

Role of surgery in pediatric ulcerative colitis

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Abstract Pediatric ulcerative colitis (UC) has a more extensive and progressive clinical course than adult UC. Therefore, more aggressive initial therapies and more frequent surgical treatments are needed. The therapeutic goal is to gain clinical and laboratory control of the disease with minimal adverse effects while permitting the patient to function as normally as possible. Approximately 5–10 % of patients with UC require acute surgical intervention because of fulminant colitis refractory to medical therapy. Mucosal proctocolectomy with ileal J-pouch anal anastomosis is currently recommended as a standard curative surgical procedure for UC in both children and adults worldwide. This review will focus on the current issues regarding the surgical indications for pediatric UC, the technical details of procedures and results of most recent published series to take the most appropriate next step to improve the surgical outcomes and patients' quality of life.

Keywords Ulcerative colitis · Surgery · Children

Introduction

Ulcerative colitis is a chronic, relapsing and remitting illness, whose incidence is rising globally [1–4]. Although its cause remains unclear, it is considered an immune-mediated disorder with a complex interplay between environmental, genetic and immunologic factors. Many patterns of presentation are possible within the pediatric age group.

The hallmark symptoms of UC include abdominal cramping, diarrhea and bloody stools, but physical symptoms vary with extent, duration and severity of the disease. Clinical experience suggests that childhood-onset disease may have a more severe phenotype being extensive in 60–80 % of all cases, twice as often as in adults and has a worse disease course, with a 30–40 % colectomy rate at 10 years, as compared with 20 % in adults [5, 6]. It is also estimated that approximately one in four pediatric patients undergo colectomy during the first decade after the diagnosis [7]. Furthermore, although significant advances have been made in medical management of UC, no change in the surgery rate has been seen between the years 1994 and 2007 [8]. Unfortunately, children may present to the surgeon after a prolonged course of failed medical management and immunosuppression, with surgery rates as high as 60 % in children with steroid-refractory UC [9]. Patients with a prolonged severe course of medically refractory disease often require prolonged hospitalization and experience increased postoperative complications [10].

UC is a chronic inflammatory bowel disease that can lead to derangements in the growth, nutritional status and psychosocial development of affected children. As the etiology of the disease has become better understood, newer therapeutic alternatives have arisen in the form of biologic therapies, which are monoclonal antibodies targeted to a specific protein or receptor. So far, there are several medical options for the induction and maintenance of disease remission, but the benefits of these medications need to be carefully weighed against the risks, especially in the pediatric population. This review will discuss the surgical indication for treatment of the disease in both the elective as well as the urgent onset with a particular focus on technical consideration and results of the most recent published series.

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Treatment of UC

Goals of therapy for pediatric UC include induction and maintenance of disease remission, improvement in quality of life, facilitation of normal growth and prevention of development and finding of colonic dysplasia or cancer of the affected bowel [11]. In recent years, new standards for the treatment of UC have evolved. The treatment of pediatric UC is sequential and tailored to the severity of disease activity [12]. As shown in Table 1, pharmacologic therapy for UC includes the following categories of medications: 5-aminosalicylates (5-ASAs), corticosteroids, thiopurine immunomodulators, calcineurin inhibitors, antibiotics, probiotics and anti-tumor necrosis factor (TNF)- α agents. While medical therapy in the setting of severe or fulminant colitis is generally preferred in children, colectomy should also be seriously considered, especially in the presence of life-threatening hemorrhage, perforation, or peritonitis. Other standard indications for surgical intervention include the following: worsening symptoms despite maximal

medical management; history of chronic corticosteroid use with significant side effects; history of long-standing, extensive disease for greater than 10 years; or delay in growth and maturation [13].

Ulcerative colitis can be cured by surgically removing the diseased colon and rectum. Historically, this was performed by creation of a permanent ileostomy, and the operation often was delayed until the patient was severely ill. However, more recently, the growing popularity of a total proctocolectomy and endorectal pull-through procedure has allowed for consideration of surgery for many patients with chronic ulcerative colitis before severe disability and major complications develop. Ulcerative colitis in children can have a negative effect on quality of life (QoL). In chronic illnesses like UC, it is important to try to clarify what factors are affecting the patient's quality of life and whether it is possible to alleviate such burdens. The QoL evaluation in inflammatory bowel disease has become a primary concern and a major objective in recent studies. It serves to appreciate the efficiency of the treatment, helps describe the nature and gravity of the disease and also to assess the prognostic. IBD has a negative impact on all aspects concerning QoL. The emotional behavior is mainly disturbed, triggering the development of depression and anxiety during and after the active disease periods. Health-related quality of life (HRQL) in patients with pediatric onset of UC is not well studied in case of surgical treatment. We reported our experience and long-term follow-up results of 28 patients who underwent endorectal pull-through (ERPT) as surgical treatment for UC with a good self-reported emotional health in most of the patients [14]. More recently, the HRQL of proctocolectomy patients with those treated with medical therapy was evaluated. Surgical patients reported to have a HRQL comparable to or better than the non-surgical patients: depression, fatigue, parent/guardian education and drugs being the main factors influencing HRQL [15]. In conclusion, surgical treatment, if compared to medical therapy, has a role also in improving QoL.

In the late 1890s, the first surgical therapy for UC, comprising colon irrigation through a temporary inguinal colostomy, was reported [16, 17]. From the beginning of the 1940s, total colectomy and ileorectal anastomosis (IRA) for restoration of intestinal continuity in patients with UC were reported and IRA became the standard surgical procedure for UC [18–20]. In pediatric experiences, Ehrenpreis [21] suggested that total colectomy and IRA can be performed safely in patients with mild-to-moderate inflammation of the rectum, provided that regular surveillance is continued. In 1947, Ravitch et al. [22] reported the first patient with UC who successfully underwent total proctocolectomy and primary straight ileoanal anastomosis (SIAA). In 1950, Bacon and Trimpi [23]

Table 1 Classes of medications used in the management of pediatric ulcerative colitis [13]

Medication class	Clinical indications	Common side effects
5-aminosalicylates	Mild-to-moderate disease	Headaches, nausea, diarrhea, photosensitivity
Corticosteroids	Acute moderate-to-severe disease	Hyperglycemia, hypertension, growth failure, weight gain, osteopenia, mood disturbances
Thiopurine immunomodulators	Maintenance of remission of moderate-to-severe disease	Bone marrow suppression, hepatitis, pancreatitis, infections, malaise, rashes
Calcineurin inhibitors	Acute severe or fulminant disease	Nephrotoxicity, infections, seizures, hirsutism, hypertension, headaches
Antibiotics	Adjunctive therapy for active disease; pouchitis	Specific to individual antibiotics
Probiotics	Adjunctive therapy for active disease; recurrent pouchitis	Limited data
Anti-TNF- α agents	Induction and maintenance of remission of moderate-to-severe disease	Hypersensitivity reactions, headaches, nausea, abdominal pain, infections

TNF- α tumor necrosis factor- α

demonstrated successful results of a staged operation concept comprising total proctocolectomy and SIAA with ileostomy construction in the first stage and ileostomy closure in the second stage. Pediatric surgeons also investigated better ways to use SIAA for UC by employing the Soave procedure for Hirschsprung's disease [24] and in 1985, Soave [25] himself reported straight SIAA in nine children. In the many experiences reported with this technique major postoperative problems were frequent bowel movements and urgency of defecation because of the low ileum capacity. Thereafter, the ileal pouch-anal anastomosis (IPAA) (also known as “restorative proctocolectomy”), for the first time described by Parks and Nicholls in 1978 (ileal S-pouch), became the most commonly practiced surgery, also in children. In 1980, Utsunomiya et al. [26] for the first time described for creation of a J-pouch anal anastomosis with good long-term functional results. The J-pouch (usually constructed with a stapling instrument) procedure has been adopted from colorectal and pediatric surgeons worldwide because of its simplicity and its superiority verified in both adult and pediatric age at many specialized institutions [27].

Surgery in children with ulcerative colitis can be elective or emergent. Elective operation is performed on patients with chronic disease who experience continued symptoms despite medical therapy, growth retardation, severe limitation of activities and an unacceptable quality of life. Risk of colorectal adenocarcinoma is an indication to elective surgical procedure, as well. Emergency indications for operation include fulminant disease refractory to medical therapy, extensive rectal bleeding and toxic megacolon. Evaluation of the child's condition should be done periodically during the course of therapy by the surgeon and the gastroenterologist to consider alternatives to long-term medical therapy.

Elective surgery

In 2012 guidelines for managing UC in ambulatory children based on a systematic review of the literature and a robust consensus process were published [28]. Guidance for the management of pediatric UC is summarized in an algorithm (Fig. 1). Consensus' conclusions of surgical considerations are that elective colectomy may be indicated in children with active or steroid-dependent UC despite maximal treatment with 5-ASA, thiopurines and anti-TNF therapy or the finding of colonic dysplasia. Concerning the latter the rate of adenocarcinoma in childhood-onset UC patients is higher than that in adult-onset UC patients and the cumulative probabilities of developing colorectal cancer is 5.5 % at 10 years after onset of UC, 10.8 % at 20 years and 15.7 % at 3 years [29, 30].

The operative techniques for restorative proctocolectomy have evolved over time. Most pediatric surgeons have used an endorectal mucosectomy followed by a hand-sewn ileo-anal anastomosis with or without creation of a pouch. Stapled SIAA, instead, involves an extrarectal dissection for proctectomy, and the anastomosis is placed higher than the “hand-sewn” [31]. Hence, a short bowel segment consisting of diseased rectal-type columnar epithelium is retained above the ATZ, the columnar cuff.

The more recent modification of this procedure, in which the ileal pouch is stapled to the anus for preservation of the anal transition zone (ATZ) without the use of the endorectal dissection, has become the standard approach for most adult surgeons [32] and this technique has been adopted also in the last cases of our series. In 1980, Knight and Griffen [33] developed the “double-staple” technique, using a circular stapler to transect a linear rectal staple line. This eliminates the need for a hand-sewn, distal purse string, which is sometimes difficult or even impossible to accurately place low in the pelvis.

The reported advantages of the double-stapled technique over the hand-sewn technique include its simplicity, speed and avoidance of trauma associated with a transanal mucosectomy by minimizing anal manipulation. As described by the same Authors 10 years later [34, 35], the use of the double stapling technique for low rectal reconstruction allows retention of a small segment of the distal rectum with sphincter preservation and offers the advantage of a very low rectal anastomosis close to the dentate line, avoiding problems with the anastomosis, such as disparate sizes of the segments of bowel. Reported experience of the straight stapled SIAA is associated to low morbidity and good functional results even if severe inflammation of the columnar cuff was associated with an increased risk of nighttime incontinence [36]. Main disadvantages of this technique are the higher long-term risk of rectal dysplasia and carcinoma that has been described in adults undergoing the J-pouch [37]. However a meta-analysis by Schluender et al. [38] in adult experience did not identify any difference in functional or manometric outcomes between the two techniques and overall, dysplasia within the ATZ is uncommon and the risk of developing cancer following RPC IPAA is even more unlikely with only 19 reported cases in the literature until 2009 [39].

However, endoscopic follow-up is mandatory to detect early dysplastic changes in the residual rectum. Comparison of hand-sewn versus stapled ileal pouch-anal anastomosis is summarized in Table 2. More recently, a new operative technique that is a modification of the double-stapled technique by combining it with an endorectal dissection from an abdominal approach has also been described: the endorectal double-stapled (ERDS) ileo-anal

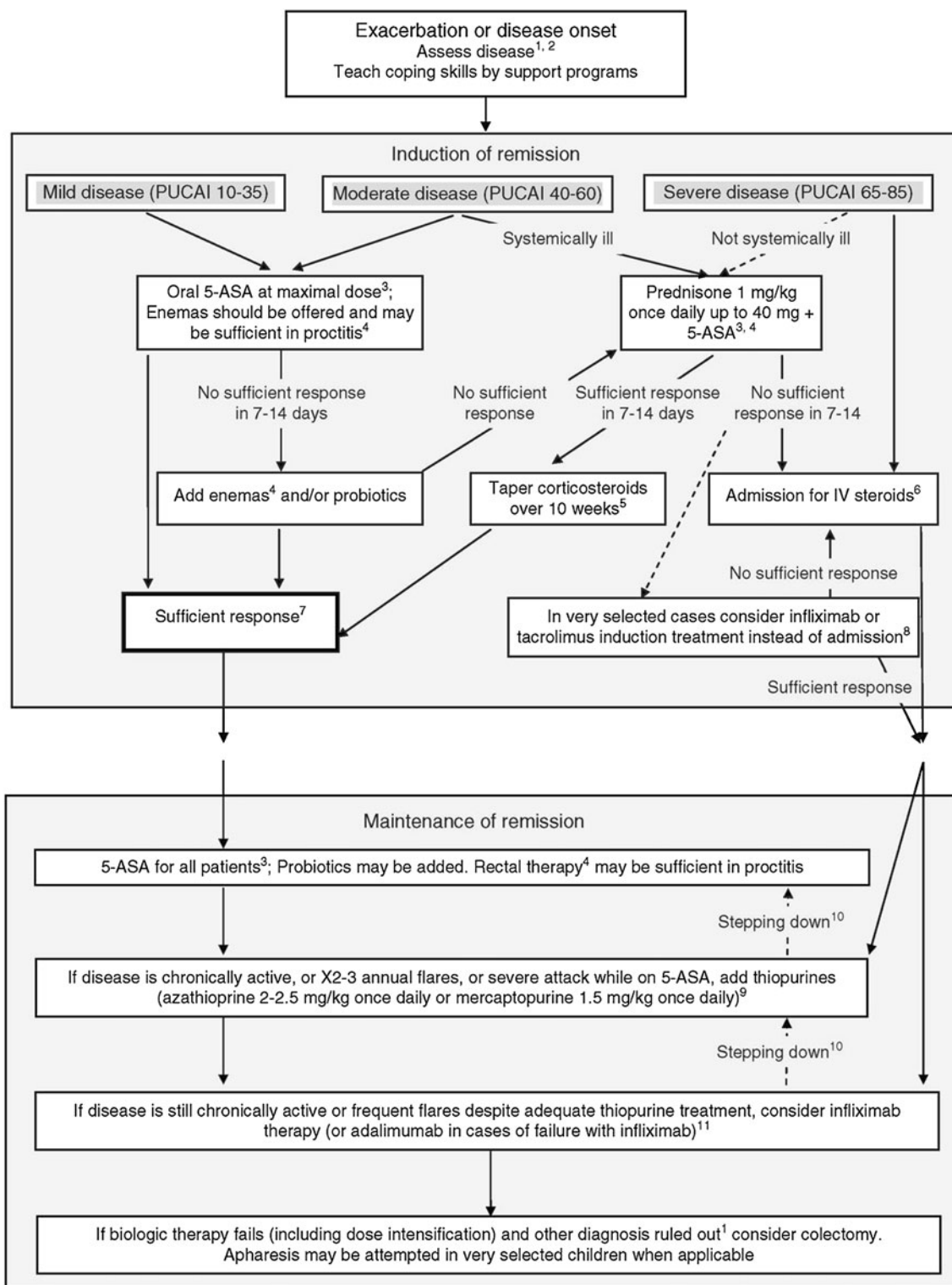


Fig. 1 Joint European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)—European Crohn’s and Colitis Organization (ECCO) therapeutic paradigm for pediatric UC [28]

pouch anastomosis. [40]. It combines the advantages of endorectal dissection with the simplicity and speed of the double-stapled technique. The endorectal dissection from an abdominal approach not only allows to get down low on

the rectum to the dentate line, but also completely avoids injury to the parasympathetic and sympathetic nerves of the pelvic plexus. The eversion of the rectal mucosal/submucosal tube onto the perineum allows clear identification of

Table 2 Comparison of hand-sewn versus stapled IPAA [75]

Hand-sewn	Stapled
Advantages	
Excellent long-term results	Excellent long-term function
No disease recurrence	Higher resting pressure
No or very low cancer risk	Improved nocturnal continence
No annual surveillance required	Easier to learn, low failure rate
	Less manipulation of anal canal
Disadvantages	
Risk of damage to anal sphincter	Possibility of disease recurrence
Technically demanding	Risk of dysplasia or cancer
	Annual surveillance required
	Chronic inflammation in ATZ

the dentate line and exact placement of the stapling device to determine ultimately the level of the anastomosis. This prevents leaving too much rectum behind and eliminates the difficulty of placing a transverse approximating stapler into a narrow male pelvis or a young child's pelvis.

Another surgical point to discuss is the different technique that can involve either a straight ileo-anal anastomosis (SIAA) or the creation of a reservoir from an ileal pouch (IPAA). From literature, restorative proctocolectomy with ileo-anal anastomosis, both with (IPAA) or without (SIAA) the creation of a pouch reservoir, has been shown to be safe and effective surgical treatment for patients with UC and FAP [41–45].

Choice of either depends on weighing the risks and benefits of each procedure. The use of a pouch has become increasingly more popular because it appears to reduce the frequency of stooling. The pouch seems to be associated with fewer bowel movements, particularly in the first year after the procedure but has the attendant risk of pouchitis, however, which may occur in 50 % of adult patients after 10 years following pull-through [46]. Pouchitis, a non-specific inflammatory condition of the ileal pouch reservoir, is the most common long-term complication in patients who have undergone IPAA, and it significantly affects patients' quality of life. The reported cumulative risk of developing pouchitis varies widely, ranging from 15 to 50 % in children with UC, and may be even higher [47].

In patients with pouchitis, 70 % had the initial episode during the first 12 months after ileostomy closure [48]. Sixty percent of the affected children will suffer from recurrent episodes and 5–10 % will develop chronic pouchitis [49]. The probability of pouch failure has been found to be 9 % at 10 years [50].

The process may relate to the original disease because pouchitis is seen infrequently in patients with familial polyposis. Pouchitis is as an inflammatory state resulting from stasis within the reservoir Symptoms including fever,

pelvic pain, bloody stools, diarrhea and malaise. Treatment with antibiotics (metronidazole or ciprofloxacin) is usually successful. Occasionally, patients may benefit from steroid enemas. The use of probiotics may be beneficial in preventing recurrence of pouchitis when the patient is in remission. Recurrent pouchitis may be a manifestation of Crohn's disease, and biopsy specimens should be obtained. It has become apparent that pouchitis is more common in larger reservoirs, which empty only partially with each defecation. In our personal experience, we perform a short pouch (about 5 cm) to reduce the risk of this complication.

In a recent meta-analysis on adult experience, pouch failure rate was found to be 4.3 % (95 % CI: 3.5–6.3) and pelvic sepsis 7.5 % (95 % CI: 6.1–9.1). Pouch failure was lower by 2.5 % in recent studies vs those published prior to 2000. Functional outcome remained stable over time, with a 24-h defecation frequency of 5.9 (95 % CI: 5.0–6.9), regardless of the technical aspects of the surgery [51].

Comparing results of straight SIAA and IPAA is not easy due to the paucity of meta-analysis, prospective studies and difficulty in comparing functional results.

The only meta-analysis published in 2006 [52] studies comparing outcomes from ileal pouch-anal anastomosis (IPAA) and straight ileo-anal anastomosis (SIAA) were identified by searching Medline, Ovid and Embase. Suitable studies were selected and data extracted for meta-analysis. Only five studied satisfied the inclusion criteria, comprising a total of 306 patients, 86 of whom (28.1 %) underwent SIAA, and the remainder, IPAA. Pouch failure was more common in the SIAA group (odds ratio 3.21; CI: 1.24–8.34), as were abdominal salvage procedures (odds ratio, 9.5; CI: 3.14–28.77). Short-term adverse events were similar between the two groups, with the exception of perianal sepsis, the higher frequency of which, in SIAA, just reached statistical significance. Bowel frequency was lower in the IPAA patients, although few studies presented functional data in a comparable form. This meta-analysis concludes that there are few good-quality studies that compare the outcomes from SIAA and IPAA, meaning that caution should be exercised in the generalization of these results, which suggest pouch procedures to be favorable in terms of reconstruction survival and functional outcome. In a more recent retrospective study, 250 children after proctocolectomy with either SIAA (112 pts) or IPAA (J-pouch: 91 pts), for the first 3 years after pull-through, were analyzed. Daytime and nighttime stooling frequencies were significantly higher ($P < 0.013$) for SIAA patients at 1–24 months after pull-through; however, stooling frequencies began approximating each other by this time. Symptomatic pouchitis (compared to enteritis after SIAA) was significantly higher in IPAA patients (odds ratio, 4.5; CI: 2.32–8.72). Frequency of pouchitis declined with time.

There was no significant difference in the incidence of surgical complications between the two groups. Finally, continence rates were strikingly good in both groups as compared to previously reported series [53]. A two-staged operation is favored by most pediatric surgeons in elective colectomy. The first operation consists of a total proctocolectomy, endorectal IPAA, and diverting loop ileostomy, while the second stage involves the closure of the ileostomy ~8–12 weeks later. The safety of performing a restorative proctocolectomy (RP) and J-pouch ileo-anal anastomosis (IPAA) without diverting ileostomy for children with ulcerative colitis (UC) is a subject of extensive debate. Several potential advantages of creating a diverting ileostomy, include avoiding consequences of pouch leak or failure, limiting stress on a fresh anastomosis, allowing recovery of anal sphincter function, and allowing de-conditioned patients time to heal before restoring GI continuity [54]. On the other hand, potential advantages to a one-stage procedure include less general anesthetics, hospitalizations, ileostomy take-down complications, atrophy of the anal sphincter muscle and issues with negative body image. There have been multiple reviews in the adult literature comparing these two treatment strategies, but comparatively few appear in the pediatric literature. A recent single-institution review comparing pediatric UC patients who underwent IPAA with or without diverting ileostomy documented equivalent short- and long-term outcomes even if questions remain regarding patient selection and quality of life impact [55]. In our experience we feel performing a temporary loop ileostomy is the preferred choice.

Acute surgery

Acute severe exacerbations of ulcerative colitis (ASC) constitute a medical emergency in both children and adults. The introduction of intravenous corticosteroid treatment dramatically reduced mortality in this otherwise life-threatening condition. Nevertheless, steroid resistance is common, making early recognition of ASC important, so that appropriate medical and, if necessary, surgical treatment can be provided in a timely fashion to minimize morbidity.

As well as for elective colectomy, guidelines for managing acute severe ulcerative colitis (ASC) in children have been recently published [56]. Based on systematic review of the literature and consensus among international experts a day-by-day decision-making algorithm for suggested management is provided (Fig. 2).

Urgent colectomy is indicated in acute severe colitis not responding to medical therapy, toxic megacolon, perforation and uncontrolled colorectal bleeding (rare).

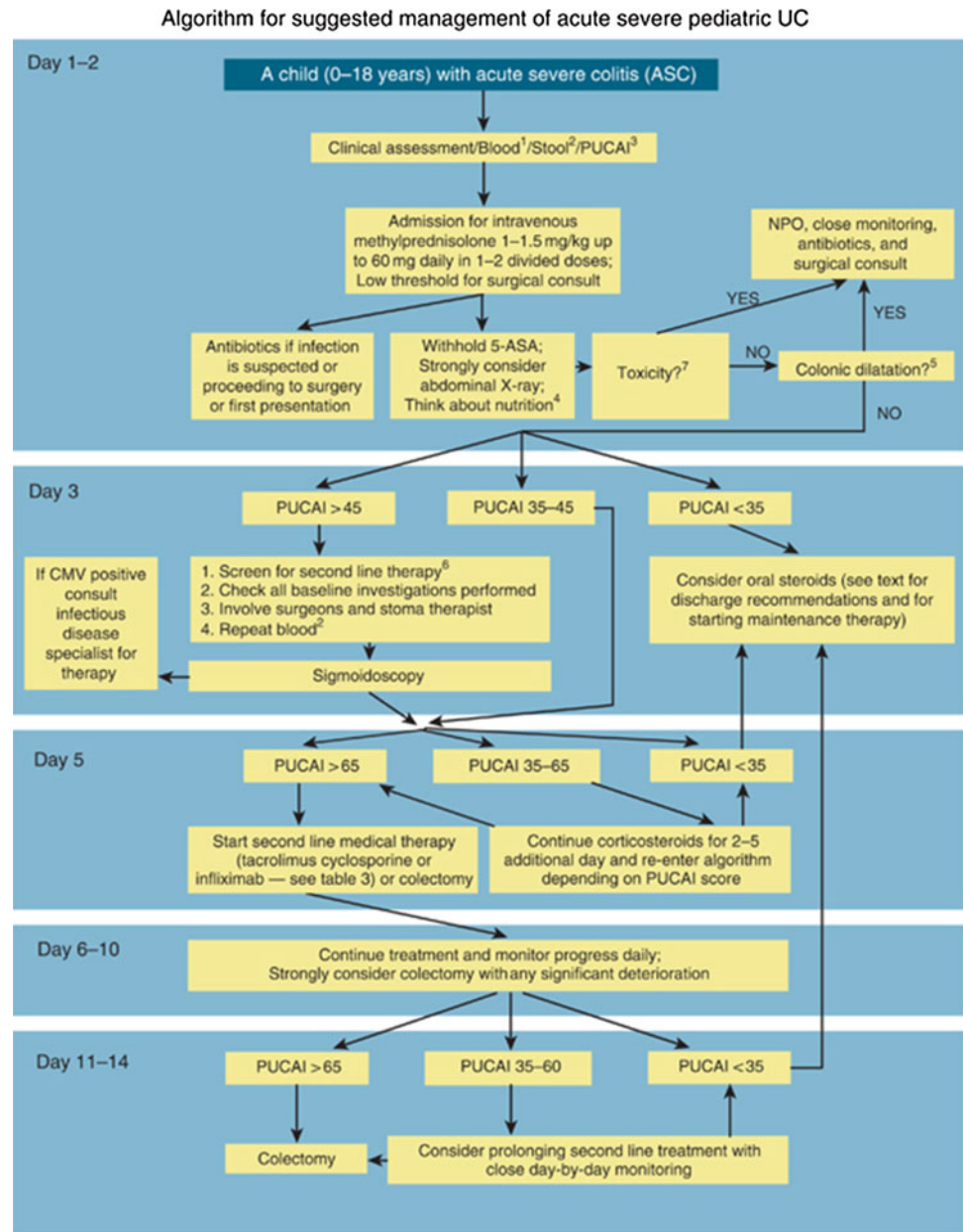
Surgery is usually the preferred therapeutic option in patients with toxic megacolon, a life-threatening event. Diagnostic criteria for toxic megacolon should consist of radiographic evidence of transverse colonic dilatation (≥ 56 mm) plus signs of systemic toxicity. If toxic megacolon has been diagnosed immediate surgical consultation is required even if it is a 24–48 h trial of conservative treatment (i.e., bowel rest, broad spectrum antibiotics and rectal tube) may be cautiously attempted in the non-severe cases (stable vital signs and no sepsis) in specialized centers only while under intense monitoring. Sequential therapy of calcineurin inhibitors followed by infliximab or vice versa may be successful in ~25–40 % of adult patients, but is associated with significant morbidity and even mortality. Therefore, most recommend timely referral for colectomy after failing one medical salvage therapy, rather than attempting another regimen. Expected response to calcineurin inhibitors and infliximab is roughly 1–2 weeks and colectomy should not be withheld in non-responders. To minimize surgical complications in treatment of ASC, guidelines state that delay in surgical intervention to enhance nutrition is not recommended, children undergoing surgery should be treated with antibiotic of appropriate spectrum and even if pre-operative steroid administration is associated with an increased risk of anastomotic leak and infectious complications, surgery should not be delayed to taper steroids.

A three-stage approach (colectomy with temporary ileostomy in the first stage, pouch construction in the second stage and ultimately ileostomy closure) should be performed in patients with steroid-refractory acute severe colitis, those on high dose steroids and/or suffering from malnutrition, and those in whom Crohn's disease has not been excluded [56].

Minimally invasive approach

Proctocolectomy procedures are performed using open or laparoscopic approaches. With increasing experience with laparoscopic colorectal surgery on pediatric age, there are no absolute contraindications to laparoscopy and the decision is based upon surgeon judgment skills and experience. In some cases only the colonic mobilization can be performed laparoscopically, with vessel transection and rectal mobilization carried out through a mini laparotomy, or a totally laparoscopic procedure can be adopted. Minimally invasive techniques are central to fast-track protocols with advantages of a decrease in inflammatory mediators, improved pulmonary function comparable to the open technique, faster return of bowel function, superior cosmetic results and reduced hospital length of stay. In the adult experience laparoscopic IPAA for UC has been

Fig. 2 Algorithm suggested for management of acute severe pediatric UC [56]



shown to be feasible, but to date the evidence present in the literature is still not conclusive. Current data suggest a shorter length of stay, shorter ileus, faster recovery and less postoperative pain, along with better cosmesis with minimally invasive surgery. On the other hand, significantly longer operative times with laparoscopy are universally reported [57].

The laparoscopic approach in both urgent and elective colorectal surgery reported in many published studies is feasible, safe, effective and associated with better short-term outcomes [58, 59]. Recent advances in experience and technology have led to laparoscopic procedures being performed through a single-incision. In children IPAA has been completed through single-incision surgery [60] as

well as in other conditions (appendectomy, gastrostomy tube placement, fundoplication, cholecystectomy, splenectomy, anterior diaphragm hernia repairs).

A large series of children who have undergone single-incision laparoscopic surgery for inflammatory bowel disease and polyposis syndromes have been recently presented [61].

Operative times, length of hospital stay, postoperative morbidity, short-term bowel function and rates of pouchitis are similar to open, laparoscopic-assisted, and laparoscopic colon and rectal surgery even if single-incision restorative proctocolectomy with protective ileostomy is recommended due to the high rate of anastomotic leak (42 %).

Discussion

Medical therapy in UC is rapidly evolving and the introduction of modern biological drugs has led to substantial changes in the traditional principles of management. Surgery continues to play an important role in UC treatment and its evolution keeps pace with the advance in medical therapy and the risk associated with it. Restorative proctocolectomy with IPAA, staged procedures and minimally invasive surgery are important treatment tools to limit postoperative morbidity and achieve excellent long-term outcomes in these patients. In an attempt to avoid surgery, aggressive medical therapy is not without complications. A complex decision-making process in a multidisciplinary fashion should take into consideration the excellent results of modern surgical therapies to avoid unnecessary morbidity. The concept of pushing conservative treatment until surgery is strictly required may be risky. As it has been shown in the adult experience mortality 3 years after elective colectomy for UC (3.7 %) is significantly lower than that after admission without surgery (13.6 %) or when an emergency operation is performed (13.2 %) [62]. Moreover, a British study recently reported a significantly higher risk to develop major complications at a 5-year follow-up for patients who received a longer course of medical therapy for acute severe UC before surgery, suggesting that the threshold for elective surgery may be too high in current practice [63]. Considering the excellent outcome of restorative surgery, heightened by the potentials of minimal invasive techniques, surgery should not be considered the last resort when everything has failed, but rather a valid alternative to an expensive and risky medical therapy [64]. UC in children is frequently severe and treatment-refractory. In pediatric as well as in adult UC, while medical therapy is well standardized, little is known regarding factors that contribute to surgical indications, complications, or long-term outcomes. Furthermore, few data are available on clinical research of how advances in medical treatment have affected surgical indications. While a Pediatric Ulcerative Colitis Activity Index (PUCAI) has been validated in determining medical therapy failure and timing for second-line therapy its use in determining timing for surgical intervention has not been studied. In adulthood experience large administrative datasets have been used to identify predictors of colectomy in patients affected by UC [65] but in pediatric population only very recently studies aimed to identify factors affecting risk of colectomy have been published. In literature, mainly three recent studies have been performed in children to identify factors associated with progression to colectomy. In the first one, children with UC presenting with hypoalbuminemia, weight loss, a family history of UC and those treated with calcineurin inhibitors frequently require restorative proctocolectomy for definitive treatment. Authors' conclusions are that early identification

and recognition of these factors should be used to shape treatment goals and initiate multidisciplinary care at the time of diagnosis [66]. In the second one, a retrospective cohort study using the Pediatric Health Information System database, developed by the Child Health Corporation of America, 8,688 patients affected by UC were studied. Of these, 240 (2.8 %) underwent colectomy and—compared with non-operative patients—factors associated with statistically significant progression to colectomy were: advanced therapies (corticosteroids and biological therapies), malnutrition, anemia, electrolyte imbalance, *Clostridium difficile* infection and TPN requirement. Another important result of this cohort study is that each successive admission with a primary diagnosis of UC is associated with a 8 % increased risk of receiving a total colectomy during that admission. These factors represent clinical variable that currently contribute to surgical decision-making in children with UC and should be more closely examined in further research [67]. The third study aimed to find biomarkers that, at the onset of disease, could distinguish patients with complicated disease behavior and a high risk for surgery from those with a more benign course. By current diagnostic modalities, it is impossible to foresee the disease outcome at the time of the diagnosis of UC, although an initial aggressive disease increases the risk of colectomy. Expression of Tryp-1 was found to be weaker in the epithelial cells of patients with aggressive disease but the mechanism and significance of that finding remained unclear. Therefore, conclusion of this study was that there is a need for further investigations on Tryp-1 and other biomarkers to identify patients with aggressively proceeding UC [68]. Identification and deepening of a subset of clinical factors that are independently associated with progression to total colectomy require future investigations to define best-practice standards to guide the treatment of these complicated patients and improve their quality of life.

Another issue to present and discuss is the need and benefit that centralization of care of surgical treatment of this condition would have. The review of English experience with UC from 1996 to 2008 was performed by Burns et al. [69].

The objective of this study was to determine outcome following RPC between 1996 and 2008 using Hospital Episode Statistics (HES) data. Specific aims were to examine national postoperative mortality, length of hospital stay (LOS), readmissions and failure rates following pouch surgery and the effect of institutional and surgeon caseload on outcome following surgical treatment. Results were that the 30-day in-hospital mortality rate was 0.5 % and the 1-year overall mortality rate 1.5 %. More than ninety per cent of surgical teams (456 of 499) carried out 20 or fewer surgical procedures over 8 years. Median surgeon volume was 4 cases. Failure occurred in 6.4 % of cases. Low-volume surgeons operated on more patients at

the extremes of age ($P < 0.001$) and a lower proportion with ulcerative colitis ($P < 0.001$). Older age, increasing comorbidity, social deprivation and both lower provider and surgeon caseload were independent predictors of longer length of stay. Older patient age and low institutional volume status were independent predictors of failure. Conclusions of this paper, together with the data presented, are that given the complexity of the surgery and postoperative care, patients would benefit by being treated in an experienced networked Inflammatory Bowel Disease Unit to decrease length of stay and failure rate.

Furthermore, in the largest published cohort of pediatric patients with UC who underwent restorative proctocolectomy a significant difference was noted between high and low-volume hospitals for medical complications and hospital LOS. [70]. Although UC in children occurs infrequently, the volume of hospital experience for pediatric cases with UC requiring proctocolectomy still contributes to improved outcomes. In larger series of adults with UC, similar relationships between hospital volume and outcomes after proctocolectomy have been reported by demonstrating low institutional volume as an independent predictor of surgical failure, higher morbidity and mortality [71]. This may imply that both the surgeon and support staff (including anesthesiology, nursing, etc.) experience contribute to the overall outcomes after colectomy for children with UC.

Quality of life is an important measure of surgical outcome for all patients and especially for children. In the pediatric population, questions concerning the long-term effects on functionality and quality of life are more pressing in magnitude and importance. IPAA removes the need for disabling, growth-modulating pharmaceuticals and permanent ileostomy, thus vastly improving the patient's quality of life but, on the other hand, it entails surgical risks and complications that continue well into the postsurgical years. These sequels bear on physical, emotional, mental, social and familial aspects, all of which are of considerable importance to the young patient and the family. The International literature documented that both in adult and pediatric experiences, functional outcomes among patients undergoing IPAA are very good [72, 73]. Interference of physical activity, emotional status and social life caused by refractory ulcerative colitis (UC) worsens patients' HRQOL, while IPAA could resolve these problems in children with UC and result in an HRQOL comparable with that in healthy children [74].

Conclusions

Surgery continues to play a pivotal role in UC treatment and its evolution keeps pace with the advance in medical

therapy and the risk associated with it. Restorative proctocolectomy with IPAA, staged procedures and minimally invasive approaches are important treatment tools to limit postoperative morbidity and achieve excellent long-term outcomes in these patients. In the last years, our personal surgical choice, in patients with no proven dysplasia, is to perform the total colectomy using a laparoscopic-assisted approach; to exteriorize and extract the colon specimen through a Pfannenstiel incision, to construct a short J-pouch by linear stapler device and to perform an ATZ sparing stapled ileal pouch-anal anastomosis with a temporary diverting loop ileostomy. The decision to construct the temporary ileostomy in our practice does not follow any strict guidelines. We typically reserve this procedure for clinical settings where there is moderate or greater tension on the ileal-anal anastomosis and/or preoperative usage of corticosteroids or other such factors that may increase the risk of an anastomotic leak or dehiscence.

Close endoscopic surveillance is mandatory: in asymptomatic cases at ileostomy take-down, once a year for the following 10 years (procedure not requiring general anesthesia) and once every 2–3 years in the late follow-up.

Aggressive medical therapy in pediatric UC is affected by high morbidity and complications. A multidisciplinary decision-making process must take into consideration the excellent results of modern surgical therapies to avoid unnecessary morbidity and to improve quality of life of patients affected by this critical condition.

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