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ECCO Guidelines/Consensus Paper

# European evidence based consensus on surgery for ulcerative colitis



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## 1. Introduction

The goal of this consensus initiated by the European Crohn's and Colitis Organisation (ECCO) was to establish European consensus guidelines for the surgical treatment of ulcerative colitis. The strategy to reach the consensus involved several steps and follows the standard operating procedures for consensus guidelines of ECCO. An open call for chairs and participants for this consensus was made (see acknowledgements and [www.ecco-ibd](http://www.ecco-ibd)). Participants were selected by the Guidelines' Committee of ECCO (GuiCom) on the basis of their publication record and a personal statement. Four working groups (WGs) were formed: WG 1 on the preoperative phase, WG 2 on the intraoperative phase, WG 3 on the postoperative phase and WG 4 on special situations. Participants were asked to answer relevant questions on current practice and areas of controversy related to the surgical treatment of ulcerative colitis based on their experience as well as evidence from the literature (Delphi procedure).<sup>1</sup> In parallel, the WG members performed a systematic literature search of their topic with the appropriate key words using Medline/PubMed/ISI/Scopus and the Cochrane database, as well as their own files. Provisional guideline statements (with supporting text) were then written by the WG chairs based upon answers to the questionnaire and were circulated among the WG members, prompting discussions and exchange of literature evidence. The proposed statements and the supporting text were submitted to an online platform for online discussion and two online voting procedures among all Consensus participants for the first voting procedure

and also for all national representatives of ECCO for the second voting procedure. The WGs finally met in Belgrade on September 25th 2013 for a final face-to-face discussion and to vote and consent on the statements. Technically this was done by projecting the statements and revising them on screen until a consensus was reached. Consensus was defined as agreement by more than 80% of participants, termed a Consensus Statement and numbered for convenience in the document. The level of evidence was graded according to the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence ([http://www.cebm.net/mod\\_product/design/files/CEBM-Levels-of-Evidence-2.1.pdf](http://www.cebm.net/mod_product/design/files/CEBM-Levels-of-Evidence-2.1.pdf)). The final manuscript was written by the WG chairs (WB, GS, AS, AD'H) in conjunction with the WG members and revised for consistency by T.Ø. This consensus guideline will be published in JCC and posted on the websites of ECCO. An update of the current guideline is planned in about 4 years. The European Society for Coloproctology has endorsed the process of producing this consensus.

The surgical treatment of ulcerative colitis was covered in the Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part2: Current management, published in JCC 2012. However it was felt that the content lacked some surgical depth and practical advice thus this first consensus on the surgical management of UC has been produced under the leadership of Surgical-ECCO. The present document is to be seen as complementary to the surgical section published in the 2012 consensus. Some consensus statements are modified or expanded and others are entirely new.

The section on pouchitis is not further elaborated here since the 2012 consensus covers this topic adequately. Apart from this the present document can be read as a stand alone document on surgical aspects of ulcerative colitis. However reading this surgical consensus in conjunction with the previous ECCO consensus documents on Ulcerative colitis will give a more comprehensive understanding of the diagnosis and treatment of the disease.

Development of IBD surgery as a surgical specialization has been rapid driven by its multidisciplinary complexity. We have seen the emergence and establishment of laparoscopic techniques, recently expanding to the use of “robots” and single port access. New variants of natural orifice surgery such as the Trans Anal Minimal Invasive Surgery (TAMIS) for proctectomy with or without an anastomosis are being explored and developed. These latter innovative techniques are not covered in this consensus since they are still at an early development stage. Parallel to this is an ever expanding range of innovative new instruments allowing us to operate more effectively and hopefully safer. The development of guidelines and consensus in IBD surgery is hampered by a lack of robust evidence in terms of randomized studies. Furthermore one of the main outcome variable in surgery, the surgeons themselves is seldom included in the evaluation of different methods and approaches. Thus the evidence base from which to draw conclusions is rather soft and this current situation is reflected in the views of the panelists and their interpretation of the literature.

## 2. Pre-operative phase

### 2.1 Indications for surgery

#### 2.1.1 Acute severe ulcerative colitis

##### 2.1.1.1. ECCO Statement 1A

Patients with bloody diarrhea  $\geq 6$ /day and any signs of systemic toxicity (tachycardia  $>90$  bpm, fever  $>37.8^\circ\text{C}$ , Hb  $<10.5$  g/dL, or an ESR  $>30$  mm/h.) have severe colitis and should be admitted to hospital for intensive treatment (EL4)

Acute severe ulcerative colitis is a potentially life-threatening condition.<sup>2,3</sup> Patients with acute severe colitis should be admitted to the hospital for appropriate investigation, close monitoring, and intensive treatment under the care of a multidisciplinary team including a specialist gastroenterologist and colorectal surgeon. The simplest, best validated and most widely used index for identifying severe UC remains that of Truelove and Witts<sup>4</sup>: any patient who has a bloody stool frequency  $\geq 6$ /day and a tachycardia ( $>90$ bpm), or temperature  $>37.8^\circ\text{C}$ , or anaemia (haemoglobin  $<10.5$ g/dL), or an elevated ESR ( $>30$ mm/h) has severe ulcerative colitis. Only one additional criterion in addition to the bloody stool frequency  $\geq 6$ /day is needed to define a severe attack.<sup>5</sup> The therapeutic approach to these patients is elaborated in Statement 5D of the second European evidence-based consensus on the diagnosis and management of ulcerative colitis.<sup>6</sup> From the surgical standpoint, it is important to emphasize the need for proper intravenous fluid and electrolyte replacement, nutritional support if the patient is malnourished, and blood transfusion to maintain haemoglobin above 8–10g/dL. All patients admitted with severe colitis require appropriate investigations to confirm the diagnosis and exclude enteric infection including flexible sigmoidoscopy and biopsy to confirm the diagnosis and exclude cytomegalovirus and other infections.

### 2.1.2 Joint treatment

#### 2.1.2.1. ECCO statement 1B

Patients are best cared for jointly by a gastroenterologist and colorectal surgeon from admission (EL5) Symptoms, physical examination and signs of systemic toxicity should be closely monitored. Any clinical deterioration should prompt consideration of an emergent colectomy

A multidisciplinary approach between the gastroenterologists and surgeons (preferably colorectal surgeon) looking after the patient is essential.<sup>6</sup> At hospital admission the surgeon should be promptly contacted, and the patient should be informed about surgical options in case of medical treatment failure. During hospital stay, the patient will be best managed with a multi-disciplinary clinical approach. Symptoms, physical examination and blood tests should be closely monitored to detect signs of systemic toxicity early. An objective evaluation of disease together with abdominal examination findings and toxicity parameters should be used in the decision-making process. Should any clinical deterioration in patients symptoms, abdominal examination findings or toxicity appear during intravenous immunosuppressive therapy, a prompt emergent colectomy should be considered. Complications such as perforation, toxic megacolon and severe gastrointestinal haemorrhage should equally prompt immediate colectomy.

#### 2.1.2.2. ECCO Statement 1C

Recommended treatment for severe ulcerative colitis is intravenous corticosteroids [EL1]. All patients should receive thromboprophylaxis (EL5)

Intravenous corticosteroids remain the mainstay of conventional therapy.<sup>6,7</sup> Corticosteroids are generally given intravenously using methylprednisolone 60mg/24h or hydrocortisone 100mg four times daily.<sup>6</sup> The most recent ECCO guidelines<sup>6</sup> should be followed in regard to medical management.

Subcutaneous prophylactic heparin or low molecular weight heparin is indicated to reduce the risk of venous thromboembolic events (VTE) which has been shown to be increased in patients with IBD compared to controls, especially during a disease flare.<sup>8</sup> Prophylactic VTE treatment should be withheld only in patients with severe lower intestinal bleeding.

#### 2.1.2.3. ECCO Statement 1D

The response to intravenous corticosteroids is best assessed objectively around the third day (EL2). Treatment options including colectomy should be discussed with patients with severely active UC not responding to i.v. corticosteroids. Second line therapy with i.v. infliximab, is appropriate (EL1). I.v. ciclosporin may be an alternative in thiopurine naïve patients (EL1). If there is no improvement within 7 days of pharmacological therapy, colectomy is recommended (EL2), without prolonging further medical therapy, in order to avoid an increase in postoperative morbidity. Third line medical therapy for acute severe ulcerative colitis is currently not indicated (EL4)

Prolonged intravenous immunosuppressive therapy is associated with increased morbidity and mortality following subsequent surgery.<sup>9,10</sup> In addition, extending intravenous corticosteroids therapy beyond 7 to 10 days carries no additional benefit.<sup>5</sup> For this reason, response to treatment should be evaluated early in the course of first-line treatment with i.v. corticosteroids, around the third day of treatment.<sup>6</sup> Simple, objective measures are needed to aid decision-making. Clinical markers such as stool frequency and body temperature, biological markers such as CRP, erythrocytes sedimentation rate, and radiographic and endoscopic appearance can be used to predict response. The correlation between these signs and the chance of colectomy is elaborated in recommendation 5F of the second European evidence-based consensus on the diagnosis and management of ulcerative colitis.<sup>6</sup> These objective measures should aid the sound clinical judgment of an IBD gastroenterologist jointly with a colorectal surgeon. It is important to ensure that the surgical options, as well as the therapeutic alternatives for second line rescue of steroid refractory disease (cyclosporine, tacrolimus, and infliximab) are considered early (on or around day 3 of corticosteroid therapy), since a delay in the decision making process, with patients remaining on ineffective medical therapy, results in a higher surgical morbidity.<sup>9,10</sup>

Infliximab has been shown to be an effective salvage therapy in patients with severe UC refractory to iv corticosteroids.<sup>11,12</sup> Cyclosporine has also been shown to be effective second line therapy in the treatment of severe UC.<sup>12,13</sup> When considering the use of cyclosporine in patients with acute severe colitis despite treatment with an appropriate dose of immunomodulation such as thiopurine, it is important to consider whether there are options for long term maintenance of remission.

In case of no improvement with second line therapy, colectomy is generally recommended to avoid further increase in surgical morbidity and potential mortality.<sup>9,10</sup> Randall et al.<sup>10</sup> retrospectively reviewed a prospectively maintained database of patients who underwent surgery for acute severe ulcerative colitis. On multivariate analysis, only duration of in-hospital medical treatment was associated with increased rate of postoperative complications with odds ratio of 1.12 (CI 1.00 – 1.24). Maser et al.<sup>9</sup> reported 10% mortality in a small group of 10 patients receiving third line of immunosuppression following failure of both intravenous corticosteroids and second line “salvage” treatment. In light of the current literature, colectomy should be strongly recommended in case of failure of a second line medical treatment within the timeframe of seven days. Reports of success of a third line immunosuppressive therapy<sup>14</sup> should be balanced against potential risks of these treatments, bearing in mind that acute severe colitis is a potentially life threatening disease. In light of the current literature, third line intravenous immunosuppressive treatment should be reserved for highly selected cases, after careful discussion between the patient, gastroenterologist and colorectal surgeon, in a specialist referral centre, preferably within a clinical trial.

### 2.1.3 Chronic refractory ulcerative colitis

#### 2.1.3.1. ECCO Statement 2

Patients' nutritional status and general conditions (including tapering of steroids when possible) should be optimized prior to elective surgery in order to decrease postoperative morbidity. The precise timing and type of surgery is essential and should be determined by both gastroenterologist and surgeon (EL5)

In elective situations (often in refractory colitis, chronically active despite optimal medication regimen, or corticosteroid dependent disease) the time lag between the decision for surgery and the procedure itself is usually several weeks, and depends on clinical practice and a variety of different factors. The patient's general condition, including nutritional status and the use of immunosuppressive medications is of great importance not only regarding surgical results and complication rate, but also for the decision on surgical strategy (restorative proctocolectomy with ileal pouch-anal anastomosis versus subtotal colectomy with end-ileostomy). For this reason, colorectal surgeon and gastroenterologist should jointly make any attempt to optimize the patient's general condition prior to surgery, and plan the surgical procedure balancing both the need to treat the patient's active disease, and the need to optimize patient's general conditions, reducing surgical risks, as pre-operative corticosteroid and immunosuppressive therapy can impact postoperative complications.<sup>15,16</sup>

Weaning off corticosteroid treatment prior to surgery (provided that this does not result in a significant exacerbation of the inflammatory disease) and improvement of nutritional status, both directly affecting the risk of surgical complications, are determinant factors for surgical outcomes optimization.<sup>15,16</sup>

The effect of biologic therapies on surgical complications is still debated,<sup>17-19</sup> while thiopurines do not increase the risks of surgery (see Statement 4D and 5).

The time lapse between indication and surgery (usually some weeks) can be used by the managing clinician for the gradual tapering of steroid dose, but may not completely eliminate the effect of anti-TNF therapy on the immune response: the half-life of the antibody is variable,<sup>20</sup> and duration of its immunosuppressive effects still remains undefined. Surgery should not be delayed in patients who recently received anti-TNF therapy. But in the absence of definitive evidence, biologic therapy is often included among the factors favouring a three-step surgical approach.

### 2.1.4 Dysplasia/carcinoma in UC

#### 2.1.4.1. ECCO Statement 3A

Presence of low grade or high grade dysplasia should be confirmed by an external second pathologist (EL1)

Even if dysplasia can be divided, according to the grade of neoplastic change, into 3 morphologic categories (indefinite, low grade-LGD, or high grade-HGD),<sup>21</sup> it is accepted that it evolves along a progressive (continuous) scale rather than in discrete categories. There is a significant interobserver variability in interpretation of the presence and the grade of dysplasia even among experienced gastrointestinal pathologists,<sup>22,23</sup> given the chronic inflammatory changes in the mucosa and the effect of concomitant medical therapies. Such limitations in the assessment of dysplasia have led to the recommendation that histological slides should be reviewed by a second expert gastrointestinal pathologist, prior to any surgical decision.<sup>6</sup>

#### 2.1.4.2. ECCO Statement 3B

Non-visible high-grade dysplasia warrants a recommendation of colectomy because of the risk of a concomitant or future colorectal cancer (EL2)

In three studies including a limited number of cases with HGD (from 6 to 24 patients) flat HGD dysplasia is associated, in 42–67% of cases, with synchronous concomitant colorectal cancer (CRC).<sup>24–26</sup> In a review of collected data from prospective surveillance trials: 15 of 47 patients (32%) with HGD developed CRC upon further follow-up.<sup>24</sup> Data from the St Mark's surveillance programme confirmed the risk, since 2 of 8 patients (25%) with HGD without colectomy progressed to CRC.<sup>27</sup> Overall, the immediate and subsequent risk of CRC in patients with flat HDG is large enough to warrant a recommendation for colectomy.<sup>6</sup>

#### 2.1.4.3. ECCO Statement 3C

The current evidence is insufficient to assess the balance of risks and benefits of colectomy for flat low-grade dysplasia. The decision to recommend colectomy or continued surveillance is best tailored to the individual after careful discussion (EL5)

Indications for the management of flat LGD in UC are less clear than for HGD: many studies do not report the outcome of LGD distinguishing between raised and flat lesions.

In three studies with a small number of patients operated on for LGD (n=10, 11, 16) 20%, 27% and 19% of the patients, respectively, were found to have CRC.<sup>24,26,27</sup> In a meta-analysis of 20 studies, for patients with LGD detected on surveillance, the overall risk of developing CRC was increased 9-fold and the risk of developing CRC or HGD was increased 12-fold.<sup>28</sup> In this same meta-analysis, the positive predictive value for progression from LGD to HGD or CRC was 14.6%.<sup>28</sup> High rates of progression have generally been reported in retrospective studies.<sup>26,29</sup> In contrast, prospective studies reported no increased progression rates in patients with LGD compared to patients without dysplasia.<sup>30,31</sup>

In conclusion, although the rate of synchronous CRC is lower for LGD than HDG, it is still considerable. The current evidence is insufficient to assess the balance of risks and benefits of colectomy for flat LGD. Thus, the decision to undergo colectomy versus continued surveillance in patients with flat LGD should be individualised and carefully discussed between the patient, the gastroenterologist and the colorectal surgeon. Colectomy will eradicate the risk of CRC, but if a patient, correctly informed about the risks, is unwilling to undergo colectomy, tight surveillance is strongly recommended.<sup>32</sup>

#### 2.1.4.4. ECCO Statement 3D

Adenoma-like raised lesions can be adequately treated by polypectomy provided the lesion can be completely excised, shows absence of dysplasia at the margins of the specimen, and there is no evidence of flat dysplasia elsewhere in the colon, either adjacent to, or distant from, the raised lesion (EL2)

#### 2.1.4.5. ECCO Statement 3E

Patients with non-adenoma-like dysplastic raised lesions, should undergo colectomy, regardless of the grade of dysplasia detected on biopsy analysis because of the high association with metachronous or synchronous, carcinoma (EL2)

Raised lesions with dysplasia in colonic segments affected by UC can be macroscopically divided into those resembling non-IBD-related sporadic adenomas (adenoma-like raised lesions) and those, which do not appear like sporadic adenomas (non-adenoma-like raised lesions). Regardless, all raised lesions should be completely endoscopically resected whenever possible and the surrounding area should undergo biopsy: surgery should be considered if dysplasia is present in the surrounding mucosa or if the mass cannot be completely resected.<sup>6</sup> Polyps in colonic segments proximal to UC involvement should be treated as sporadic adenomas.

#### 2.1.4.6. ECCO Statement 3F

The recommended operation in case of dysplasia/cancer is proctocolectomy with ileal pouch-anal anastomosis, taking into account oncologic principles (EL5). There is no evidence to support an oncologic advantage of mucosectomy and hand sewn anastomosis over stapled anastomosis in this setting. (EL2) Colectomy with ileorectal anastomosis could be considered in selected patients (EL5)

In patients with a preoperative diagnosis of dysplasia/cancer proctocolectomy should include oncologic lymphadenectomy with ligation of the vessels at their origins. Restorative surgery is obtainable in most patients, while an abdomino-perineal excision with end-ileostomy is warranted in patients with very low rectal cancer where adequate distal clearance cannot be obtained or in whom the anal sphincter is damaged. No data support an oncologic superiority of mucosectomy over stapled anastomosis in the presence of dysplasia or CRC: cancers are reported both in patients with a stapled anastomosis as well as in those who have had a mucosectomy, and there is evidence that a mucosectomy does not necessarily clear all remnants of mucosa.<sup>33</sup> In addition, there is evidence that the stapled technique is as safe under these circumstances as hand sewn.<sup>34–36</sup> However it seems reasonable, when the indication for surgery is cancer or high grade dysplasia of the lower rectum, to perform a mucosectomy and anastomosis at the dentate line.

In highly selected cases of HGD or CRC located in a proximal colonic segment, in presence of a mild rectal disease, colectomy with ileorectal anastomosis may be considered, following careful discussion with the patient regarding the increased risk of neoplastic transformation, as high as 8.7% at 25-year disease duration for ileorectal anastomosis compared to 1.8% for IPAA.<sup>37</sup>

## 2.2 Risk factors for colectomy and for post-operative complications

### 2.2.1 Perioperative risk assessment

#### 2.2.1.1. ECCO Statement 4A

Patients with coexisting primary sclerosing cholangitis have a high risk of developing pouchitis (EL3)

#### 2.2.1.2. ECCO Statement 4B

Patients within inflammatory bowel disease type unclassified are potential candidates for proctocolectomy and ileoanal pouch surgery. However, a subtotal colectomy with ileostomy is recommended to allow proper histological evaluation of the colectomy specimen (EL5). Completion proctectomy with a pouch is standard in patients with ulcerative colitis, and could be considered in selected patients with Crohn's disease, well informed of a higher failure rate



A number of variables have been associated with a higher colectomy rate in patients with ulcerative colitis (UC). Although the identification of early predictors of colectomy would be potentially useful, none of the described risk factors are currently directing medical therapy.

### 2.3 Clinical presentation

More severe disease activity,<sup>38–40</sup> more extensive UC<sup>38,41–45</sup> presence of extra-intestinal manifestations,<sup>46</sup> a younger age at diagnosis,<sup>44,47</sup> and non smoking,<sup>42,45,48–50</sup> have all been associated with higher colectomy rates. Furthermore, in a North-American trial using the Nationwide Inpatient Sample 2004, anemia, requirement for blood transfusion, malnutrition, and total parenteral nutrition were independent predictors of colectomy.<sup>51</sup>

In a Belgian cohort study evaluating the efficacy of cyclosporine, patients refractory to azathioprine, showed a significant higher colectomy rate on the long-term.<sup>52</sup> This observation was later confirmed in other cohort studies.<sup>53–55</sup>

### 2.4 Baseline serological, fecal and genetic markers

Elevated C-reactive protein, elevated fecal calprotectin, and decreased albumin levels have been associated with colectomy.<sup>39,43,56–59</sup> Other serological markers, such as perinuclear antineutrophilic cytoplasmic (pANCA) and anti *Saccharomyces cerevisiae* antibodies (ASCA) have not been associated with long-term colectomy risk.<sup>57,60,61</sup>

Genetic variations in HLA, MDR1 and MEKK1 have also been associated with colectomy risk in UC, but are lacking confirmation.<sup>53,60,62</sup>

### 2.5 Baseline endoscopic disease activity

In the pre-biological therapy era, the IBSEN cohort demonstrated that patients with mucosal healing at one year had a lower risk of colectomy at 5 years.<sup>63</sup> In two trials evaluating the efficacy of IV steroids and IV cyclosporine in acute severe UC, severe endoscopic lesions at baseline were associated with a significantly higher colectomy rate during follow-up.<sup>56,64</sup>

### 2.6 Short-term clinical, biological and endoscopic response to treatment

The well-known Oxford criteria in patients with acute severe UC were based on a trial evaluating predictors of bad outcome on day 3 of IV steroid therapy.<sup>65</sup> Of note, 85% of patients with more than eight stools on day 3, or a stool frequency between three and eight together with a CRP >45mg/l, would require colectomy. Therefore, rescue therapy with cyclosporine, infliximab or surgery seems warranted if the Oxford criteria are met.

Several investigators showed that in outpatients with moderate-to-severe UC receiving infliximab as well as in hospitalized patients treated with infliximab for acute severe IV steroid-refractory UC, both clinical response and mucosal healing in the short-term were predictive of colectomy-free survival in the longer-term.<sup>39,59,66–68</sup> Furthermore, in a Belgian cohort study, the absence of a normalization of CRP levels in the short-term (absence of biological response) was also associated with the need for colectomy in the longer-term.<sup>57,60</sup> Similarly, a normalization of fecal calprotectin levels ( $\leq 100\mu\text{g/g}$ ) after induction therapy with anti-TNF agents was predictive of sustained clinical remission after one year, but an influence on colectomy-free survival was not reported.<sup>59</sup>

## 2.7 Serum levels

Higher IFX serum levels have been associated with a better long-term outcome of IFX treated patients, including lower colectomy rates.<sup>69</sup> A recent Belgian study, demonstrated that serum IFX levels  $\geq 3\mu\text{g/mL}$  at week 14 were predictive of colectomy-free survival.<sup>57</sup>

### 2.7.1 Risk factors for postoperative complications

Pouchitis is the most common post-operative complication in patients undergoing pouch surgery.<sup>70</sup> Genetic, demographic, clinical and serological risk factors for pouchitis have been extensively studied. Reported risk factors for pouchitis include younger age at colectomy,<sup>60</sup> smoking status,<sup>71,72</sup> regular use of NSAIDs,<sup>71,72</sup> extensive ulcerative colitis,<sup>73</sup> the presence of backwash ileitis,<sup>60,74</sup> and extraintestinal manifestations, particularly primary sclerosing cholangitis.<sup>60,75,76</sup>

Variations in TLR1, TLR9, CD14, ILR1N and NOD2 have been associated with the development of pouchitis.<sup>60,76,77</sup> Seropositivity for pANCA,<sup>71,78,79</sup> anti-CBir1 flagellin,<sup>78</sup> antibodies to outer membrane porin,<sup>60</sup> or chitobioside carbohydrate-specific antibodies<sup>60</sup> seems to be another risk factor for pouchitis.

### 2.7.2 Preoperative medical therapy

#### 2.7.2.1. ECCO Statement 4C

Prednisolone 20 mg daily or equivalent for more than six weeks prior to surgery is a risk factor for surgical complications (EL3). Therefore, corticosteroids should be weaned if possible. Failure to wean from prednisolone 20 mg daily or equivalent for more than six weeks prior to surgery, should postpone pouch construction to a second stage (EL5)

There are good data suggesting that corticosteroids (CS) increases short-term complications after colectomy for UC. One study compared patients' outcomes after colectomy in regard to the administration of steroids, with or without concomitant azathioprine/ 6-MP. There was a significant higher risk of any (odds ratio=3.69) or major infectious complications (odds ratio=5.54) after the procedures in patients who were taking steroids at the time of surgery.<sup>80</sup> Another study demonstrated higher incidence of postoperative infectious complications in patients who received a higher cumulative dose of steroids before they were submitted to pouch surgery.<sup>81</sup> In a Belgian cohort study from, moderate-to-high dose of CS (at least 20mg of prednisolone at first surgery) was associated with short-term postoperative pouch-specific complications (OR 10.20 [95% CI: 2.47–42.12] (p=0.001), surgical site infectious complications (OR 7.96 [95% CI: 2.17–29.22] (p=0.002) and infectious complications overall (OR 5.19 [95% CI: 1.72–15.66], (p=0.003).<sup>82</sup> These studies suggest that patients with corticosteroids at surgery may have lower complication rates with subtotal colectomy first, avoiding a pouch construction at the first operation.

#### 2.7.2.2. ECCO Statement 4D

Pre-operative thiopurines do not increase the risk of postoperative complications (EL3). Colectomy for ulcerative colitis immediately following or in the medium term after the use of cyclosporin appears to have no higher rate of postoperative complications (EL3)

One study from the United States demonstrated that after pouch surgery for UC, previous exposure (from 7 up to 30 days before the operation) to azathioprine/ 6-MP did not affect the rates of short-term and late postoperative complications.<sup>83</sup> The same pattern was observed in the study from Abera et al., previously discussed.<sup>80</sup>

#### 2.7.2.3. ECCO Statement 4E

As long as the data surrounding pre-operative use of anti-TNF agents remain conflicting it is recommended that surgeons avoid the use of single stage proctocolectomy and ileoanal pouch in anti-TNF treated patients. (EL 5)

Preoperative use of infliximab does not appear to increase the risk of infectious complications. There may however be an increase in short-term surgical complications. One retrospective observational study from the Mayo Clinic (USA) demonstrated that previous (ever) exposure to IFX increased the rate of complications in pouch surgery. In this series, they found that the IFX patients had higher risk of anastomotic leakage, pouch-specific and infectious complications than the controls. Again, IFX was identified as the only independent factor related to infectious complications (OR=3.5).<sup>18</sup> Another study from the Cleveland Clinic (Ohio, USA) demonstrated similar results. They found that the odds ratio for early complications was 3.54 (p=0.004), for sepsis was 13.8 (p=0.011) and for late complications was 2.19 (p=0.08). They concluded that previous (ever) IFX should lead the patients to a 3-stage procedure regarding the high risk of poor outcomes.<sup>17</sup>

On the other hand, other studies revealed opposite results. Data from Belgium, demonstrated that high doses of steroids and pouch surgery without a defunctioning ileostomy, but not IFX (within 12 weeks of surgery), were independent factors for higher complication rates after restorative proctocolectomy with ileal pouch anal anastomosis.<sup>82</sup> Retrospective data from USA<sup>84</sup> and from Denmark<sup>85</sup> (both with IFX within 12 weeks of surgery) also concluded that IFX did not increase morbidity after surgical treatment for UC. The largest sample of patients studied with the aim of detecting the influence of IFX on surgical complications in UC came from Denmark, in a nationwide registration with more than 1200 patients that included 199 IFX (within 12 weeks of surgery) exposed individuals; they also found no significant increase in complications after surgery on the IFX previously exposed patients.<sup>86</sup> A study from the Netherlands suggested that patients submitted to a one-stage procedure (pouch construction without a diverting ileostomy) had a higher rate of pelvic sepsis if they had previous IFX, suggesting again that in these patients a total colectomy with end ileostomy should be considered.<sup>87</sup> A meta-analysis including most studies regarding this topic cited in this section demonstrated that recent or ever used IFX as an independent factor increased the rate of total postoperative complications (OR =1.80), but not significant if only looking at inflammatory complications.<sup>88</sup>

#### 2.7.2.4. ECCO Statement 4F

Where possible, preoperative physiological optimisation and application of the principals of enhanced surgical recovery appear to convey an outcome advantage in terms of hospital stay and post operative morbidity (EL 1)

Many studies have demonstrated the advantages of enhanced recovery protocols after colorectal surgery, with a shorter hospital stay and lower overall complication rates.<sup>89</sup> These principles can be applied in the surgical management of ulcerative colitis, but specific studies in the management of this disease are still needed.

## 2.8 Intraoperative phase

### 2.8.1 General

#### 2.8.1.1. ECCO Statement 5A

Laparoscopic surgery is safe and feasible for the elective surgical treatment of ulcerative colitis and confers better short-term outcomes at the expense of longer operative times and increased procedural costs (EL 2). Long-term advantages of a minimally invasive approach are a reduction in adhesion formation and a better-preserved fecundity in addition to a reduced incidence of hernias (EL 3)

Laparoscopic IPAA is an appealing alternative to open surgery and it is performed with increasing frequency in many centers. Feasibility and safety of the laparoscopic technique has been shown in various studies.

A RCT in 2004 failed to demonstrate differences in short term benefit or in quality of life for laparoscopic versus open surgery.<sup>90</sup> However, this study only included operations, which were laparoscopic assisted. A second RCT designed in 2006 to compare blood loss and need for perioperative blood transfusion during totally laparoscopic versus open IPAA had severe difficulties recruiting patients.<sup>91</sup> A meta-analysis published in 2007 showed a longer operative time and less blood loss in laparoscopic surgery but no significant differences in postoperative adverse events between laparoscopic and open surgery.<sup>92</sup> In 2009, a Cochrane review was published,<sup>93</sup> demonstrating no difference in mortality or complications between open and laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous polyposis. Operative time was longer but cosmesis better for the laparoscopic approach. In 2011 data from an ASCRS database were published reporting a significant reduction in both major and minor complications in laparoscopic IPAA.<sup>94</sup> The laparoscopic approach was associated with advantages including reduced intraoperative blood loss and earlier recovery as demonstrated by shorter length of hospital stay. Recently two reports on a significant better preservation of female fecundity after laparoscopic IPAA were published.<sup>95,96</sup> This is in line with a report on a reduction in visceral and pelvic adhesions after laparoscopic IPAA.<sup>97</sup>

#### 2.8.1.2. ECCO Statement 5B

The optimal management of the remaining rectum following colectomy for acute severe colitis is unclear. The data to support mucus fistula, Hartmann's pouch or subcutaneous position of the distal bowel remain conflicting (EL 4)

The management of the remaining rectum following colectomy for acute severe colitis includes three options: intra-peritoneal rectal stump closure (Hartmann's pouch), creation of a mucous fistula by exteriorizing the rectosigmoid remnant or to position the closed

rectosigmoid remnant in the subcutaneous tissue in an attempt to prevent peritonitis in the event of a stump blow out.

Rectal stump leakage resulting in pelvic sepsis occurs in 6–12%.<sup>98</sup> Trans-anal drainage of the Hartmann's pouch could be considered to prevent acute rectal stump blowout. The creation of a mucous fistula (in the left iliac fossa, suprapubic or in the same opening as the ileostomy) necessitates a longer rectosigmoid stump.

There are no randomized studies that compare the three techniques. Three retrospective studies were published. The largest compared Hartmann's pouch (n=99) to subcutaneous placement of the closed rectal stump (n=105).<sup>99</sup> There was no difference in pelvic sepsis but a significant higher wound infection rate for the last group. A second study compared local and systemic morbidity related to the rectal stump in the three mentioned groups.<sup>98</sup> In this study, the incidence of pelvic sepsis was higher in the Hartmann group (12%) compared to a mucous fistula or subcutaneous stump placement. Persistent rectal disease was more common in the Hartmann group and subsequent pelvic dissection was more difficult compared to the other two techniques. In a third study Hartmann's pouch (n=27) was retrospectively compared to subcutaneous stump placement (n=10) which resulted in 2 anastomotic leaks in the Hartmann group and 3 secondary stump dehiscence's in the subcutaneous group.<sup>100</sup>

### 2.8.2 Surgical approach in urgent colectomy

*The considerations below are not applicable to the emergent setting with an unstable patient and the results of urgent colectomy cannot be generalized to critically ill patients in need of an emergent colectomy.*

#### 2.8.2.1. ECCO Statement 5C

A laparoscopic approach in emergency colectomy results in shorter hospital stay and in reduction of postoperative infectious complications (wound infections, deep abscess) and where appropriate expertise exists should therefore be the approach of choice (EL 2)

When an emergency colectomy for fulminant ulcerative colitis is necessary, it is possible to perform a laparoscopic or open colectomy. In a recent systematic review of laparoscopic versus open colectomy for non-toxic colitis, laparoscopic surgery resulted in less wound infections and intra-abdominal abscesses and a shorter hospital stay.<sup>101</sup> However, these results may be altered in critically ill patients in need for an emergency colectomy.

In recent years a few studies have been published focusing on laparoscopic emergency colectomy in acute ulcerative colitis. The first study from the Mayo Clinic used a prospective database to determine safety, feasibility, and short-term outcomes of three-stage minimally invasive surgery for fulminant ulcerative colitis. Of 50 procedures 72% was performed with laparoscopic-assisted and 28% with hand-assisted techniques. Completion proctectomy with ileal pouch-anal anastomosis was performed in 42/50 patients with a low conversion rate (2.3%). During the postoperative period there were no anastomotic leaks or mortality.<sup>102</sup> In a second study short-term outcomes of laparoscopic versus open total abdominal colectomy and end ileostomy for severe UC were compared. Using a prospective database, 72 patients with fulminant ulcerative colitis undergoing surgery were investigated. Thirty-one patients underwent a laparoscopic colectomy and 41 patients an open colectomy. The laparoscopic group had less narcotic usage, faster return of bowel function and shorter length of hospital stay. Furthermore the laparoscopic group underwent subsequent restorative proctectomy

49days sooner and ileostomy closure 17days sooner than the open colectomy group.<sup>103</sup> In a third study a retrospective analysis was performed to compare peri- and postoperative complications in laparoscopic and open colectomies in an urgent or emergency setting. Of 90 patients 29 were operated laparoscopically. Laparoscopic subtotal colectomy was associated with improved cosmesis, reduced intraoperative blood loss, negligible wound complications, and shorter hospital stay in comparison to the open colectomy group.<sup>104</sup> All three studies conclude that emergency laparoscopic colectomy for fulminant ulcerative colitis is a safe and feasible alternative to open colectomy and offers some clinical benefits. However, it should be noted that these studies were performed in high-volume hospitals with significant laparoscopic and inflammatory bowel expertise.

### 2.8.3 Rectal dissection

Most surgeons perform a modified TME dissection today (=anterolateral close rectal dissection in combination with a posterior dissection in the TME plane).

The main argument for close dissection is to minimize the risk of

#### 2.8.3.1. ECCO Statement 5D

In absence of dysplasia or cancer of the rectum a close rectal resection can be performed. Anterolateral resection posterior to Denonvillier's fascia might preserve the autonomic nerves better and thus minimize the risk for urogenital complications (EL 4)

damage to the pelvic autonomic nerves and to better preserve sexual function.<sup>105–108</sup>

Sexual dysfunction affects up to 3% of men following pouch surgery and therefore sperm banking could be recommended.<sup>105,106</sup> It has also been postulated that mesorectal preservation diminishes septic complications.<sup>109</sup> The idea is based on the premise the retained mesorectal fat would allow for better pelvic filling and reduces the risk of a presacral sinus if the anastomosis leaks.

#### 2.8.4.1. ECCO Statement 5E

The J-pouch is the standard of care due to its simplicity to construct and good long-term function outcome (EL 2)

### 2.8.4 Pouch and anastomosis

A good pouch function depends mostly on patient's sphincter function, pouch volume and compliance.<sup>110</sup> Several pouch designs have been described: S-, J- and W-pouches.<sup>111</sup> A meta-analysis including 1519 patients reported no significant difference in surgical outcome in terms of pelvic sepsis, early pouch failure or mortality.<sup>112–114</sup> Operating time is shorter for J-pouches. The number of bowel movements tends to be higher in J-pouches, as a consequence of a smaller pouch volume.<sup>112,115–121</sup> The difference in number of bowel movements diminishes after longer follow up, and disappears mostly in long follow up series.<sup>115,119</sup> Pouch design is therefore predominantly of importance during the pouch maturation period. S-pouches have a higher incidence of evacuation difficulties due to the longer outlet limb of the pouch, which frequently makes pouch intubation necessary.<sup>112,113,118</sup> All pouch offer the patient a similar ability to defer defecation.<sup>114</sup> Only very few patients experience urgency, which is an important drawback on quality of life.

#### 2.8.4.2. ECCO Statement 5F

In performing pouch surgery a stapled anastomosis is preferred as it results in decreased nocturnal incontinence. However a long rectal cuff/retained rectum (>2 cm) with a subsequent risk for inflammation and/or dysplasia should be avoided (EL 3)

The retained rectal stump in a stapled anastomosis should be minimal (<2cm) to minimize the risk of subsequent cuffitis and/or dysplasia at the site of the rectal remnant. It is recognized that a stapled anastomosis may fail technically during the procedure and therefore all surgeons performing pouch surgery should be competent to perform a hand-sewn endo-anal anastomosis. Mucosectomy and hand sewn anastomosis results in poorer continence (even at 12months of follow-up), lower anal resting pressures and a permanent loss of the recto-anal inhibitory reflex.<sup>122-125</sup> Recovery of the recto anal inhibition reflex (RAIR) has been linked to less nighttime soiling.<sup>126</sup> However all sensation levels and related pressures are unaffected by the recovery of RAIR.<sup>122,127</sup>

Despite the absence of clear evidence a recent survey demonstrates that a low-stapled ileo anal-pouch anastomosis has become the standard of care (>95%).<sup>128</sup>

In a more recent meta-analysis including only randomized data no advantage in functional or manometric outcome was noted in a stapled anastomosis versus hand-sewn anastomosis group.<sup>129</sup>

### 2.8.5 Alternative procedures

#### 2.8.5.1. ECCO Statement 5G

In patients not amenable to restorative surgery a total proctocolectomy with permanent ileostomy is the procedure of choice. An intersphincteric perineal dissection may improve perineal wound healing (EL 4)

Intersphincteric proctectomy (ISP) has been recommended since the early 60s. There is lack of randomized data (ISP versus conventional proctectomy) however it appears logical to spare the pelvic floor and EAS (external anal sphincter) to provide optimal pelvic floor closure and reduce the risk of perineal wound healing problems. In 1984 Zeitels et al. and Leicester RJ et al. recommended a more widespread use of the technique, as perineal healing was more constant.<sup>130,131</sup> In 2000 Adam and Shorthouse recommended intersphincteric dissection and selective use of omental transposition for optimal outcome in UC and reported no persistent perineal sinus (0/27 patients).<sup>132</sup>

#### 2.8.5.2. ECCO Statement 5H

Kock's continent ileostomy is a valid alternative for end ileostomy. Even though half of the patients with a continent ileostomy will need one or more reoperations, long-term survival for the pouch as well as quality of life are good. Motivated patients who are candidates for Kock's pouch should be referred to centers with expertise in this procedure (EL3)

The Kock's pouch (continent ileostomy) was devised by Nils Kock in 1969.<sup>133</sup> The procedure became popular until IPAA was introduced in the 1980's.

Today, Kock's pouch is not an alternative to IPAA, but is an alternative to conventional end-ileostomy for patients with failed IPAA, or for those who are not candidates for IPAA (sphincter injury etc.) and for those who have considerable problems with an ileostomy (leakage, skin problems, etc.).

The Kock's pouch has been discredited by many surgeons due to a high reoperation rate. About half the patients will need reoperation, nipple valve sliding is the most common indication. However, most series today have a 10year continent pouch survival around 90%.<sup>134,135</sup> Quality of life with a Kock's pouch seems superior to an end-ileostomy. According to a study from the Cleveland clinic patients with an end-ileostomy were more than twice as likely to report social, work, and sexual restrictions compared to Kock's continent ileostomy.<sup>134</sup>

#### 2.8.5.3. ECCO Statement 5I

Under optimal circumstances ileorectal anastomosis is a reasonable alternative to IPAA. Outcome advantages such as lower morbidity, preserved female fecundity need to be weighed against the need for rectal surveillance and subsequent proctectomy in 50% of cases (EL 3)

The good long term functional outcome after IPAA and a rather unpredictable functional outcome after ileorectal anastomosis on a noncompliant and inflamed rectum and the subsequent fear of rectal cancer explains the reluctance of many surgeons to perform IRA for ulcerative colitis today.<sup>136</sup> IRA consists of a less complex procedure with lower morbidity rates and with reasonable clinical results in highly selected patients. Patients considered for IRA are usually those presenting with a relatively spared rectum (or a healed rectum under medical therapy), good rectal compliance and normal sphincter tone. In these selected patients the defecation habits are almost the same as for the IPAA patients, however urgency is more common in most published series with IRA (22-33%).<sup>137,138</sup> Urgency is the most common cause of failure after IRA. The reported probability of having a functioning IRA has ranged from 74 to 84% at 10years and from 46 to 69% at 20years.<sup>136,137,139,140</sup>

### 2.8.6 Loop ileostomy

#### 2.8.6.1. ECCO Statement 5J

Evidence suggests that a temporary loop ileostomy at the time of ileo-anal pouch surgery reduces the risk for clinical leakage by 50%. (EL 2) However, in selected patients a temporary ileostomy can be avoided (EL 2)

IPAA can be performed as a one, two or three stage procedure. In emergent conditions a total colectomy with end ileostomy will precede the pouch procedure. In elective cases the procedure is performed either as a two (with a defunctioning ileostomy) or one stage procedure. The reported risk for anastomotic leakage and pelvic sepsis in expert centers is approximately 10%.<sup>141</sup> Defunctioning ileostomy reduces the septic consequences of leakage but also the rate of leakage itself. No randomized trials have been reported.

Proponents of a two-stage procedure claim a reduced morbidity and mortality of anastomotic leakage and pelvic sepsis.<sup>142-144</sup> Pelvic sepsis not only can have immediate potential life threatening consequences but also is associated with pouch dysfunction and ultimate



pouch failure.<sup>145</sup> Temporary diversion results in improved physiological recovery of the anal canal. Stoma closure is safe with low morbidity.<sup>146</sup> Furthermore patients seem to value the advantages of the pouch more after having experienced an ileostomy.

Proponents of a one-stage procedure claim a reduced overall hospital stay and reduced morbidity (linked to an ileostomy: e.g. skin problems and dehydration, and linked to ileostomy closure). Diversion ileitis is avoided and continued use of the anal sphincter would result in better function. Furthermore sepsis is well managed without diversion in majority of cases and without impact on pouch function in the long term.<sup>147-149</sup>

There seems to be a tendency to promote a selective approach based on patient characteristics, which has recently been reported in a 5-point nomogram.<sup>128,148,150-153</sup> Some surgeons recommend pouch intubation with regular irrigation and claim the same benefits as for diversion but without the complications of a stoma.<sup>99</sup>

There have been several reports on risk factors for pelvic sepsis after IPAA: although not universally accepted most common predictors for morbidity are: age, male patients, preoperative corticosteroid use and hand sewn anastomosis. A recent meta-analysis comprising 17 reports and including almost 1500 patients<sup>100</sup> (765 without ileostomy and 721 with ileostomy) found that although anastomotic leakage was more common in the group without the stoma at the time of pouch surgery (OR: 2.37; 95% CI, 1.39–4.04;  $p=0.002$ ) pouch related sepsis was not different for both groups. Furthermore both stricture of the pouch-anal anastomosis (OR, 0.31; 95% CI, 0.10–0.98;  $p=.045$ ) and pouch failure (OR, 0.30; 95% CI, 0.12–0.74;  $p=.009$ ) were significantly reduced in the no-stoma group. Small bowel obstruction was more common in the stoma group (OR, 2.37;  $p=0.002$ ).

In summary, restorative proctocolectomy for ulcerative colitis should be covered with a loop ileostomy especially in the presence of risk factors. Temporary intubation of the pouch should be considered in those selected patients with a one-stage procedure.

## 2.8.7 Volume of surgery

### 2.8.7.1. ECCO Statement 5K

There is clear evidence that high volume surgeons in high volume units achieve lower pouch failure rates as well as better pouch salvage (EL 2) Centralization should lead to refer patients to centers that perform at least 10 pouches per year (EL 5)

It has been demonstrated in numerous publications that volume of surgery and specialization has a beneficial effect on patient outcome. Recent studies show significantly lower mortality rates in high volume hospitals for various surgical procedures.<sup>154</sup> In a 2007 systematic review the authors conclude that in particular high surgeon volume was associated with improved patient outcome.<sup>155</sup> Two studies were published that focused on learning curve in ileal pouch-anal anastomosis surgery and volume analysis for restorative proctocolectomy. The first study used a risk-adjusted cumulative sum (CUSUM) model to monitor outcomes in IPAA surgery performed by 12 surgeons in a single center from 1983 to 2001.<sup>156</sup> It was calculated that the learning curve to perform stapled IPAA surgery for trainee staff is 23 cases and for hand sewn IPAA surgery: 31 procedures. In a recent observational study in England, the effect of institutional and surgeon caseload on outcome following pouch surgery was analyzed.<sup>157</sup> Thirty percent of institutions performed less than 2 procedures a year and 91.4% performed 20 or fewer procedures during 8 years. High-volume centers (>8.4 procedures annually) reported significant less pouch failure than mid- and low-volume centers.

## 2.9 Postoperative phase

### 2.9.1 Risks and complications

#### 2.9.1.1. ECCO Statement 6A

Emergency colectomy for Ulcerative Colitis has population based mortality and morbidity rates of 5-8% and 27-51% respectively (EL 3). In specialized centres with a timely surgical policy mortality rates of less than 1% can be achieved (EL2)

Emergency colectomy for acute colitis in ulcerative colitis is associated with a mortality rate of 5–8% and morbidity rates of 27–51%.<sup>158,10,159,160</sup> Higher mortality rates are to be expected when the colon is perforated.<sup>161</sup> Risk factors increasing morbidity are prolonged conservative treatment and hospitalization prior to surgery<sup>10,162</sup> advanced age and co-morbidity.<sup>163</sup> According to the systematic review<sup>158</sup> the most frequent complications are wound infection (18.4%), intra-abdominal abscess (9.2%), small bowel obstruction (6.2%), ileostomy related complications (5.5%), hemorrhage (4.6%). Septicemia was observed in 18% of the patients, pneumonia in 11%, thromboembolic complications in 7.2%, pulmonary embolism in 7% of patients. In a systematic review abdominal abscesses are reported at a frequency of 3.4% and 12.6% after a laparoscopic and open emergency colectomy respectively.<sup>101</sup> A publication bias might explain the favourable results.

#### 2.9.1.2. ECCO Statement 6B

A leaking ileoanal anastomosis usually needs to be defunctioned if not done so at the initial operation (EL5)

Mortality after elective IPAA is rare (0–1%). Postoperative complications are high though. The incidence of early postoperative complications in a high volume center was 33.5% in a large retrospective study (3707 patients).<sup>70</sup> More recent metaanalysis show a tendency to a decrease in pouch failure rate and pelvic sepsis rate (4.3% resp. 7.5%)<sup>164</sup> which might reflect surgery in more specialised centers.

Weston et al. meta-analysed the leak rate of restorative proctocolectomy with or with an ileostomy.<sup>151</sup> The leakage rate was diminished but not abolished by a covering ileostomy (4.3% versus 9.3%, OR, 2.37; 95% CI, 1.39–4.04;  $P=.002$ ). The routine creation of an ileostomy after restorative proctocolectomy is adopted by most colorectal surgeons because it may reduce the disastrous clinical consequences of leakage.<sup>165,166</sup> Moreover pelvic sepsis has a significant negative impact on long term pouch function and is correlated with long term failure rate. However the lower leakage rate of an ileoanal anastomosis covered by an ileostomy must be balanced against the morbidity and mortality of the creation and closing of an ileostomy. (L3a, RG C). In almost all cases a leaking anastomosis must be defunctioned if not done so at the initial procedure.<sup>167,168</sup>

#### ECCO Statement 6C

Small Bowel Obstruction is a common complication seen after UC surgery. The reported frequency is up to 30%, however most episodes can be treated without surgery (EL 4)

After restorative proctocolectomy overall incidence of SBO varies between 13–30% and increases with length of follow up.<sup>169-173</sup> Most events are treated conservatively, but up to 25% of patients

need surgical treatment.<sup>170</sup> Ileostomy increases the risk of SBO events and frequency of surgical treatment. Laparoscopy didn't decrease the number of SBO episodes.<sup>169</sup>

#### 2.9.1.4. ECCO Statement 6D

Patients undergoing surgery for UC have an increased risk of thromboembolic complications. Risk-reducing and preventative strategies are advised in these patients (EL 3)

Patients suffering from UC are at increased risk of thromboembolic events.<sup>174-177</sup> In a large review of US surgical patients the incidence was 3.3%. They were at higher risk of death (4% vs. 0.9%).<sup>176</sup>

Postoperative bleeding from the IPAA is rare (1.5%), but if it happens, it is mainly caused by bleeding at the staple line.<sup>178</sup> Pouch suture line inspection immediately after creation may prevent postoperative bleeding. Postoperative treatment is usually conservative and consists of evacuation of clots, epinephrine enema, hemostatic treatment through pouchoscopy. Early postoperative ischemia of IPAA is rarely reported in the literature. It could lead to leak or separation of ileo-anal anastomosis or abdominal sepsis.<sup>170</sup> It occurs in up to 4.3% in some series. Ischemia could be created by tension of the ileocolic pedicle, thrombosis of ileocolic artery or volvulus.<sup>179,180</sup> Pouchoscopy and CT angiography are the main diagnostic procedures. Well timed pouch extirpation is warranted in case of pouch necrosis. Volvulus of the pouch might be a one of the causes of ischemia. Immediate derotation and fixation is necessary.

## 2.9.2 Loopileostomy closure

#### 2.9.2.1. ECCO Statement 6E

The optimal timing of ileostomy closure after IPAA seems to be from 8 weeks and beyond. (EL4). A contrast enema before closure is common practice to rule out silent anastomotic leaks (EL 5)

Loop ileostomy closure is typically undertaken 8–12 week after construction allowing sufficient time for recovery from the initial resection. Loop ileostomy closure can have significant impact on the patient with morbidity rate of up to 33%.<sup>168</sup> In a recent systematic review the reported rates of small bowel obstruction following loop ileostomy closure was 7.2%, 1/3 of them required re-laparotomy, anastomotic leak rates were 1.4%, enterocutaneous fistula 1.3%, wound infections 5.0%, and stoma site hernias 1.3%.<sup>167</sup>

Loop ileostomy closure after laparoscopic colorectal surgery is associated with a significantly shorter operative time and hospital stay, as well as with lower rates of postoperative complications than after open surgery.<sup>181</sup> Ileostomy closure can be performed using either a stapled or a sutured technique and although opinion differs as to the optimal closure technique a recent meta-analysis revealed no significant differences in short-term outcome between the two approaches.<sup>182</sup> Early closure (within 2weeks) of a covering ileostomy is an option if imaging has shown an intact anastomosis.<sup>183,184</sup> A contrast enema before closure is common practice to rule out silent anastomotic leaks before closure.<sup>185</sup>

## 2.9.3 Follow-up

#### 2.9.3.1. ECCO Statement 6F

In the absence of risk factors such as neoplasia and PSC, no specific pouch follow-up protocol is required in asymptomatic patients (EL 2)

The prevalence of high-grade dysplasia, low-grade dysplasia and indefinite for dysplasia was 0.15 (range 0–4.49), 0.98 (range 0–15.62) and 1.23 (range 0–25.28 per cent) respectively in a systematic review of dysplasia after restorative proctocolectomy.<sup>36</sup> Dysplasia was equally frequent in the pouch and rectal cuff or anal transitional zone. Dysplasia and cancer identified before or at operation seemed to be significant predictors of the development of pouch dysplasia. Data from this systematic review have been confirmed by others indicating that even if the indication for colectomy has been dysplasia or cancer, the risk of having dysplasia in the rectal cuff or pouch was very low.<sup>186,187</sup> No specific follow-up is therefore recommended after restorative proctocolectomy in the absence of risk factors.

#### 2.9.3.2. ECCO Statement 6G

Early endoscopy is recommended in symptomatic patients with pouch dysfunction, in order to distinguish between pouchitis, cuffitis or other responsible conditions (EL 4)

In patients with UC, proctocolectomy with ileal pouch-anal anastomosis (IPAA) may be followed by signs and symptoms related to pouchitis (occurring in up to 50% of patients at 10years) or to other conditions (irritable pouch syndrome, CD of the pouch, ischemic pouch, cytomegalovirus, CMV or *Clostridium difficile* infection).<sup>188,189</sup>

Timing of clinical follow up is related to the development of these signs and symptoms in subgroups of patients, although not standardized schedule is currently available. In the early postoperative period, patients may require liquid infusions due to watery diarrhea or electrolytes imbalances, although specific timing of hematochemical and clinical assessment should be tailored on a patients' basis. Daily clinical experience suggests a clinical and routine hematochemical assessment (CBC, serum iron, ferritin, electrolytes, CRP, serum albumin and creatinin) within 3months from surgery, although earlier assessment may be required (EL5, RG5). Subsequent clinical evaluations should be assessed on a patients' basis.

In UC patients with IPAA with signs and symptoms compatible with pouchitis (liquid stools, urgency, tenesmus, pelvic discomfort, electrolytes imbalance), pouchoscopy should be performed in order to discriminate between pouchitis and other conditions (irritable pouch, ischemic pouch, CMV or *C. difficile* infections, CD of the pouch).<sup>190</sup> Timing of the endoscopic follow up is related to the specific indication (EL5, RG5).<sup>191</sup>

## 2.9.4 Adjuvant medication

#### 2.9.4.1. ECCO Statement 6H

Loperamide is an effective drug to reduce the stool frequency in patients with an ileoanal pouch (EL 1b). Cholestyramine and psyllium may be useful in reducing stool frequency (EL 5)

Opioid analogues like loperamide are used to reduce the increased bowel frequency observed in patients with UC patients after restorative proctocolectomy with IPAA. The evidence for this is limited since only a few studies addressed this topic. In 1998, an open-label study<sup>192</sup> aimed to assess the clinical efficacy of loperamide and its effect on pouch motility in 14 patients with an ileoanal reservoir with parameters recorded for 24h while taking no medication and for 24h while receiving 8mg loperamide. Loperamide decreased median bowel frequency (4.0 vs 5.5; P=0.03) and 24-h stool weight (413g vs 610g; P=0.03) but not individual stool weights. In 2001, the effect of loperamide hydrochloride on bowel function was investigated in 8 patients with IPAA (8 for UC, 2 for FAP) in a blinded,

three-tailed, case-controlled and randomized crossover trial, using a daily dose of 12mg either orally (4mgt.d.s.) or as suppository (6mg b.d.). Mean daily stool frequency during the oral loperamide phase was lower than during both the placebo ( $P=0.05$ ) and suppository ( $P<0.02$ ) phases.<sup>193</sup> In a randomized, placebo-controlled, double-blind, crossover study the effects of loperamide versus placebo were investigated in 30 patients with IPAA. Findings suggested that while loperamide increased resting anal pressure by approximately 20% ( $P<0.05$ ), squeeze pressure was not affected. Loperamide also did not appear to affect pouch volume or contractility. A reduced bowel frequency and an improved nighttime continence, with less soiling ( $P<0.05$ ) and need to wear a protective pad was reported to be associated with loperamide use.<sup>194</sup> Cholestyramide and psyllium might be useful in reducing the bowel frequency and in binding the stool, although evidence is lacking. However, uncontrolled clinical observations suggest that cholestyramine may reduce the bowel frequency related to fat malabsorption, although the dose should be tailored on an individual basis (EL5). No standardized doses of supplements (Vitamin B, folate acid, iron) are available for preventing/treating related deficiencies in UC patients with IPAA. Indication for using these supplements should be assessed during the follow up of UC patients with IPAA. Instead of determining the levels of vitamin B and folate acid, patients with pouches can be advised to take these supplements routinely.

## 2.9.5 The leaking anastomosis

### 2.9.5.1. ECCO Statement 6I

The presacral abscess of a defunctioned leaking pouch-anal anastomosis can be treated with a wait and see policy, drainage (transanal or transgluteal) with irrigation or vacuum endoscopic therapy (EL4)

Subsequent restoration of continuity is often possible but with a risk of compromised pouch function (EL3).

No robust data exists how to treat a leaking anastomosis or pelvic sepsis other than transanal irrigation, percutaneous drainage or as last option surgery. Chronic pelvic sepsis is associated with poor pouch function, long term pouch failure and development of persisting presacral sinus.<sup>165,166,195–197</sup> It seems of great importance to treat the pelvic sepsis aggressively in order to avoid the long term sequelae. Recently, the Endosponge®, a low vacuum system inserted in the presacral cavity with the flexible endoscope has been used in the treatment of even near complete dehiscence of ileoanal anastomosis with favourable results.<sup>198–200</sup>

## 2.10 Special situations

### 2.10.1 Sexual function, fertility and delivery

#### 2.10.1.1. ECCO Statement 7A

Active UC is associated with poor sexual function. In general terms sexual function improves after IPAA. However proctectomy can risk impotence and loss of ejaculatory function in men and reduced fecundity and dyspareunia in women (EL2). Sexual function should be discussed when counseling patients about treatment options (EL5)

UC patients have a poor sexual function and a reduced desire for childbearing associated with fears of disease worsening or functional

concerns, in particular following restorative proctocolectomy, of which a decrease in fertility and sexual dysfunction are acknowledged complications.<sup>108,201–205</sup>

The largest published series of IPAA to date reports sexual dysfunction in 1 in 7 patients, a figure similar to the reported level of social and work restrictions.<sup>70</sup> Nonetheless, those patients also report persisting excellent quality of life and increased overall sexual satisfaction in a meta-analysis.<sup>201,206</sup> Indeed, 2 prospective evaluations showed an improvement in sexual function in both genders 12months after IPAA when compared to preoperative levels.<sup>108,207</sup> These findings are important in overall clinical care of patients with UC and should be addressed when counseling patient about treatment options.

Cohort studies and meta-analysis have demonstrated that open IPAA reduces female fecundity,<sup>208–210</sup> most probably because of adhesions affecting the fallopian tubes.<sup>211</sup> Conversely, studies of patients with familial adenomatous polyposis who had an ileorectal anastomosis (IRA) showed no reduction in fecundity.<sup>212,213</sup> Half to two-thirds of patients still live with their IRA after 20years.<sup>136,139,140</sup> Yet, in IRA the retained rectum remains exposed to inflammation and to a residual risk of cancer that mandates surveillance.<sup>214–216</sup> On the other hand, IRA does not disturb sphincter function, unlike IPAA, does not impair fecundity, and can be discussed as a temporizing option. In males, the potential complications of a pelvic procedure that are avoided by an IRA include retrograde ejaculation and erectile dysfunction,<sup>202</sup> which both may make conception more problematic.

Growing evidence suggests that laparoscopic IPAA may allow curative surgery while limiting the negative consequences on female fecundity.<sup>95,96</sup> Indeed, infertility rates after laparoscopic IPAA were lower than after open IPAA. This was explained by reduced pelvic adhesions after laparoscopic IPAA.<sup>217</sup>

#### 2.10.1.2. ECCO Statement 7B

Even if there is conflicting evidence to support both vaginal delivery and caesarean section in patients who have undergone IPAA, caesarean section is recommended (EL5). Management can be individualized following an appropriate discussion and counselling with the patient, the (colorectal) surgeon, and the obstetrician (EL 5)

A recent population based study from Sweden showed that women with UC and no previous surgery had a nearly 2 fold increased risk of an elective cesarean section,<sup>218</sup> although a vaginal delivery remains the safest way for both mother and baby. Prior abdominal surgery increases this figure, both because of concern about anal continence and because an emergent cesarean section in face of abdominal adhesions may turn hazardous. Vaginal delivery has a 0.5–3.5% risk of inflicting significant maternal sphincter tears,<sup>219,220</sup> the risk being highest at the first delivery.<sup>221</sup> On the other hand, multiple deliveries have been shown to prolong pudendal nerve terminal motor latency.<sup>222,223</sup> People with an IPAA have a very limited margin for maintaining fecal continence compared to the general population. This is because many factors considered important for normal continence, such as solid stools, rectal sensation, and recto-anal nervous interplay are absent in people with an IPAA. Consequently they rely heavily on their sphincter for maintaining continence.

Principally on these grounds many surgeons recommend that their patient have a caesarian section rather than a vaginal delivery, translating in a cesarean section rate of 49% in a meta-analysis<sup>224</sup>

and an unsettled controversy in the literature.<sup>188,225</sup> Nonetheless, the same meta-analysis concluded that vaginal delivery appeared safe and did not affect anal continence, with pouch function only affected during the third trimester and returning to baseline within 6 months after delivery. However, pouch function seemed to deteriorate faster in the long-term follow-up (beyond 5 years) after vaginal delivery,<sup>226</sup> in particular when vaginal delivery was at high risk of obstetric injury (instrumental delivery, episiotomy, baby weighting more than 4000g, emergent cesarean section, and delivery with a second stage of labour over 2 hours).<sup>225</sup> Hence, an informed decision about the mode of delivery requires a thorough discussion between the patient, her colorectal surgeon, and the obstetrician weighting in risk factors, patient's values, and elements of the literature.

## 2.10.2 Perianal problems

### 2.10.2.1. ECCO Statement 8A

In patients with ulcerative colitis suffering from perineal pathology caution should be exercised when considering surgical intervention [EL 5]

The real incidence of perianal problems in patients with UC is not clearly quantified. In the past, the overall perianal complications rate was reported in the range of 3.7% to 32%, considering all “anorectal complications” (including haemorrhoids, skin tags, anal strictures, etc.). However, these rates were misleading because colonic Crohn's disease (CD) and Indeterminate Colitis (IC) were first recognized in the 1960s and 1970s respectively.<sup>227</sup> Since improper surgical management of haemorrhoids and anal fissure may affect anal sphincter mechanism and the possibility of performing an adequate ileo-anal anastomosis, the treatment should be as conservative as possible. When necessary, surgery should be performed by a colorectal surgeon aware of IPAA procedure.<sup>227</sup> Recent reports have shown an incidence of perianal disease, namely abscesses and fistulas, in UC population of 5%, and in surgical UC series of 7%.<sup>228,229</sup> In a recent case-control study on 758 UC patients, Zabana et al. found that 70% who developed perianal disease did not meet diagnostic criteria of CD, despite diagnostic reassessment. Perianal disease was more frequent in men (62%) and it was associated with a more aggressive disease, requiring steroids, immunomodulators and biological treatments. These patients seem to have a higher hospitalization and colectomy rates.<sup>229</sup>

### 2.10.2.2. ECCO Statement 8B

In the presence of perianal fistulas and/or abscesses it is important to simultaneously control both sepsis and rectal inflammation, and to consider the possibility of Crohn's disease (EL 3). In previously healed perianal disease there is no absolute contraindication to forming an ileoanal pouch (EL 5)

Since different diagnostic and therapeutic options are available for the treatment of perianal disease, a general approach should be followed through adequate control of sepsis (abscess drainage and seton placement), sphincter preservation, low damage to anal and perianal tissues, evaluation of mucosal inflammation, and differential diagnosis with CD. Once the diagnosis of CD is excluded, there are no controlled data on medical and surgical management of perianal disease in UC. The Consensus agreed that if the inflammation

of the rectum is absent or mild, diagnostic and surgical ECCO guidelines for perianal Crohn's Disease should be used.<sup>189</sup> In the presence of perianal fistulas and/or abscesses with moderate or severe UC activity, the simultaneous control of both sepsis and inflammation is mandatory. ECCO guidelines for the medical treatment of Ulcerative Colitis should be followed.<sup>6</sup> In the presence of an abscess at clinical examination, the drainage should be performed before any other diagnostic procedure. Uncontrolled perianal sepsis in UC patients under steroids and/or immunosuppressant treatment can lead to Fournier's gangrene, a rapidly progressive, life threatening condition that require emergency surgery.<sup>230</sup> Contrast-enhanced MRI should be the initial procedure for the study of perianal UC, since it gives additional information on rectal and perirectal structures; Endoscopic Ultrasound (EUS) has similar sensitivity, but inferior specificity than MRI, and it cannot be performed in the presence of stenosis and painful abscesses; Transperineal Ultrasound (TPUS) could be used in the presence of anal stenosis or abscesses<sup>231</sup>; US methods can be improved with hydrogen peroxide enhancement; Computed Tomography (CT) is preferred in emergency settings. Fistulography is no more recommended. All these methods achieve the best results when combined with examination under anaesthetics (EUA). EUA is reported to have an accuracy of 90% in the hands of an experienced colorectal surgeon, but most important, it permits contemporary identification of all fistulae tracts, loose seton positioning, and abscess drainage.<sup>189</sup> Simple perianal fistulae should be treated, only if symptomatic, with loose seton placement and antibiotics (metronidazole and ciprofloxacin). Complex fistulae should always be treated by abscess drainage and loose seton placement. Concomitant luminal disease should be treated with antibiotics, a combination of topical and oral compounds, immunomodulators or biologicals when appropriate, depending on extension and severity of the inflammation.<sup>6</sup>

Since perianal disease seems to be associated with a more aggressive disease course, some of these patients will finally require colectomy.<sup>227,229</sup> In case of IPAA is needed, a prior perianal disease increases the risk of developing an ileoanal anastomotic leak and postoperative perianal complications,<sup>228</sup> and it is an independent negative predictor of long-term pouch survival.<sup>228,232</sup> In selected and well informed patients, with previously healed perianal disease, IPAA should be performed with a temporary diverting ileostomy.<sup>227</sup>

## 2.10.3 Colorectal Cancer

### 2.10.3.1. ECCO Statement 9A

In UC patients with highgrade dysplasia or colorectal cancer (CRC) the colon and rectum should be removed with en bloc oncologic resection of lymph nodes in all colonic segments due to the high risk of multiple synchronous tumors and preoperative under staging (EL 2)

In the past, almost 10% of UC patients who underwent resection were found to have a colorectal cancer (CRC) in the specimen.<sup>233</sup> Eaden et al., in a meta-analysis on 116 studies, reported an overall incidence of CRC in UC of 3.7%, increasing to 5.4% in the presence of pancolitis. The cumulative risk of CRC was reported to be of 2% at 10 years, 8% at 20 years, and 18% at 30 years.<sup>22</sup> A systemic review by Bernstein reported 42% of patients with high-grade dysplasia and 43% of patients with DALM having a synchronous CRC at immediate colectomy.<sup>24</sup> In a recent series from the Cleveland Clinic,



synchronous dysplasia or cancer in the specimen of patients with preoperative diagnosis was 48% and 12% respectively.<sup>234</sup> Strictures associated to even low-grade dysplasia are malignant in 20%-24% of the cases.<sup>235</sup> A consistent number of patients (11.7%), having a colectomy for dysplasia or cancer and found to have a CRC in the operative specimen, had Dukes' C or D postoperative staging.<sup>27</sup> Due to the high risk of multiple tumor locations and preoperative under staging, total proctocolectomy for dysplasia or cancer should be performed with adequate lymph nodes removal in all colonic segments. However, there are some technical implications in these settings. Patients with CRC of the ascending colon should receive adequate oncologic operation with removal of the terminal ileum, ileo-colonic vessels ligation, and regional lymph nodes excision, so they have to be informed about the diminished possibility of performing an adequate IPAA. Patients with dysplasia or cancer in any colonic segment, but with negative rectal biopsies and a rectum which can be easily examined, should receive a more conservative procedure with Denonviller's fascia preservation and an accurate "nerve sparing" procedure.

#### 2.10.3.2. ECCO Statement 9B

In the presence of a rectal cancer requiring radiotherapy, it should be performed in a neo adjuvant setting (EL 4)

The role of restorative proctocolectomy in the setting of UC complicated by rectal adenocarcinoma is unclear. Main oncologic concerns are that an active UC treated by radio and/or chemotherapy in neo-adjuvant setting may complicate with massive bleeding<sup>236</sup>; the presence of the pouch could interfere with the administration of chemotherapy; and postoperative radiotherapy could compromise the integrity of the pouch. Post operative pelvic radiotherapy can be associated with worse functional outcomes when administered for those who have had an anterior resection for rectal cancer.<sup>237</sup> Similar effects may be seen in the setting of an ileoanal pouch. Taylor et al. in their series of patients with familial adenomatous polyposis suggested that advanced rectal cancer treated with adjuvant radiotherapy may be associated with worse function.<sup>238</sup> Remzi et al. have suggested that radiotherapy should not be used post operatively even if the diagnosis of rectal cancer is made after surgery.<sup>239</sup> In the situation where inflammatory disease activity is absent the best option for patients needing radiotherapy is to receive it in the neo-adjuvant setting. On the contrary, pouch radiation inevitably lead to pouch failure. Another option should be a staged procedure with radiation following a subtotal colectomy with Hartman's closure and ileostomy. In general, radiation treatment is associated with an elevated risk of pouch failure (16% vs 7%), but the oncologic outcome do not seems to be affected.<sup>240-243</sup>

#### 2.10.3.3. ECCO Statement 9C

In UC patients with colorectal cancer undergoing proctocolectomy with IPAA and likely to require adjuvant chemotherapy a defunctioning ileostomy is strongly advised (EL 4)

Patients requiring surgery for colorectal cancer who might require adjuvant therapy need careful consideration. Preoperative staging may prove inaccurate and in order to reduce side effects of any adjuvant therapy on pouch function, a staged procedure should be performed.<sup>240,241,243</sup> In fact, adjuvant therapy cessation

for pouch related intolerance could worsen cancer prognosis, while adjuvant therapies could adversely influence pouch function.<sup>240</sup> Patients with CRC and a reliable preoperative clinical Stage I or II (in particular rectal cancer that seems to be easier staged) should be treated with restorative proctocolectomy with or without diverting ileostomy.<sup>242</sup> UC patients treated with IPAA and needing post-operative adjuvant therapy should receive standard dosage of chemotherapeutic agents. The risk of diarrhea associated with chemotherapy for colorectal cancer is estimated to be as high as 82%. A third of these patients usually experience grade III or IV diarrhea.<sup>244</sup> Specific data on this topic are absent, but IBD patients seem to be at higher risk for developing severe diarrhea during chemotherapy, due to the toxic effects of cytotoxic drugs or a flare of the IBD itself. A regimen of continuous infusion 5-FU alone, in combination with leucovorin, or in combination with oxaliplatin should be best tolerated. Bolus infusions of 5-FU and combination therapy of irinotecan with 5-FU should be avoided because of severe diarrhea and the possibility of sepsis. Diarrhea should be empirically treated with aminosalicylates.<sup>236</sup> In the presence of an ileostomy or an ileoanal pouch, diarrhoea may be severe enough to need modification of chemotherapy dosing.

#### 2.10.4 Surgery for pouchitis and cuffitis

The diagnosis of pouchitis requires the presence of symptoms, together with endoscopic and histological abnormalities. Extensive UC, extraintestinal manifestations, being a non-smoker, p-ANCA positive serology and NSAID use are possible risk factors for pouchitis. The most frequent symptoms of pouchitis are increased number of liquid stools, urgency, abdominal cramping and pelvic discomfort. Fever and bleeding are rarely present. The majority of patients respond to metronidazole or ciprofloxacin, although the optimum modality of treatment is not clearly defined. Anti-diarrhoeal drugs may reduce the number of daily liquid stools, independently of pouchitis. In chronic pouchitis a combination of two antibiotics is effective, and oral budesonide is an alternative. Infliximab should be effective for the treatment of chronic refractory pouchitis. Probiotic therapy with VSL#3 has shown efficacy for maintaining antibiotic-induced remission and for preventing pouchitis.<sup>189</sup>

For patients who have persistent symptoms, alternative diagnoses

#### 2.10.4.1. ECCO Statement 10A

Patients with chronic pouchitis refractory to all medical therapy should be referred to a colorectal surgeon for consideration of permanent ileostomy with pouch exclusion or excision (EL4)

should be considered, including undiagnosed Crohn's disease, pouch-anal or ileal-pouch stricture, infection with CMV or *Clostridium difficile*, collagenous pouchitis, cuffitis, anatomical disorders, or irritable pouch syndrome. Approximately 10-15% of patients with acute pouchitis develop chronic pouchitis.<sup>226,245-247</sup> Patients with chronic, refractory pouchitis do not respond to conventional therapy and often have on-going symptoms. This refractory condition may ultimately be a cause of pouch failure. In large institutional series, the risk of pouch failure is about 10% at 10years and chronic pouchitis accounts for 10% of the failures. Little data exist to help decide between excluding or excising a failed pouch. What data there is suggests that excision may confer a better outcome in terms of quality of life.<sup>140,170,248-251</sup>

#### 2.10.4.2. ECCO Statement 10B

Rectal cuff inflammation (cuffitis) or retained rectum may induce symptoms similar to pouchitis or irritable pouch syndrome, although bleeding is more frequent (EL2). Topical 5-ASA has shown efficacy in treating cuffitis (EL4)

Cuffitis can cause pouch dysfunction with symptoms that mimic pouchitis or irritable pouch syndrome (IPS), especially after double-stapled IPAA. A coexisting pouch disorder should be excluded, but bleeding is a characteristic feature of cuffitis. Endoscopy is diagnostic and care has to be taken to examine the cuff of columnar epithelium between the dentate line and pouch-anal anastomosis. In an open-label trial, 14 consecutive patients with cuffitis treated with mesalazine suppositories 500mg twice daily experienced a reduction in the total Cuffitis Activity Index (derived from the PDAI). Symptom, endoscopy, and histology scores were significantly reduced. 92% of patients with bloody bowel movements and 70% with arthralgia improved after therapy.<sup>188,190</sup> The symptoms of retained rectal mucosa are those of proctitis, including bleeding, burning and urgency, with frequent passage of small amounts of stool. These patients are at risk of neoplastic transformation.<sup>252-254</sup> In a series of 217 patients with stapled IPAA an inflamed mucosa distal to the anastomosis was present in 22% of the patients, and retreatment was needed in 13%.<sup>255</sup> Tulchinsky et al. reported a series of 22 patients submitted to major revisional surgery for retained rectal stump with a successful rate of 68%.<sup>248</sup>

#### 2.10.5 Non inflammatory pouch dysfunction and pouch failure

*Definition: Failure of the pouch is defined as the excision of the pouch or indefinite defunctioning.*

*Definition: Redo ileal pouch-anal anastomosis (IPAA) is defined as an operation for malfunctioning pouch or pelvic septic complications, with pelvic dissection, pouch disconnection, pouch revision, reconstruction or advancement, and reanastomosis.*

#### 2.10.5.1. ECCO Statement 11A

Non-inflammatory causes of pouch dysfunction include pouch anal stricture, problems with pouch capacity, efferent limb dysfunction (S-pouch), retained rectal stump, and chronic presacral sepsis. Deciding on appropriate management requires careful surgical evaluation (EL5)

There are no randomised trials to ascertain the best surgical procedure for UC. Despite this limitation there are many retrospective series and prospective observational studies from tertiary centres to determine outcomes from surgery for UC. Reliable data from over 9,000 patients have been reported to date.<sup>256</sup> Overall pouch failure is reported to range from 0,5% to 24% of cases; the frequency increases over time, reaching the higher values during long-term follow-up.<sup>252,256</sup> Postoperative pelvic sepsis ranges from 2.5% to 26.7% and acute and chronic septic complications, such as fistulas and sinuses, account for 50% to 65% of the causes for pouch removal. Poor pouch function due to mechanical outlet obstruction accounts for 35% to 55% of pouch excisions. Different techniques for pouch construction (e.g. "J" vs "S" shape) and ileo-anal anastomosis (e.g. hand-sewn vs stapled) are reported to have different and specific complications. The main complications are anastomotic strictures, afferent and efferent limb problems, retained rectum, and small

reservoir. Chronic inflammations of the pouch or the cuff and neoplastic transformation are the cause of pouch removal in 5-10% of the cases. Pouch prolapse, pouch intussusception, mega-pouch, irritable pouch syndrome, anismus and sphincter dysfunctions, are rare conditions, responsible for 2-3% of redo IPAA surgery.<sup>15,196,257-262</sup>

Since IPAA surgery is not only an anatomical reconstruction, but also a "quality of life" intervention, the first step in the diagnosis of pouch disorders is a careful clinical history and examination. This can guide the clinician to discriminate the nature of the problem (s) affecting the pouch and to design the adequate diagnostic workup. Endoscopy is essential in order to obtain information on the mucosa status, such as cuffitis, pouchitis, and Crohn's disease. Both endoscopy and pouch enema are useful for evaluation of pouch distensibility, afferent and efferent limb disorders, mucosal prolapse, and pouch torsion. Essential for most disorders is to obtain 2D/3D imaging through a tomographic device. Computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (either endoanal or transperineal) are very sensitive to identify and characterize septic problems and most of mechanical disorders.<sup>231</sup> Unfortunately, no diagnostic tools are available to discriminate the presence of fibrosis.<sup>196,263-265</sup> As proposed in the ECCO indications for perianal Crohn's disease, in case of fistulas, abscesses, sinuses, and IPAA stenosis, examination under anaesthesia (EUA) is very important for diagnosis and contemporary treatment of most conditions. The association of EUA, performed by an experienced IBP surgeon, together with one of the tomographic imaging devices (CT, MRI, US) give the best levels of accuracy.<sup>189</sup>

A large proportion of patients who experience postoperative pouch problems are successfully treated by transanal approach, with or without faecal diversion. Transanal resolution of IPAA stenosis by dilation is effective in 45% to 95% of the cases, but often, more than one procedure is necessary to obtain satisfactory results. The most important prognostic factor for the success of the dilation is absence of fibrosis. Septic complications are also managed by EUA, especially where abscess drainage, simple perianal fistulas and sinuses are concerned. Fistulotomy, fistulectomy, loose seton placement, sphincterotomy and pouch-flap advancement are all feasible for the treatment of post-pouch complications. Multiple and/or complicated perianal fistulas, large pre-sacral sinuses, as well as pouch-vaginal fistulas often need a temporary ileostomy for prolonged periods.<sup>196,248,257,261,266,267</sup>

#### 2.10.5.2. ECCO Statement 11B

Redo pouch surgery is a complex but effective procedure for appropriate indications. The procedure should be performed only in highvolume centers by dedicated and experienced surgeons, and in highly motivated patients (EL 2)

Redo pouch is necessary when the IPAA has to be disconnected and the pouch revised or reconstructed through a combined transabdominal and transperineal approach. Identification of the precise pouch dysfunction is mandatory in order to optimize surgical strategy. In general, indications for pouch revision can be divided in mechanical and infectious or inflammatory. Mechanical causes of malfunctioning may be identified such as a stenosis of IPAA, an efferent limb that is too long in an "S" pouch, a blind limb of a "J" pouch which is too long, kinking of the afferent limb, twisting of the pouch, pouch intussusception, small pouch volume, megapouch, and a long rectal stump. Ideally, obstructing problems should be managed using

the existing pouch by disconnection of the IPAA and redo transanal handsewn anastomosis, while for volume problems specific procedures have been proposed in order to reduce or enlarge the volume of the pouch. Septic complications require more often a complete reconstruction because the pouch itself is frequently involved. Inflammatory disorders, such as chronic refractory pouchitis and Crohn's disease should be managed by aggressive medical treatment, and in case of failure a permanent ileostomy may be necessary. Cuffitis may need a complete mucosectomy and handsewn anastomosis, whether through transanal or combined access.<sup>52,141,196,248,256-271</sup> In general, redo pouch surgery seems to have better results when performed for mechanical than for septic complications. When performed by experienced surgeons in tertiary centres, redo pouch is a safe and effective procedure. More than 600 patients are reported in the literature to undergo salvage surgery for pouch failure, with no mortality rate and a perioperative complication rate that ranges from 19% to 51%. The outcomes after revisional surgery are also encouraging, having a salvage rates ranging from 50% to 100%. In those studies with a 5-years follow-up or longer, the pouch survival was estimated between 75% and 85%. Even if measured with different methods, the Quality of Life (QoL) after revisional pouch surgery has been assessed by several Centres and the results are reported as satisfactory from 50% to 93% of the patients.<sup>141,257,260,267,271</sup> Both in terms of postoperative complications and functional results there is a trend among authors in favour of preserving the existing pouch versus reconstruction and in case of an indication for mechanical problems versus septic complications.<sup>52,141,201,248,261,262,266-269</sup>

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### Conflict of interest statement

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

The ECCO Consensus Guidelines are based on an international consensus process.

Any treatment decisions are a matter for the individual clinician and should not be based exclusively on the content of the ECCO Consensus Guidelines.

The European Crohn's and Colitis Organisation and/or any of its staff members and/or any consensus contributor may not be held liable for any information published in good faith in the ECCO Consensus Guidelines.

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