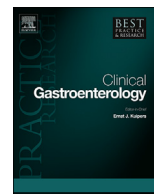




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## Surgery in ulcerative colitis: When? How?

Gaetano Gallo<sup>a, b</sup>, Paulo Gustavo Kotze<sup>c</sup>, Antonino Spinelli<sup>d, e, \*</sup><sup>a</sup> Department of Medical and Surgical Sciences, O.U. of General Surgery, University of Catanzaro, Catanzaro, Italy<sup>b</sup> Department of Colorectal Surgery, S. Rita Clinic, Vercelli, Italy<sup>c</sup> Colorectal Surgery Unit, IBD Outpatient Clinics, Catholic University of Paraná, Curitiba, Brazil<sup>d</sup> Humanitas University, Department of Biomedical Sciences, Via Manzoni 113, 20089, Rozzano, Milano, Italy<sup>e</sup> Humanitas Clinical and Research Center, Colon and Rectal Surgery Unit, Via Manzoni 113, 20089, Rozzano, Milano, Italy

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### ABSTRACT

Ulcerative Colitis (UC) is an idiopathic chronically-remitting inflammatory bowel disorder characterized by a contiguous inflammation of the colonic mucosa affecting the rectum that generally extends proximally in a continuous manner through the entire colon. Patients typically experience intermittent exacerbations, with symptoms characterized by bloody diarrhea associated with urgency and tenesmus. The anatomical extent of mucosal involvement is the most important factor determining disease course and is an important predictor of colectomy.

The precise etiology of UC is unknown. However, a combination of genetic predisposition and environmental factors seems to have a key role in the development of the disease. UC usually is mildly active but it can be a life-threatening condition because of colonic and systemic complications, and later in the disease course due to the development of colorectal cancer. Interestingly, even if pathogenetic features detected in patients with sporadic CRC can be also found in UC-related colorectal cancer (UC-CRC), this latter is, usually, driven by an inflammation-driven pathway rising from a non-neoplastic inflammatory epithelium to dysplasia to cancer. Thus, a long-term follow-up with colonoscopy surveillance has been recommended.

Approximately 15% of UC patients develop an acute attack of severe colitis, and 30% of these patients require colectomy. The initial treatment strategy in UC typically follows the traditional step-up approach. One third of the patients will not respond to steroid therapy and cyclosporine and infliximab are the most common salvage agents employed in these cases in order to avoid emergent surgery. Unfortunately, although a significant short-term benefit have been observed after infliximab treatment, the colectomy rate have remained stable. Surgery in UC depends on the stage of the disease as well as patient's status and is divided into the following settings: urgent, emergent and elective. Despite many efforts the surgical management of UC remains a significant challenge. A multidisciplinary management of UC is key in order to define the best timing and the best procedure for each patient in an individualized basis.

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### 1. Introduction

Ulcerative Colitis (UC) is an idiopathic chronic inflammatory bowel disorder of the colonic mucosa affecting the rectum that generally extends proximally in a continuous manner through the entire colon. Intermittent exacerbations are typical, with symptoms characterized by bloody diarrhea associated with urgency and tenesmus [1]. The anatomical extent of mucosal inflammation is

the most important factor determining disease course and is an important predictor of colectomy [2]. At diagnosis, 30–50% of patients have disease confined to the rectum or the sigmoid colon (distal colitis), 20–30% have left-sided colitis, and approximately 20% have pancolitis [3].

The precise etiology of UC is unknown. However, genetically susceptible individuals seem to have a dysregulated mucosal immune response to commensal gut flora, which results in bowel inflammation [4]. UC usually is mildly active but it can be a life-threatening condition because of colonic and systemic complications, and later in the disease course due to the development of colorectal cancer [5]. Interestingly, even if pathogenetic features

\* Corresponding author. Humanitas University, Department of Biomedical Sciences, Via Manzoni 113, 20089, Rozzano, Milano, Italy.

E-mail address: [antonino.spinelli@hunimed.eu](mailto:antonino.spinelli@hunimed.eu) (A. Spinelli).

detected in patients with sporadic CRC can be also found in UC-related colorectal cancer (UC-CRC), this latter may not follow the common progression from normal epithelium to cancer but usually is driven by an inflammation-driven pathway [6].

Approximately 15% of UC patients develop an acute attack of severe colitis, and 30% of these patients require colectomy [7–9]. Furthermore, 10% of patients will need surgery during the first year of illness [10], in many cases as emergency procedures. Recently, a significant short-term reduction in the colectomy rates have been observed after infliximab treatment [11]. Unfortunately, the long-term effect of biological therapy in preventing colectomy is still unclear [12,13].

Surgery in UC is divided into the following settings: urgent, emergent and elective (Table 1). Emergency operations can be performed for life threatening complications such as massive hemorrhage, perforation or severe medically refractory disease in which surgery should not be delayed beyond a few hours, while urgent surgery should be undertaken during toxic megacolon [15]. Conversely, elective surgery is indicated in cases of persistent disease activity, despite optimized medical therapy, stricture formation, extra-intestinal manifestations or for associated dysplasia or cancer.

As colectomy severely affects quality of life, the timing of surgery remains a crucial decision in the management of UC and a close interaction between gastroenterologists and colorectal surgeons is mandatory for optimal patient outcome.

## 2. Surgery: when?

The three main indications for surgery in UC remain [1]: acute severe colitis; [2]: refractory UC; [3]: associated dysplasia and carcinoma. In the following session, we will describe in detail specific characteristics of each indication.

### 2.1. Acute severe colitis

Acute severe ulcerative colitis (ASUC) can be the initial presentation in up to 10% of UC patients [15,16]. It can be a serious, potentially life-threatening condition [17] and patients that meet the Truelove-Witts criteria [18] (>6 bloody stools per day plus at least one of the following: (1) temperature greater than 37.8 °C; (2) pulse greater than 90 beats per minute; (3) haemoglobin less than 10, 5 g/dL; (4) erythrocyte sedimentation rate greater than 30 mm/h) should be admitted to hospital for treatment with intravenous corticosteroids, which remain the first-line treatment for ASUC, due to their high risk for colectomy [19]. The overall response rate of steroids in ASUC is almost 70% [20], with a 30% rate of colectomy in the short-term, after the first course of therapy [21]. In the absence of response to this first-line treatment, after 3–5 days, a rescue therapy using cyclosporine, tacrolimus or anti-TNF (usually infliximab) can be considered. A third-line medical therapy is often associated with significant delay and high risk of severe complications and should not be considered in cases of ASUC, unless in specific clinical trials in tertiary referral centers [22]. Objective evaluation of response rates using the Oxford or the Sweden indexes are recommended [23,24]. In addition to the Truelove-Witts

criteria, the ECCO guidelines also include C-reactive protein (CRP) > 30 mg/L as an additional parameter [25].

Furthermore, patients with ASUC should have full blood count, electrolytes, urea, creatinine, liver function tests, magnesium, lipid profile, abdominal X-ray and flexible sigmoidoscopy with multiple colonic biopsies to rule out Cytomegalovirus colitis. A full colonoscopy is usually not recommended in patients with ASUC due to the risk of colonic perforation [26,27]. Endoscopically, ASUC is usually defined by mucosal friability, spontaneous bleeding and ulcerations, usually as a Mayo 2–3 endoscopic subscore [25]. Clostridium difficile infection is associated with increased morbidity and mortality in UC patients [28,29]. For this reason, the concomitant diagnosis of infectious colitis must also be additionally excluded [30].

After patient hospital admission other measures, such as fluid and electrolyte replacement, blood transfusion, venous thromboembolism prophylaxis and nutritional support should be taken into account and decided in a case-by-case analysis. Surgeons must be involved in the care of hospitalized patients since admission, and these patients usually must be seen multiple times a day in order to precisely recognize surgical indications, as fast deterioration of the clinical status can occur in a matter of hours [25].

The absolute indications for surgery usually comprise the major complications of ASUC: toxic megacolon, perforation, severe colorectal bleeding and multiple organ dysfunction syndrome (MODS).

Toxic Megacolon (Fig. 1) is defined as total or segmental non-obstructive hypotonic dilatation of the colon, exceeding 5.5 cm in diameter in the transverse colon on plain abdominal X-ray film [31]. In the absence of a significant response after 48–72 h of an intensive intravenous steroids regimen, colectomy with ileostomy and preservation of the rectum is the generally accepted procedure. Perforation can be common during toxic megacolon and can occur in 0.3% of patients with ASUC [32]. The detection of perforation is often revealed only at CT or during surgery. The procedure of choice is subtotal colectomy with proper treatment of the rectal stump,



Fig. 1. Toxic megacolon in a patient admitted due to acute severe colitis. Dilatation of more than 5.5 cm of the transverse colon is observed. Picture courtesy of Paulo Kotze.

**Table 1**  
summary of main surgical indications in three different settings in the management of UC.

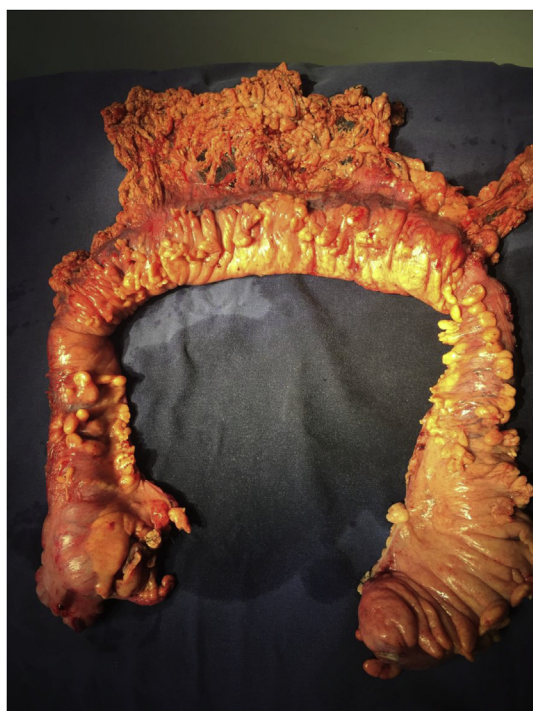
| Elective  | Urgent  | Emergent  |
|---|---|---|
| <ul style="list-style-type: none"> <li>• Failure of medical therapy</li> <li>• Stricture formation</li> <li>• Extra-intestinal manifestations</li> <li>• Dysplasia or Cancer</li> </ul> | <ul style="list-style-type: none"> <li>• Acute severe colitis (5–7 days after failure of intensive medical therapy)</li> <li>• Toxic Megacolon</li> </ul> | <ul style="list-style-type: none"> <li>• Perforation</li> <li>• Massive hemorrhage</li> <li>• Multiple organ dysfunction syndrome (MODS)</li> </ul> |

which can be closed in the pelvis or exteriorized as a rectosigmoid mucous fistula in the lower part of the incision. Toxic Megacolon in stable patients should not be considered a contraindication to the laparoscopic approach as preserving abdominal wall integrity is critical in these patients. Furthermore, a hand-assisted approach can give an appropriate balance of speed and safety by reducing the trauma of the abdominal wall. In ASUC, surgery is mandatory for any patient whose condition worsens or fails to improve after 5–7 days of an intensive medical treatment (Fig. 2) [33–35]. Delayed surgery for acute severe colitis is associated with increased risk of postoperative complications [36,37] and a multidisciplinary management between gastroenterologists and colorectal surgeons is critical to correctly choose the optimal timing of surgery.

## 2.2. Refractory UC

According to the ECCO (European Crohn's and Colitis Organisation) guidelines, refractory UC includes both steroid dependency and immunomodulators or biologic-refractory UC [38]. Following an extended period under steroid therapy refractory-UC patients have a high risk of septic complications and poor conditions of anastomotic healing [39,40]. As an attempt to avoid complications, a staged procedure is preferred in these cases [23].

Failure of medical therapy is usually defined as persistence of active disease despite optimal medical therapy. It consists in the most common surgical indication in the elective setting in the management of UC. Good common sense between the gastroenterologists and surgeons must come on board in defining failure to medical treatment. Commonly, gastroenterologists will tend to always try alternative medical therapies, as newer agents are being approved over the years, as an attempt to control disease activity. However, it is common that this chase for an ideal medication can result in exhausted patients, usually with impaired nutritional status, non-functional colons and with not perfect conditions to be submitted to major abdominal surgery. Again, a multidisciplinary



**Fig. 2.** Acute severe colitis. Surgical specimen after initial subtotal colectomy in an urgency basis. Picture courtesy of Paulo Kotze.

approach needs to better define the proper timing for surgery in these situations.

## 2.3. Associated dysplasia-Cancer

UC-related colorectal cancer (CRC) represents less than 1% of all CRC, with higher risk in patients with long-term UC as compared with the general population [41,42]. In particular, the risk of CRC begins to increase 8–10 years after the initial diagnosis [42,43]. For this reason, all patients should undergo yearly screening colonoscopy, with random or guided by chromoendoscopy biopsies, after 8 years of disease onset to evaluate the microscopic extent of the disorder and exclude dysplasia [25,44,45].

Several studies described the incidence of UC-CRC [46–49]. Eaden et al. in a meta-analysis including 116 studies, reported a cumulative risk of 18.4% after 30 years of disease duration [50]. However, a more recent systematic review, based on 81 studies and 181,923 patients, reported a decrease of the incidence rate from 4.29/1000 patient-years in the 1950s to 1.21/1000 patient-years in the last decade [51].

Anatomical extent of colitis is also an independent risk factor for UC-CRC (higher risk in extensive colitis) as well as young age [52,53]. Other risk factors for CRC in UC patients include the following items: duration of disease [41–43], concurrent primary sclerosing cholangitis [54] and family history of CRC [55].

The main goal of surveillance programs is to detect dysplastic alterations. According to the ECCO guidelines, dysplasia detected during surveillance procedures must be classified into three categories: polypoid, non-polypoid and endoscopically invisible [25]. The first one is usually endoscopically removable by routine methods. Meanwhile, the second requires immediate colectomy, being this latter strongly correlated with metachronous or synchronous carcinoma [56]. Both of them may need close monitoring at 3–6 month before reverting to annual surveillance. Endoscopically invisible dysplasia is referred to a dysplasia detected within random biopsies in the absence of visible lesions during colonoscopy. In cases of high-grade dysplasia (HGD) surgery is clearly recommended. Conversely, the decision to undergo surgery in patients with low-grade dysplasia (LGD) should be individualized evaluating the balance of risk and benefit. In fact, about 30–50% of patients with LGD progress to HGD or CRC and a synchronous CRC may already be present in more than 20% of patients [57,58]. Indeed, before considering surgery for dysplasia in UC, the histologic diagnosis should be confirmed by a consensus between two experienced gastrointestinal pathologists [25].

## 3. Surgery: HOW?

### 3.1. Reconstructive surgery (restorative proctocolectomy with ileal pouch-anal anastomosis [IPAA])

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA), first described by Parks and Nicholls in 1978, is currently the procedure of choice for the elective surgical treatment of UC in patients who have good sphincter function and no risk factors for postoperative complications [59,60]. IPAA avoids the need for a permanent stoma with stable functional results and good quality of life. In general, it is the most performed surgical procedure in UC, mostly in patients with primary sclerosing cholangitis, associated dysplasia or cancer and patients with severe rectal involvement.

Scoglio et al. [61] compared two meta-analysis which included studies published before and after 2000 [62,63]. The rate of complications after IPAA declined over time. Interestingly, functional outcomes were similar in studies published before and after 2000. There can be many considerations that need to be evaluated during

preoperative evaluation before IPAA. The three most important factors are: patient's age, female fertility and sexual function impairment in both men and women (dyspareunia, impotence and retrograde ejaculation).

IPAA was usually not offered to patients older than 50, because older age can be associated with increased risk of complications and worse functional outcomes [64]. However, recent studies have shown similar results in different age groups, in terms of functional outcomes and long-term complications [65–69]. Conversely, IPAA surgery at a younger age is associated with greater likelihood of stricture development.

Another potential complication is the risk of infertility and sexual impairment. Previous studies have shown that both sexual function and the postoperative pregnancy rates seem to be reduced after IPAA [70–72]. Both can be explained by nerve injury, scarring and adhesions in the pelvic (i.e. obstruction of the fallopian tubes) [73,74] or anatomic distortion related to rectal dissection. Again, according to the ECCO guidelines, a laparoscopic approach is associated with better preservation of female fertility and might be the preferred choice where expertise and adequate technology are available [25].

IPAA can be performed with either mucosectomy of the rectal mucosa, with a hand-sewn anastomosis to the dentate line, or with the double-stapling technique. Another alternative is the transperineal single-stapling technique, usually the choice after transanal completion proctectomy. The first procedure guarantees the complete removal of the rectal mucosa but is technically demanding and might damage the anal transitional zone leading to a worse functional outcome. The second preserves the anal transitional zone leaving a rectal cuff of no more than 1–2 cm, to minimize the risk of malignant transformation, and is usually associated to better functional results despite the risk of cuffitis, due to the presence of inflammation in the remaining tissue [75].

Although some case reports of dysplasia and cancer development have been described in the literature [76,77], in both approaches, with hand-sewn or with a stapled anastomosis, the risk of having dysplasia or cancer in the rectal cuff or pouch remains very low [78,79]. A recent study from the Cleveland Clinic analyzed 3203 patients undergoing an IPAA between 1984 and 2009. The authors concluded that the risk of neoplasia is low and preoperative dysplasia or cancer were the only independent factors associated with an increased risk of dysplasia [80]. Furthermore, neoplasia of the specimen is a strong predictor of pouch-related cancer, suggesting a close monitoring after pouch-surgery [81,82]. Thus, in case of dysplasia or cancer, proctectomy should include total mesorectal excision, increasing the risk for pelvic nerve damage as compared to the technique that is usually performed in IBD cases, notably the close rectal dissection [83].

Appropriate staging of surgery is a matter of some debate. Construction of the pouch should be avoided in the acute phase of UC due to a high risk of pelvic bleeding, sepsis and injury to pelvic nerves. In these cases a staged procedure with colectomy first and a temporary end ileostomy is preferred. Nevertheless, in a three-stage approach, colectomy can be performed more rapidly than IPAA and unstable patients may benefit from shorter operating time. Moreover, the time gap between colectomy and IPAA would allow improvement in nutritional status and weaning off any types of IBD related medication, what can improve the postoperative outcome after pouch construction and anastomosis in a second procedure, usually performed 6 months after colectomy. A three-stage approach should be adopted in patients with ASUC who are exhausted of medical therapy, usually malnourished and have several previous medications (mostly steroids) in use. Despite all these issues, Hicks et al. have demonstrated that the only risk factor for worse outcomes in this situation is represented by the surgeon's experience [84].

### 3.2. Subtotal colectomy with Brooke ileostomy

Brooke ileostomy, after total colectomy, was first described by Professor Bryan Brooke in 1952 [85]. Currently, subtotal Colectomy with Brooke ileostomy remains the optimal procedure in case of ASUC, as well as in the majority of exhausted chronic refractory patients. Furthermore, it may be indicated in patients who are elderly, with poor sphincter function or malignant lesions of the low rectum, who will receive pelvic radiation or will undergo associated proctectomy [86].

Subtotal colectomy with Brooke ileostomy has several advantages. It is a purely abdominal procedure, with no need for pelvic dissection, and can be easily performed by a well-trained general surgeon. Moreover, in unclear cases, it gives the possibility to perform a complete pathological investigation of the colonic specimen, allowing the later choice of the best reconstructive surgical procedure, without any kind of influence linked to the timing or the risk of having IPAA for Crohn's disease patients [14]. In fact, several studies have highlighted the considerable rate of change in diagnosis between UC and Crohn's colitis after colectomy [87,88].

The major disadvantage of the subtotal colectomy and end ileostomy is the possibility of leaving the patient with a long lasting, or even a permanent stoma. The choice on how to manage the rectal stump remains critical even in the era of IPAA. The creation of a mucous fistula, through the opening of the tip of the rectal stump, can reduce the risk of pelvic sepsis and the consequent post-operative morbidity. Mucous fistula can be brought out in the left lower quadrant, within the end of the median laparotomy incision, or in the same stoma aperture as ileostomy leaving a long rectal/rectosigmoid stump. In this last option patient should deal with another stoma until definitive surgery.

Another option, in which the rectal stump remains closed, include creation of an intraperitoneal Hartmann's pouch. In this case the rectum is interrupted at the level of the sacral promontory and left stapled or sutured in the pelvis. A permanent suture could facilitate future identification.

The closed rectal stump can be also placed subcutaneously, such that stump leakage results in superficial wound complications without the morbidity of an intraperitoneal sepsis.

Pellino et al. [89] described a novel technique in which the rectal stump was secured in a subcutaneous position in the left iliac fossa or at the end of the median laparotomy incision and was lavaged with betadine and saline if signs of local stump-related sepsis occur during post-operative period. 7 out of 20 patients experienced early stump-related septic complication and in 5 of these patients the authors were able to avoid opening of the rectal stump and the discomfort due to the creation of a second stoma.

According to Trickett et al. [90] the incidence of pelvic sepsis when the rectal stump is closed seems to be related to its locations. In particular, short intrapelvic stumps have the highest rate (33%) if compared with intraperitoneally (6–12%) and subcutaneously (3–4%) placed stumps [91–93]. The authors conclude that the lowest pelvic sepsis rate is associated with subcutaneous placement despite the higher wound infection rate.

More recently, Gu et al. [94] compared postoperative outcomes after subcutaneous or intraperitoneal (Hartmann stump) rectal stump placement and concluded that a subcutaneously placed rectal stump leak is more frequent but associated with decreased morbidity.

Furthermore, even if some surgeons, after leaving a closed rectal stump, place a rectal drain to minimize the risk of stump blow-out there are no data supporting this practice.

Other disadvantages of the subtotal colectomy and Brooke ileostomy include acute and chronic stoma complications, electrolyte abnormalities (dehydration or even renal dysfunction)

and urinary and gallstones formation. In patients with staged procedures, having an initial subtotal colectomy and end ileostomy is usually linked to longer period of surgical treatment, higher associated costs and overall surgical morbidity, as other reconstructive procedures are usually needed. In the era of biological therapy, this procedure is usually the first to be undertaken in chronically refractory patients, in the modified 2-stage or the 3-stage approaches.

### 3.3. Total colectomy with ileorectal anastomosis (IRA)

Total colectomy with ileorectal anastomosis (IRA) is usually an operation of exception, and can be a reasonable alternative to IPAA in selected patients with UC. This is usually the case of patients with associated advanced metastatic colorectal cancer, because of their short life expectancy [61]. Furthermore, because of no need for extensive pelvic dissection and a consequent reduced risk of sexual and urinary dysfunction, IRA can be the treatment of choice in younger women eager to get pregnant [95]. This technique can only be indicated in cases where the rectum can be spared in terms of disease activity, or subsequently controlled with rigorous medical therapy. Conversely, patients with poor sphincter function, severe rectal disease and poorly compliant rectum should not be offered an IRA. Due to the high risk of subsequent cancer and persistent rectal inflammation, surveillance of the retained rectum after IRA is mandatory [96]. Urgency is the most common cause of IRA failure and several studies reported an elevated number of bowel movements per day [97–99]. Unfortunately, this is not a definitive operation, especially for young patients, and completion proctectomy can be often indicated in cases of recurrent proctitis, dysplasia or cancer [100,101].

### 3.4. Minimally invasive surgery (MIS)

The application of laparoscopic techniques to restorative proctocolectomy and IPAA was first described by Peters in 1992 [102]. Since then, minimally invasive surgery (MIS) has become an accepted alternative to open surgery. The main advantages of this approach are the decreased surgical trauma as compared with open surgery, reduced analgesic medication requirement, reduced postoperative complications and length of hospitalization, as well as an improvement in intraoperative visualization [103–111].

Furthermore, high rates of fecundity can be observed if MIS is compared with open surgery [112], as well as the obvious advantage of a better cosmesis [113–115]. Chung et al. [116] performed a multivariate analysis identifying laparoscopy as the only factor independently associated with a shorter time interval between the second and the third operation of the three-step restorative proctocolectomy and demonstrating that patient who undergo laparoscopic subtotal colectomy are able to complete their subsequent procedures earlier than those patients whose undergo open colectomy. These results were consistent with what had been described by Maartense and Ouassi [117,118].

A recent Cochrane review of 11 trials including 607 patients undergoing IPAA for UC or familial adenomatous polyposis failed to demonstrate differences between open and laparoscopic surgery in terms of mortality, morbidity, reoperation and readmission, being the operative time significantly longer in the laparoscopic group [119]. However, MIS has expanded significantly over the last years and there have been several reports that have investigated the superiority, in terms of both short- and long-term outcomes, of the laparoscopic approach for UC patients [120].

Gu et al. identified 204 patients submitted to laparoscopic total abdominal colectomy for UC and reported that preoperative high-dose steroid exposure and low BMI are, respectively, independent

risk factors for postoperative morbidity (39%) and for reoperation (7%), within 30 days of colectomy. Their results fall within the ranges reported in literature for both parameters [121].

The potential advantages of laparoscopy are related to the experience of the centers in which it is performed. Literature is clear on the importance of centralization showing how surgeon and hospital volume impact colorectal surgical outcomes. In fact, the best outcomes occur in high volume hospitals with high volume surgeons (i.e. a dedicated colorectal surgeon).

Other MIS approaches, as robotic surgery [122] and single incision laparoscopic surgery (SILS) [123], has also been successfully used in IPAA surgery. Nevertheless, the cost of robotic procedures is higher than that of conventional multiport laparoscopic surgery [124], and SILS is more appropriate for experienced laparoscopic surgeons. Therefore, further studies are needed to better position these techniques in therapeutic algorithms. MIS is clearly the future of colorectal surgery. However, MIS in UC is technically demanding with a steep learning curve and should be offered only in specialist tertiary care centers.

### 3.5. Timing of ileostomy closure

A temporary loop ileostomy is the preferred choice of most surgeons as an associated procedure during restorative proctocolectomy and IPAA [125]. It can reduce pouch-related septic complications [126] which can occur in 10% of restorative proctocolectomies [127–129], but can also be associated with morbidity rates of more than 10% [130–132].

Wong et al. [133] compared the complication rates on ileostomy closure at or after 3.2 months vs. closure before 3.2 months. They didn't find significant differences in the proportion of small bowel obstruction or anastomotic complications. On the contrary, early closure (before 3.2 months) was associated with a higher rate of wound infections. The authors concluded that closure should not be planned before 3 months.

## 4. Conclusions

The surgical management of UC remains a significant challenge. Several issues on the timing of the procedures need to be carefully evaluated. In the acute setting, surgeons' involvement is essential since hospital admission, as conditions can fastly deteriorate, and surgical indication can be masked by intrinsic difficulties in the clinical evaluation of the patients. In these cases, staged procedures with initial subtotal colectomy and end ileostomy as a first step, followed by further reconstructive techniques, constitute the best and safest approach. In stable patients, MIS can be initially offered, with significant advantages. However, in unstable patients, with toxic megacolon, sepsis or MODS, laparotomy can be the approach for a rapid procedure.

In the chronic setting, failure of medical therapy is the most common indication for surgery in UC, followed by associated dysplasia or cancer. As these patients are usually exhausted of medical therapy, with impaired nutritional status, a staged procedure is commonly indicated, with pouch construction and IPAA performed as a second stage, after improvement of clinical status. Laparoscopic techniques currently constitute the best approach in the surgical management of UC and are linked to several advantages over conventional procedures. A multidisciplinary management of UC is key in order to define the best timing and the best procedure for each patient in an individualized basis.

#### 4.1. Practice points

- Ulcerative Colitis (UC) is an idiopathic chronic inflammatory bowel disorder of the colonic mucosa affecting the rectum that generally extends proximally in a continuous manner through the entire colon
- The precise etiology of UC is unknown, but is most probably the result of the interaction of genetic and environmental factors
- Approximately 15% of UC patients develop an acute attack of severe colitis, and 30% of these patients require colectomy
- The primary goals of medical therapy in the treatment of UC are to induce remission of symptoms and maintain it on a long-term basis
- Infliximab, used as rescue therapy after failure of steroids in UC, appears to be effective in reducing the need for urgent colectomy, although its efficacy in the long-term is not proven
- Surgery in UC depends on the stage of the disease as well as patient's status and is divided into the following settings: urgent, emergent and elective
- The three main indications for surgery in UC remain [1]: acute severe colitis [2]; refractory UC [3]; associated dysplasia and carcinoma.
- Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is currently the procedure of choice for the elective surgical treatment of UC in patients who have good sphincter function and no risk factors for postoperative complications
- Subtotal Colectomy with Brooke ileostomy remains the optimal procedure in case of ASUC, as well as in the majority of exhausted chronic refractory patients
- Total colectomy with ileorectal anastomosis (IRA) is usually an operation of exception, and can be a reasonable alternative to IPAA in selected patients with UC (advanced metastatic colorectal cancer and younger women eager to get pregnant)

#### 4.2. Research agenda

- The reduction in hospitalization and surgical intervention for patients affected by ulcerative colitis after the introduction of biologic treatment is still in doubt.
- Laparoscopic colectomy and restorative IPAA represent the standard of care in the treatment of UC requiring reducing post-operative pain, time to stoma function and overall hospital stay. Furthermore, laparoscopy also leads to longer operative time with its results related to the experience of the centers in which is performed. Further studies are needed to clarify these points.
- Robotic surgery and single incision laparoscopic surgery (SILS) has also been successfully used in IPAA surgery. Nevertheless, the cost of robotic procedures is higher than that of conventional multiport laparoscopic surgery, and SILS is more appropriate for experienced laparoscopic surgeons. Therefore, further studies are needed to better position these techniques in therapeutic algorithms

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