0.35% (95% CI 0.34–0.36) at 20 years from IPAA [141]. Pouch-related cancers are usually diagnosed at advanced stages, and survival is poor. The risk of developing primary (de novo) pouch cancer is very low (0.02% 20 years after IPAA) [141]. Mucosectomy does not seem to abolish the risk of subsequent pouch-related cancer [142], but avoiding it increased eight times the risk of cancer arising from the residual anorectal mucosa (OR 8, 95% CI 1.3–48.7; $p = 0.02$) [141]. The presence of dysplasia or cancer on the proctocolectomy specimen increases the risk of pouch-related malignancy (OR 8.8, 95% CI 4.61–16.80) [141, 143]. Very rarely, squamous cell carcinomas and other pouch-related cancers can occur [144–146]. In a systematic review on dysplasia after RP, the pooled prevalence of dysplasia in the pouch, anal transitional zone or rectal cuff was 1·13% (range 0–18 75%) and was equally frequent in all three locations [147]. Pouchoscopy with multiple biopsy from the pouch body, rectal cuff and anal transitional zone is the main tool for detecting dysplasia during surveillance. It is recommended annually in high-risk pouch patients, such as patients 10 years after UC diagnosis, with a preoperative diagnosis of UC-associated neoplasia, with type C histological changes, with a long retained rectal stump, in addition to those who have chronic inflammatory conditions of the pouch, a family history of colorectal cancer or concomitant sclerosing cholangitis [3, 148]. Patients with high-grade dysplasia of the anal transitional zone and pouch-related adenocarcinoma should be offered abdominoperineal excision of the pouch [141]. Conversely no specific follow-up is recommended in asymptomatic patients with no risk factors after IPAA [2, 3, 5].

Management of a pouch leak

Item 17
Anastomotic leak after ileal pouch–anal anastomosis (IPAA) should be treated conservatively when possible. Anastomotic dehiscence is associated with worse functional outcomes in the long term (EL3).
[Agreement: "Agree" 94.1%, "Partially agree" 5.9%, round I]
Item 18
An ileostomy should be performed if not already present, and percutaneous or surgical drainage of the presacral abscess or the application of vacuum-assisted closure therapy have been described as treatments (EL4). Redo anastomosis or redo pouch are feasible

procedures and should be performed when necessary in tertiary centres (EL3).
[Agreement: "Agree" 100%, round I]

The incidence of anastomotic leak after IPAA was shown to be 15% in a recent multicenter study [84]. Pelvis sepsis occurred in 9.4% of patients in an analysis of the UK pouch registry [70]. Anastomotic leak after IPAA has been proven to be associated with significantly worse functional outcomes in the long term [127, 149]. Conventional management includes the construction of an ileostomy if not already present, followed by transanal or percutaneous drainage of the presacral abscess. Single-center studies using transanal vacuum-assisted closure therapy showed good short-term outcomes in terms of complete healing and ileostomy closure rate [150, 151]. A recent report demonstrated that this treatment was associated with improved pouch function and a lower incidence of pouch failure compared to conventional management [152].

Should conservative treatment of the leak fail, alternative and more invasive procedures include transanal or transabdominal redo IPAA, with or without redo or revision of the existing pouch [122, 153]. The redo and revision procedures may be associated with higher rate of complications and worse outcomes, should be chosen according to the type and severity of the leak and performed in tertiary centers [154].

Functional outcome, fertility, and Qoç

Item 19
RP can impair sexual function with a risk of impotence and loss of ejaculatory function in men and dyspareunia in women. A plane of dissection close to the rectum or an incomplete mesorectal excision are advised, unless rectal cancer is present (EL2). In young female patients RP can increase the risk of subfertility (EL1). A laparoscopic approach seems to be associated with better preservation of female fertility than an open approach (EL3) Functional results of open and laparoscopic approaches are similar (EL3).
[Agreement: "Agree" 88.8%, "Partially agree" 5.6%, "Disagree" 5.6%, round II]

Men who undergo RP for UC may have retrograde ejaculation and erectile dysfunction due to the pelvic dissection which may make conception difficult [155]. However, no change or even an improvement in sexual function occurs after surgery [156]. The risk of infertility could increase by two- to threefold in patients having RP compared with patients receiving medical management [157, 158]. Adhesions involving the Fallopian tubes, hydrosalpinx and destruction of fimbria, are the most frequent mechanisms for female infertility after surgery [159]. The real entity of this problem is still controversial, with reduced fertility ranging

from 30 to > 70%. A recent population-based analysis [160] showed that RP leads to a reduction in birth rates in females and higher fertility in males. There are many recent studies that report how infertility rates after laparoscopic RP are significantly lower than those seen after open surgery [103, 161] and this can be explained by a reduction of pelvic adhesions. However, similar rates of infertility have also been reported in patients undergoing either laparoscopic (61.1%) or open (65%) IPAA [91, 162].

Item 20
There are in sufficient data about QoL level afterRP. Conversely health related QoL improves after RP and is no different from that of the general population (EL2). RP and total proctocolectomy with ileostomy appear equivalent in terms of overall health-related QoL (EL3).
[Agreement: "Agree" 70.6%, "Partially agree" 11.8%, "Neutral" 11.8%, "Disagree" 5.9%, I round]

With the introduction in clinical practice of RP, great interest has been shown in improving QoL and many reports have been published to define this [163]. Despite this, if one considers the accepted definition of QoL [164], namely " an individual's perception of his or her position in life in the context of the culture and vague systems in which he or she lives in relation to goals, expectations, standards and concerns", there are no publications that have actually analyzed this aspect of QoL [165]. On the contrary, many studies have evaluated the so-called "Health-related QoL" (HRQoL) that is a part of QoL, defined as the "patients' own evaluation of functioning in the physical, psychological and social domains" [166]. HRQoL is measured using fewer domains and it is not as extensive as QoL. HRQoL has been analyzed in medium- and high-quality studies, which concluded that it improved after RP for UC and reached a level similar to that of the healthy population [165]. Patients with UC who undergo proctocolectomy appear to have good HRQOL, regardless of which reconstructive option they undergo (proctocolectomy with ileostomy or IPAA). This is probably related to the fact that the removal of the diseased colon itself improves HRQoL after surgery [167].

Pouchitis

Item 21
The diagnosis of pouchitis requires a combination of symptoms plus endoscopic and histological abnormalities (EL3). Several factors have been associated with pouchitis, including pANCA, pancolitis, primary sclerosing cholangitis, being a non-smoker., low fruit intake, and use of nonsteroidal anti-inflammatory drugs (NSAIDs) (EL3).

Structural issues of the pouch should be ruled out in patients with pouchitis [EL5]
[Agreement: "Agree" 94.1%, "Partially agree" 5.9%, round I]

Pouchitis is a non-specific inflammation of the ileal reservoir and is the most common complication after an IPAA for UC [1]. It can occur in up to 50% of patients 10 years after IPAA for UC, but its cumulative incidence is much lower, ranging from 0 to 10%, in patients with an IPAA following familial adenomatous polyposis (FAP) [1]. The reasons for a higher frequency of pouchitis in UC patients remain unknown. A recent study demonstrates that UC patients have more peri-pouch fat than FAP patients, which might, in part, explain their difference in prevalence of pouchitis and chronic antibiotic-refractory pouchitis [168].

Symptoms include increased stool frequency and liquidity, abdominal cramping, urgency, tenesmus and pelvic discomfort, but rectal bleeding, fever and extra-intestinal manifestation may also occur [1]. After IPAA, fecal incontinence may occur in the absence of pouchitis, but is more common in patients with pouchitis. The differential diagnosis for pouch dysfunction in patients with IPAA should include CD of the pouch, cuffitis, ischemia, collagenous pouchitis, C. difficile or cytomregalovirus pouchitis, non-specific ileitis caused by NSAIDs and irritable pouch [1].

Pouchoscopy and pouch mucosal biopsy should be performed in patients with symptoms compatible with pouchitis, to confirm the diagnosis [1, 64, 128]. Biopsies should be taken from the pouch mucosa and from the afferent limb above the pouch, but not along the staple line. Evaluation of pouchitis disease activity and response to treatment requires use of validated indices, but substantial reliability was observed only for the endoscopic items of ulceration and ulcerated surface in the pouch body [169]. Introduction of a template improved documentation of flexible pouchoscopy significantly [170]. Endoscopic features include diffuse erythema, edema, granularity, friability, bleeding, loss of vascular pattern, mucous exudates, hemorrhage, erosions and ulceration [1]. Erosions and/or ulcers along the staple line do not necessarily indicate pouchitis [1].

The etiology of pouchitis is unknown. Reported risk factors for pouchitis include extensive UC, backwash ileitis, extra-intestinal manifestations (especially primary sclerosing cholangitis), being a non-smoker and regular use of NSAIDs [1, 171]. Interleukin-1 receptor antagonist gene polymorphisms and the presence of pANCA are also associated with pouchitis. Another risk factor is the use of antidepressants or anxiolytics, which suggests that these patients may have had irritable bowel syndrome even before pouch surgery.

Most importantly, mechanical causes of pouchitis must not be overlooked, including ischemia (which can be responsible for segmentary pouchitis) or problems with pouch

emptying, which can result in stasis, bacterial overgrowth and inflammation. Structural/mechanical problems of the pouch can benefit from revisional surgery, avoiding unnecessary and predictably ineffective medical treatment [122, 128, 172–178].

Item 22
Acute pouchitis is successfully treated in the majority of patients with metronidazole or ciprofloxacin (EL2). Ciprofloxacin seems associated with less side effects; but side effects of long-term antibiotic therapy are frequent (EL2). Antidiarrheal drugs may reduce the number of daily liquid stools, independently of pouchitis (EL5).
[Agreement: "Agree" 100%, round I]

As reported by Magro et al. [1], pouchitis can be divided into remission (normal pouch frequency) or active pouchitis (increased bowel frequency with endoscopic appearance and histology consistent with pouchitis) on the basis of symptoms and endoscopy. Active pouchitis may then be divided into acute or chronic, depending on symptom duration [1].

Acute pouchitis management is largely empirical, antibiotics being the mainstay of treatment [1]. Both metronidazole and ciprofloxacin significantly decrease the Pouchitis Disease Activity Index (PDAI) score, but there seems to be significantly greater benefit with ciprofloxacin than with metronidazole in terms of the total PDAI, symptom score, and endoscopic score, as well as fewer adverse events. For the treatment of acute pouchitis, ciprofloxacin appears to be more effective in inducing remission than metronidazole [1]. The use of long-term antibiotics must be weighed against potential complications associated with pouchitis and antibiotics [179].

A direct causal relationship between individual microbiota changes and inflammation has not yet been established, but manipulation of the ileoanal pouch microbiota may be a novel therapeutic target to explore [180].

Item 23
A combination of two antibiotics is usually effective in chronic pouchitis (EL3). Alternative treatments include oral budesonide, oral beclomethasone dipropionate (EL3), and topical tacrolimus (EL3), whereas IFX is effective for the treatment of chronic refractory pouchitis (EL4). Should pouchitis be refractory to IFX, adalimumab, vedolizumab and ustekinumab may represent alternative treatments (EL4).
[Agreement: "Agree" 82.3%, "Partially agree" 11.8%, "Disagree" 5.9%, round I]

The threshold for chronicity is symptom duration of >4 weeks [1], with up to 10% of patients developing chronic pouchitis and an even smaller subgroup having refractory pouchitis. Chronic pouchitis may lead to pouch failure.

Combination antibiotic therapy or oral budesonide may be effective. Moreover, oral beclomethasone dipropionate has been shown to be effective in chronic refractory pouchitis [1]. As regards anti-TNF agents, there is clearly more benefit in CD-like complications of the pouch than in refractory pouchitis, highlighting the need to differentiate these two entities both in daily practice and clinical trials [181]. Recent studies suggest that vedolizumab is effective and can be safely used for chronic antibiotic refractory pouchitis patients [182–184]. Lastly, ustekinumab appears to be a safe and effective treatment for chronic pouchitis and CD of the pouch in biologic-naïve patients and those who failed anti-TNF or vedolizumab therapy [185].

Pouchitis recurs in more than 50% of patients [1]. Potential complications of pouchitis include abscesses, fistulae, stenosis of the IPAA and adenocarcinoma of the pouch [1]. The latter complication is rare and almost only occurs when there is pre-existing dysplasia or carcinoma in the original colectomy specimen [141, 144, 146].

Well designed, adequately powered studies are needed to determine the optimal therapy for the treatment and prevention of pouchitis.

Pregnancy and delivery in patients with ileal pelvic pouches

Item 24
Patients with IBD have normal fertility, except for women after IPAA because of the impact of pelvic surgery (EL2). Pre-conception counselling is very important (EL5). A laparoscopic approach can decrease infertility rates (EL2).
[Agreement: "Agree" 94.4%, "Partially agree" 5.6%, round II]

Infertility is defined in most studies as inability to conceive after 1 year of unprotected intercourse; recently this is defined as subfertility suggesting that follow-up in case series should be prolonged.

Most studies included both patients with end ileostomy or RP/IPAA and considered open surgery, with infertility rates ranging from 20 to 90% (in the general population, the fertility rate is 2–8%) [186].

There are two retrospective studies on IPAA [91, 187] with large cohorts (300 and 306 women) showing a severe impairment of fertility with high need for in vitro fertilization (IVF) (In the first study, the infertility rate was 56% post-IPAA compared with 38% pre-IPAA).

One metanalysis reviewing infertility in IPAA showed an infertility rate of 63% with a relative risk of infertility of 3.91 (95% CI 2.06–7.44) [157].

Some authors reported lower rates of infertility with laparoscopic surgery [161, 188]. However, a recent study [162]

conducted on 161 women with IPAA, who tried to conceive, found no difference in infertility rates between laparoscopic (61.1%) and open IPAA (65%, $p = 0.69$); laparoscopic IPAA was associated with a significantly reduced time to conceive (3.5 months vs 9 months, respectively, log-rank $p = 0.01$). In recent years, some techniques have been proposed to prevent infertility during surgery, including oophoropexy, intraoperative, adhesiolysis, interposition of the omentum, pedicled graft to separate ovaries from pelvis [189, 190].

Risk factors for infertility are older age (over 40) and blood perioperative transfusions [191].

Preoperative counselling regarding fertility is necessary. Embryo storage is a possibility for future IVF [192, 193].

Item 25
Pregnancy can cause temporary alterations in pouch function (mainly incontinence), above all in the third trimester, with resolution of symptoms after delivery (EL2.) IPAA does not affect childbirth outcome (EL2).
[Agreement: "Agree" 94.4%, "Partially agree" 5.6%, round II]

Pregnancy has a direct effect on pouch function, above all in the third trimester, through the abdominal wall distension and enlargement of the uterus [194, 195]. In a series of 43 women followed at the Mayo Clinic, there was an increase of stool frequency, incontinence and pad usage with return to prepartum status after delivery [196]. All studies on the outcome of pregnancy in women post-IPAA report a favorable outcome [186, 197]. There is no scientific evidence about specific vitamin deficiencies during pregnancy in these patients, so their folate intake does not differ from that of healthy women.

Item 26
There is no correlation between pouch function and route of delivery (EL2). The route of delivery is a multidisciplinary choice, taking inro account the clinics, patient preference and obstetric factors (EL5). IPAA is a relative indication for elective cesarean section (EL5).
[Agreement: "Agree" 94.4%, "Partially agree" 5.6%, round II]

One of the most controversial aspects of IPAA surgery has been the preferred route of delivery. There is no consensus regarding the optimal method of delivery, even if nowadays the preferred method is cesarean section to prevent sphincter injury rather than a true obstetric indication (present in fewer than 50%) [198].

Cesarean delivery is associated with all the complications of abdominal surgery including adhesion formation and prolongation of recovery, besides the risk of intraoperative injury to the pouch. Also, cesarean section during labor may not prevent anal incontinence [199].

However, vaginal delivery may increase the risk of pudendal nerve damage anal sphincter injury, thus increasing incontinence [200].

Although several studies of pregnancies after IPAA have shown vaginal delivery to be as safe as cesarean delivery in terms of pouch function, physiological measurements and imaging studies suggest that there is a higher risk of sphincter injury with vaginal than with cesarean delivery. One large study comparing pouch function after vaginal delivery and cesarean section did not report any differences [201]. However, Remzi et al. observed an increased number of sphincter injuries (anterior sphincter defect) after vaginal delivery (50% after vaginal delivery vs 13% after caesarian section, p 0.012), confirmed with US [202].

The latest guidelines of the European Crohn's and Colitis Organisation [193] and the Toronto Consensus Statement [203], designate only active perianal disease as an absolute indication to cesarean section, IPAA is considered as a relative indication.

In a retrospective series from the USA analyzing the percentage of cesarean sections in women with IBD, all IPAA patients had a cesarean delivery (ten patients out of a total of 65 UC patients) [204].

Other treatment options

Colectomy with ileorectal anastomosis (IRA)

Item 27
Total colectomy with IRA is a reliable and less invasive option with lower morbidity in patients with a relatively healthy rectum compared to IPAA. Adequate rectal compliance is mandatory for good functional outcomes: urgency may be more frequent and invalidating than after IPAA (EL 4).
[Agreement: "Agree" 88.8%, "Partially agree" 5.6%, "Disagree" 5.6%, round II]
Item 28
IRA does not compromise subsequent IPAA. The main advantage is the preservation of fertility and sexual function in young patients (EL3).
[Agreement: "Agree" 88.2%. "Neutral" 5.9%. "Disagree" 5.9%, round I]
Item 29
Patients should be informed about the need for close endoscopic surveillance after IRA due to the risk of rectal dysplasia/cancer, as well as about the high overall failure rate (EL 3).
[Agreement: "Agree" 88.2%. "Neutral" 11.8%. round I]

Total colectomy with ileorectal anastomosis (IRA) is a relatively simple procedure as compared with IPAA, with low morbidity (8–28%) [205]. IRA may be a reliable option in patients with a relatively healthy rectum (minimal disease or disease responsive to medical therapy without dysplasia) without high risk of subsequent dysplasia (primary sclerosing cholangitis, a family history of CRC, prior colon cancer or dysplasia). A normally distensible rectum with adequate compliance is mandatory for good functional results. Patients with IRA have fewer bowel movements and less night time soiling, but increased urgency (68% vs 21%) compared with patients with IPAA. HRQoL may be similar [206].

IRA should be offered to young patients who desire to defer the risk of sexual and fertility disturbances following pelvic dissection. Even if laparoscopy has been associated with lower rates of infertility in some studies [103, 161], during laparoscopic IPAA pelvic dissection is still performed. To date there is no conclusive, strong evidencethat the laparoscopic approach actually reduces the infertility risk [91, 162]. At present, infertility risk should be still discussed with the patient before laparoscopic IPAA. Rectal excision in benign disease in men may lead to impotence (4%) and loss of ejaculation (17%); it causes sexual dysfunction in up to 28% of women [207]. Brown et al. [3] suggested that women of reproductive age who have not yet had children should be offered IRA although laparoscopy seems to reduce the infertility rate.

IRA may be a good stoma-free option for teenagers, allowing a quick return to school and avoiding potentially severe complications of IPAA that can have a severe negative impact on psycho-social development.

The main causes of IRA failure are proctitis, poor function, high dysplasia or cancer. In the largest multicenter cohort, the failure rate at 10 and 20 years was 27% and 40%, respectively. Severe acute colitis as an indication for colectomy was associated with a lower failure rate than refractory colitis [208]. A meta-analysis showed a cumulative incidence of 2% and 14% for rectal carcinoma at 10 and 20 years, respectively. A history of CRC was the most important risk factor, and several studies did not report rectal cancer within 10 years of diagnosis [143]. There are no clear and universally accepted surveillance strategies (endoscopic technique, biopsy protocol, time interval) [209]. Primary sclerosing cholangitis, dysplasia and colon cancer justify special attention in rectal surveillance [208]. Flexible endoscopy with multiple biopsies of the rectum is generally recommended from 8 to 10 years post-IRA [210].

Continent ileostomy

Item 30

Continent ileostomy (Kock's pouch) may be an alternative to end-ileostomy in selected patients who are not candidates for an IPAA or in whom an IPAA cannot be performed. (EL4).
[Agreement: "Agree" 88.9%, "Partially agree" 11.1%, round II]

Whenever an ileoanal pouch anastomosis is not possible or has failed, the option of a continent ileostomy should be discussed with carefully selected patients [211, 212]. A restorative Ileoanal pouch anastomosis may be contraindicated in patients referred for redo ileoanal pouch or in patients with previous sphincter injury or in patients with anal disease or cancers extending to the anal canal. Similarly, a continent ileostomy may be needed in case an ileoanal pouch anastomosis cannot be safely achieved because of inadequate mesenteric length [128, 213]. Careful patient's selection is mandatory in view of the high rate of complications and reoperations.

Item 31
Continent ileostomy (Kock's pouch) represents an alternative in patients with an existing conventional ileostomy when the existing ileostomy is having an adverse effect on QoL (EL4).
[Agreement: "Agree" 82.3%, "Partially agree" 5.9%, "Neutral" 5.9%, "Disagree" 5.9%, round I]

The overall goal of continent ileostomy surgery must be to provide better QoL for the patient than that which would be obtained with a conventional end ileostomy [213].

A study from Ojerskog et al. [214] compared HRQoL in patients before and after conversion from a conventional end ileostomy to a continent ileostomy. They demonstrated improved working capacity after conversion to a continent ileostomy and reported that the greatest effect was seen in leisure activities and quality of sexual life.

According to a study from the Cleveland Clinic, HRQoL was lower in all scales in patients with an end ileostomy compared with those with a Kock's continent ileostomy [215]. Patients must be fully informed of the complication and reoperation rates of continent ileostomy surgery.

Item 32
Complications and reoperation rates are high following continent ileostomy (Kock's pouch) surgery (EL3)
[Agreement: "Agree" 94.1%, "Partially agree" 5.9%, round I]

Many surgeons have discredited the Kock's pouch procedure given the high rate of reoperation reported: approximately 50% of patients need reoperation, with nipple valve sliding being the most common indication [1]. A published series of 330 patients from the Cleveland Clinic [215] reports an overall reoperation rate of 70% with nipple valve

sliding being the most common indication, and with 10- and 20-year pouch survival rates of 87% and 77%.

Proctocolectomy with terminal ileostomy

Item 33
Compared toIPAA, proctocolectomy with end ileostomy is a relatively simple one stage procedure associated with lower morbidity (EL3).
[Agreement: "Agree" 94.1%, "Disagree" 5.9%, round II]
Item 34
Proctocolectomy with end ileostomy should be always discussed with the patient as a reliable option: although proctocolectomy with terminal ileostomy and IPAA may potentially provide similar QoL (EL3).
[Agreement: "Agree" 100%, round II]
Item 35
Correct preoperative soma siting and proper stoma construction may positively affect patients' QoL after proctocolectomy with end ileostomy (EL4).
[Agreement: "Agree" 100%, roundII]

Proctocolectomy with end ileostomy (PCEI) is a one-stage, relatively straightforward procedure, compared with IPAA. PCEI should be always discussed with the patient as reliable surgical option. A systematic review reported equivalent QoL after IPAA and PCEI [167]. PCEI could be proposed in case of predictive risk of poor pouch function (e.g., weak sphincters), increased risk of pouchitis (primary sclerosing cholangitis, extraintestinal manifestations, NSAID use), and pre- or postoperative pelvic radiotherapy.

The long-term complications following PCEI are generally less frequent and severe than those after IPAA (24% vs 52%) [216], with stomal problems, delayed perineal wound healing, small bowel obstruction and nerve injury being the commonest. Anal mucosectomy and excision of the rectum at the anorectal junction may eliminate the problem of perineal wound healing [217]. A recent review highlighted the relevance of close rectal dissection in benign disease, particularly in transanal-mesorectal surgery. Perimuscular dissection may reduce nerve injury and perineal wound healing problems leaving a smaller pelvic dead space [218].

The closure of the lateral gut fixing the right preserved mesocolon to the anterior abdominal wall may reduce the risk of obstructing twisting ileostomy [219]. A recent review reported 42 cases of adenocarcinoma at the end ileostomy in UC patients. This uncommon complication may suggest the importance of inspection in long-standing ileostomy [220].

HRQoL after PCEI will strictly depend on a well-constructed stoma [221]. It is mandatory to pay special attention to preoperative stoma site marking and ileostomy technique. The enterostomal therapist plays a crucial role [222].

A recent RCT showed that intracutaneously sutured ileostomies may reduce stoma leakage in contrast to transcutaneously sutured ones (52.4% vs 41.4%), but are associated with similar overall stoma related complications and HRQoL [223]. A relatively recent systematic review [167] confirmed that both IPAA and PCEI may have equivalent HRQoL.

Segmental resections

Item 36
According to recent data, segmental resection may be a safe surgical option in a highly selected group of UC patients, especially the elderly with a limited duration and extent of disease. A limited colonic resection can preserve colorectal function and QoL. Further evidence is needed to support this surgical strategy. (EL 4).
[Agreement: "Agree" 72.2%, "Partially agree" 22.2%, "Neutral" 5.6%, round II]

Total proctocolectomy with or without pouch reconstruction is the ideal option for UC patients needing surgery is. Recent data suggest that in highly selected patients more conservative surgery could be an option.

It has been suggested that segmental resections might be an alternative in selected patients, with no increased risk of colorectal cancer-associated mortality [224].

The risk of metachronous colorectal carcinoma appears to be low [225], so segmental resections are particularly attractive for those patients who have been diagnosed with UC later in life and who have a milder burden of disease.

Khan [226] reported in a recent retrospective study on 24 patients with colorectal cancer in UC who underwent segmental resection compared with 35 patients who underwent total proctocolectomy. No patient who underwent a partial colectomy developed a new cancer in the retained colonic segment during the follow- up period of 7 years.

The anatomical extent of disease is known to be correlated with the risk of colorectal cancer, so younger patients with pancolitis who are diagnosed with colorectal cancer are surely not suitable for segmental resection and need total proctocolectomy.

Even if the reported literature is very limited, recent data suggest that in elderly patients with comorbidities, high-impact surgery such as proctocolectomy with IPAA or end ileostomy may be too aggressive and it may be reasonable to offer a more conservative resection with close medical and endoscopic follow-up. The patients should undergo active surveillance with at least annual endoscopy with multiple biopsies [227].

A previous colonic resection does not appear to affect subsequent IPAA, so this surgical option could be kept in

mind for young patients as "temporary" solution with regard to fertility and sexual function [228, 229].

Conclusions

Even if the overall agreement rate was acceptable, the committee felt that there are several areas of UC management that need further attention.

These include the role of segmental resections, continent ileostomy and preoperative medications.

Future studies should assess these aspects of treatment.

The resulting recommendations are to be intended as suggestions and need to be applied carefully, after taking into account the individual features of each patient and after a clear discussion with the patient about all the available options for each specific condition, and realistic expectations.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval The present paper was exempt from approval.

Informed consent Informed consent was not needed for this study. No procedures on patients were performed by the authors for this study.

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