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Review Article

Surgical Management of Ulcerative Colitis in Children and Adolescents: A Systematic Review from the APSA Outcomes and Evidence-Based Practice Committee☆

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ABSTRACT

Introduction: The incidence of ulcerative colitis (UC) is increasing. Roughly 20% of all patients with UC are diagnosed in childhood, and children typically present with more severe disease. Approximately 40% will undergo total colectomy within ten years of diagnosis. The objective of this study is to assess the available evidence regarding the surgical management of pediatric UC as determined by the consensus agreement of the American Pediatric Surgical Association Outcomes and Evidence-Based Practice Committee (APSA OEBP).

Methods: Through an iterative process, the membership of the APSA OEBP developed five *a priori* questions focused on surgical decision-making for children with UC. Questions focused on surgical timing, reconstruction, use of minimally invasive techniques, need for diversion, and risks to fertility and sexual function. A systematic review was conducted, and articles were selected for review following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Risk of Bias was assessed using Methodological Index for Non-Randomized Studies (MINORS) criteria. The Oxford Levels of Evidence and Grades of Recommendation were utilized.

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Results: A total of 69 studies were included for analysis. Most manuscripts contain level 3 or 4 evidence from single-center retrospective reports, leading to a grade D recommendation. MINORS assessment revealed a high risk of bias in most studies. J-pouch reconstruction may result in fewer daily stools than straight ileoanal anastomosis. There are no differences in complications based on the type of reconstruction. The timing of surgery should be individualized to patients and does not affect complications. Immunosuppressants do not appear to increase surgical site infection rates. Laparoscopic approaches result in longer operative times but shorter lengths of stay and fewer small bowel obstructions. Overall, complications are not different using an open or minimally invasive approach.
Conclusions: There is currently low-level evidence related to certain aspects of surgical management for UC, including timing, reconstruction type, use of minimally invasive techniques, need for diversion, and risks to fertility and sexual function. Multicenter, prospective studies are recommended to better answer these questions and ensure the best evidence-based care for our patients.
Level of Evidence: Level of evidence III.
Study Type: Systematic review.

1. Introduction

Ulcerative colitis (UC) is the most common type of inflammatory bowel disease in North America. It is characterized by chronic or recurrent colonic mucosal ulceration, bloody diarrhea, weight loss and abdominal pain. The overall incidence of UC is increasing, and nearly 20% of all patients with the disease will be diagnosed in childhood [1]. Children typically present with more severe and extensive disease. Eighty percent of children present with pancolitis and approximately 40% will undergo total colectomy within ten years of diagnosis [2]. Due to the timing of diagnosis during this critical period of physical, intellectual, and psychosocial development, the higher rate of colectomy, and their longer lifespan without a colon, it is imperative pediatric surgeons understand the best surgical treatment strategies and their associated outcomes.

The objective of this study is to review best practices in the surgical management of pediatric UC by answering clinical questions as determined by consensus agreement of the APSA Outcomes and Evidence based Practice Committee. These include questions regarding surgical timing, reconstruction, the use of minimally invasive techniques, the need for diversion, and the long-term risks to fertility and sexual function in the pediatric population.

2. Methods

2.1. Research questions

The study was registered with Open Science Framework. The membership of the APSA OEBP Committee developed five questions *a priori* for the systematic review through an iterative process.

1. What is the optimal reconstruction for pediatric and adolescent patients after total proctocolectomy for ulcerative colitis?
2. What is the optimal timing for elective reconstructive surgery for ulcerative colitis?
   a. Elective resection and reconstruction (one, two or three stage procedure)
   b. Following total abdominal colectomy in acute severe colitis
   c. Review the above questions with regard to time off steroids or biologics, optimal age, or other drivers for surgery
3. Are there benefits or disadvantages to minimally invasive procedures for ulcerative colitis?
4. When should diversion be considered at the time of ileo-anal anastomosis?
5. What are the rates of sexual dysfunction and infertility following proctocolectomy and reconstruction?

2.2. Search strategy

Electronic searches were created and completed in February 2020 with the assistance of a health sciences librarian experienced with systematic searches. The following databases were queried: PubMed [NLM], Scopus [Elsevier], Cochrane Central Register of Controlled Trials [Wiley], Web of Science [Thomson Reuters], and Google Scholar. The librarian developed a search strategy in PubMed, and then translated that strategy for each database platform as appropriate. Medical subject headings (MeSH) terms and keywords were used to search the concepts and related concepts of UC and pediatrics. Results were restricted to January 1, 2009 through December 31, 2019, human-only studies, and English language. Appendix Acontains the PubMed search strategy for each question. While questions 1–4 were constrained to pediatric populations or pediatric cohorts within larger mixed studies, the literature surrounding infertility and sexual dysfunction included adult patients given its later relevance to children.

2.3. Study selection for inclusion/exclusion

Screening of studies for inclusion or exclusion followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology [Fig. 1]. Screening of titles and abstracts was performed in quadruplicate (A.B., E.R., R.R., R.M.R.) with conflicts resolved by re-review and group consensus if all or ¾ voted to include or exclude a study that was considered majority. Studies where 2/4 voted to include were discussed and consensus reached. Included abstracts were divided by question and the full-text manuscript review was performed in a similar fashion with reasons for exclusion noted. Each phase of screening for inclusion/exclusion was performed using Rayyan [3] (https://rayyan.qcri.org). Studies were assigned to the five research questions; some articles addressed more than one study question.

Studies were included if the patient population was only pediatric, or if there were clearly some pediatric patients included. Studies that clearly did not include pediatric patients were excluded. We chose to include studies with both adult and pediatric patients due to UC often being diagnosed in late adolescence and sometimes managed by adult colorectal surgeons. Studies were also included if they had a mix of patients with inflammatory bowel disease (UC and Crohn disease), as well as if they had patients with both UC and Familial adenomatous polyposis (FAP), as long as these cohort numbers were clearly defined, and outcomes could be linked to disease process. Level of evidence was classified according to Oxford Center for Evidence-Based Medicine (OCEBM) guidelines [4]. The Methodological Index for Non-

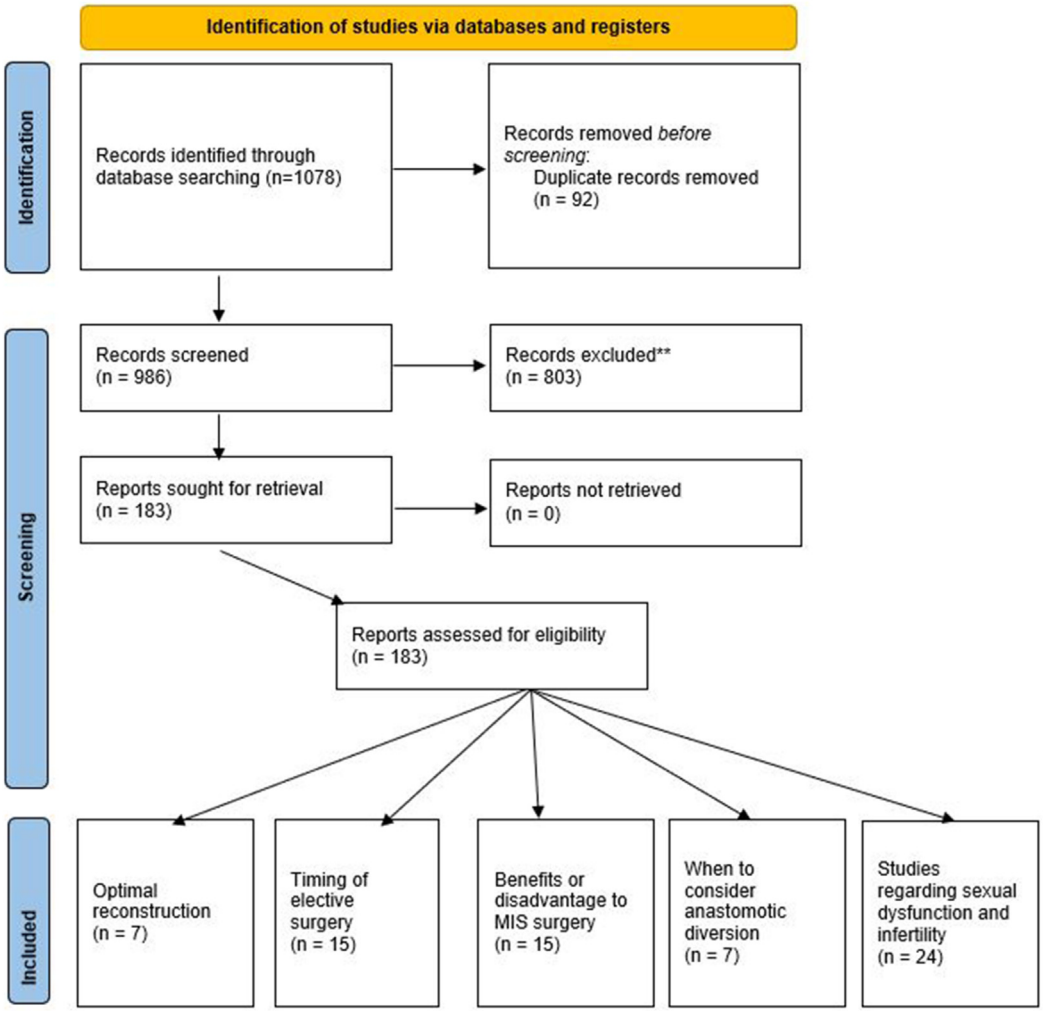

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. 1078 records were identified through database searches and 986 records remained after duplicates were removed. 183 full-text articles were assessed for inclusion and 68 articles were included in the qualitative synthesis. Some articles addressed more than one of the pre-identified questions.

Randomized Studies (MINORS) was chosen to assess methodological quality given that we had no randomized studies to assess.

3. Results

3.1. Question 1

What is the optimal reconstruction for pediatric and adolescent patients afterproctocolectomy for ulcerative colitis?

Variability exists around multiple technical aspects of reconstruction following proctocolectomy in UC including.

- Anastomosis type (straight ileal pull through vs. pouch creation)
- Shape of pouch if present (J, W, S)
- Anastomotic technique (stapled vs. hand sewn)
- Location of anastomosis (ileorectal anastomosis vs. ileoanal)
- Length of the pouch

It is unclear whether any of these surgical choices affect short-term morbidity (surgical site infections, anastomotic leak, abscess, bowel obstruction, or re-operative risk) or long-term outcomes (pouchitis, continence, pouch loss) [5–8].

Six studies in our review addressed this question [4,6–9,11]. In five of the six studies, the number of pediatric/adolescent patients in the study was clearly stated. Most studies had both pediatric and adult patients, as well as patients with CD and FAP. The studies were all retrospective and assessed different outcome measures (Table 1). MINORS criteria to evaluate methodological quality of these studies ranged from 6 to 16.

3.2. Recommendations and observations

IPAA instead of ileoanal anastomosis for reconstruction after pediatric proctocolectomy for ulcerative colitis generally leads to fewer bowel movements per day. The complication of pouchitis is seen with IPAA. Based on current available evidence however, there is no clear type, shape, or location of anastomosis for reconstruction after pediatric proctocolectomy for ulcerative colitis that overall results in better patient outcomes, therefore we recommend that surgeons perform the reconstruction procedure they have the most experience with.

- Level of Evidence 3–4; grade of recommendation D.

3.3. Question 2

What is the optimal timing for elective reconstructive surgery for ulcerative colitis?

Table 1
Studies evaluating outcomes after IPAA based on reconstruction type.

Study	Year	MINORS (max 24)	Patients	Reconstruction			Follow up mean yrs (range)	Comments
				IPAA	IA	other		
Ba'ath *et al.*	2007	7	227 peds 102 UC 22 surgical (*17 definitive*)	11	3	IR (2) Ileostomy (1)	NR	10/11 IPAA with daytime continence 3 with IA all still diverted due to stool frequency
Barrena *et al.*	2011	8	107 UC peds 29 surgical (28 definitive)	12	16		12 (0.4–18)	No difference in stool frequency. Pouchitis seen with J pouch in 1/3
Mattioli *et al.*	2015	11	62 UC peds	50	8	4 NR	12 months	More frequent stools and daytime soiling with IA
Rokke *et al.*	2011	11	134 UC Unk peds	9 (W) 125 (J)	N/A		7.4 (0.5–17)	No difference in complications
Seetharamaiah *et al.*	2009	14	203 168 UC 35 FAP Unk peds	91 (J)	112		2	Higher stool frequency with IA, more med use with IA
Sunde *et al.*	2016	16	103 99 UC Unk peds	56 (J) 47 (K)	N/A		11 (J pouch) 3 (K pouch)	More pouchitis with J pouch. No difference in SF-36 scores

Abbreviations: IPAA = ileal pouch anal anastomosis; IA = ileoanal anastomosis; IR = ileorectal anastomosis; NR = not reported; N/A = not applicable; W= W pouch; J = J pouch.

a. Elective resection and reconstruction (one, two or three stage procedure)
b. Following total abdominal colectomy in acute severe colitis
c. Review the above questions regarding time off steroids or biologics, optimal age, or other drivers for surgery

A total of 15 manuscripts were included focusing primarily on age at surgery, the effects of operating at younger ages, and the timing surrounding the use of immunosuppressive medications. No articles were identified that answered part “b" of our initial question. The optimal timing for reconstruction is important to minimize post-operative complications. Many patients with UC are managed with immunosuppressive therapy that may adversely impact outcomes. Additional concerns include the effect of surgery on growth and nutrition, as well as the long-term functional outcomes that can occur after restorative proctocolectomy.

3.3.1. Elective resection and reconstruction (one, two or three stage procedure)?

Gray et al. evaluated the use of the pediatric ulcerative colitis activity index (PUCAI) for determining the appropriate surgical management (two-stage vs. three-stage) in pediatric patients with UC (A single stage procedure is a colectomy with concordant reconstruction without an ostomy while a two-stage procedure adds a diverting ostomy. A three-stage procedure separates the colectomy from the subsequent reconstruction.) The PUCAI score is determined by evaluation of 6 factors: abdominal pain, rectal bleeding, stool consistency, number of stools per 24 h, nocturnal stools, and activity level. The authors evaluated 60 patients and found that individuals with a lower PUCAI uniformly underwent a combined or two-stage procedure. They noted a cutoff score of 45 predicted a safely performed two-stage procedure [9].

3.3.2. What is the optimal timing for elective reconstructive surgery for ulcerative colitis with regard to time off steroids or biologics, optimal age, or other drivers for surgery?

Ulcerative colitis, Crohn's disease (CD) and indeterminate colitis are different categories of colitis. In a study of 25 pediatric patients diagnosed with non-infectious colitis prior to the age of 10 years, 21 children were initially diagnosed with UC or indeterminate colitis. Five of these children were ultimately reclassified with CD at a median age of 13.4 years, thus potentially altering their surgical management. The authors recommend delayed creation of an ileal pouch anal anastomosis in children with early onset colitis [10].

Two single-institution retrospective studies addressed timing of surgery in children 18 years and younger as it differs by patient age. Complication rates and functional outcomes were compared. One manuscript showed that over a 20-year period, the median age at time of first intervention decreased from 13.9 years to 11.5 years. This has not translated into increased complication rates [11]. The second study demonstrated no differences in surgical complication rates when comparing younger (5–12, n = 22) versus older (13–18 n = 43) patients [12].

Three retrospective studies specifically compared adult patients with pediatric patients. Wu et al. performed a single center study of 104 pediatric patients compared to 1135 adult patients. The authors used 18 years of age as the cutoff. Pediatric patients had a higher rate of pouch related complications, post-operative pouch-related hospitalizations, and higher post-operative use of anti-tumor necrosis factor agents. It does not appear that these led to pouch failure as long term pouch retention was similar in both groups, with a median follow-up of 10.5 years [13]. The other two reviews focused on the long-term success rates of pouch surgery in pediatric versus adult patients. No long term difference in pouch function or pouch failure rates between pediatric patients and adults were shown [14,15].

Nine manuscripts evaluated the impact of immunosuppressant therapy on surgical outcomes [16–24]. Table 2 shows the results of these studies.

Two studies showed an increased rate of both early and late post-operative complications in children treated with high dose steroids [18,22]. Children who were operated on at a younger age in the setting of high-dose steroids showed faster post-operative catch up growth – perhaps due to the ability to wean off steroids [22]. Despite initial studies that suggest a potential increase in immediate post-operative complications, more recent and larger studies suggest that the use of anti-TNF-alpha agents, such as infliximab, is safe during the 8–12 week period before surgical therapy and does not increase complication rates.

3.4. Recommendations and observations

PUCAI may help guide whether a two-stage or three-stage procedure is optimal. Waiting until adolescence before performing

Table 2
Effect of immunosuppressant medication on surgical outcomes.

Article	Immunosuppressant	# of Study Patients	Age (yrs)	Findings
Uchida et al., 2010	Prednisolone	16	<15	Four patients had early complications; 6 patients had late complications. Faster catch up growth was seen in children under 11 who underwent colectomy.
Markel et al., 2008	Various	51	<18	Preoperative steroid use associated with higher postoperative wound infection rate. Other immunosuppressive agents did not affect outcomes.
Uchida et al., 2017	Various	136	<19	Preoperative immunosuppressants did not significantly affect incidence of surgical site infections.
Schaufler et al., 2012	Various	51	<17	Preoperative exposure to thiopurines or calcineurin inhibitors within 30 days of surgery of infliximab within 90 days did not increase the postoperative complication rate.
Larsen et al., 2016	Anti-TNF-alpha	1468	<17	Increasing number of children treated with anti-TNF-alpha medication within 5 years of diagnosis. Decreasing number of children receiving operative therapy for UC during the same time.
Kennedy et al., 2012	Infliximab	11	<19	Postoperative complications higher in infliximab group with small bowel obstruction significantly more common.
Norgard et al., 2012	Anti-TNF-alpha	199	<16	Nationwide database review. Pre-operative use of anti-TNF alpha agents did not increase the risk of post-operative complications
Mir et al., 2014	Infliximab	47	<19	Preoperative exposure to infliximab within 8 weeks of surgery did not significantly increase postoperative complications.
Lightner et al., 2018	Vedolizumab	13	<19	Compared with 36 patients receiving anti-TNF therapy. No patient experienced a 30-day postop SSI or non SSI infectious complication

a J-pouch reconstruction may prevent reclassification to Crohn's disease in patients diagnosed with IBD at a young age. Aside from the concern of a diagnostic dilemma, performing surgery at a younger age does not seem to increase the rate of complications or worsen outcomes. Steroids may increase the rate of complications following surgery and this must be considered when pursuing surgical therapy that will allow a child to wean off steroid therapy and exhibit catch up growth and improved nutrition. Immunosuppressants including infliximab, thiopurines, calcineurin inhibitors, and vedolizumab do not seem to increase the postoperative complication rates of surgical site infections when given in the perioperative period.

- MINORS criteria scores for the reviewed manuscripts ranged from 8 to 16.
- Level of Evidence 3–4; grade of Recommendation D

3.5. Question 3

Are there benefits or disadvantages to minimally invasive procedures for ulcerative colitis?

Recent adult studies have demonstrated that minimally invasive techniques for IPAA have improved outcomes such as post-operative pain, length of stay, time to oral intake, and cosmesis. This section assesses the benefits of minimally invasive techniques in the surgical management of UC in pediatric patients.

Fifteen studies identified by this review compared laparoscopic and open procedures. All had different outcome measures. Most studies included both adult and pediatric populations without specifying numbers of included pediatric patients. Of note, two studies [25,26] addressed fertility outcomes and will be discussed in the Question 5 section. In both studies, a laparoscopic approach was associated with improved fertility compared to an open technique.

3.5.1. Laparoscopic vs. open resection: short-term outcomes

Four studies with only pediatric and adolescent patients found that although laparoscopic procedures were associated with longer operative times, other outcomes were similar or improved when compared to an open approach [30–33]. Three were retrospective and one used a prospective database. While the laparoscopic approach was associated with longer operative times [30], it was also associated with shorter length of stay in three studies [30,32,33], a lower incidence of post-operative small bowel obstruction in two studies [31,32], and similar or improved complication profile compared with open procedures in 3 studies [31–33].

Three retrospective studies included pediatric or adolescent patients among their primarily adult cohorts [34–36]. Laparoscopy again was associated with longer operative times [35,36] but was also associated with shorter length of stay in two studies [34,35] and less intraoperative blood loss [35,36]. Complication rates were similar between laparoscopic and open approach [35,36].

Three studies utilized the National Surgical Quality Improvement Program pediatric database to examine outcomes. While limited by the specifications of the database itself, in these studies the laparoscopic approach compared favorably with the open approach to surgery [37–39]. In two studies, the laparoscopic approach was associated with fewer minor complications [38,39]. One study also showed a decrease in length of stay after laparoscopic surgery [39].

3.5.2. Long-term continence outcomes

Three studies including pediatric or adolescent patients as part of their cohorts addressed this outcome and found an association of similar or improved continence outcomes with the laparoscopic approach [40, 41, 42). In one study of 58 laparoscopic and 91 open IPAA for UC, laparoscopic approach was associated with less stooling at night (1-2 stools nighttime, 86.2% vs 69.4%; >2 stools, 13.8% vs. 30.6%, $p = 0.024$). However, this difference disappeared after controlling for the type of anastomotic technique (stapled vs. hand sewn) [27]. Another study compared a minimally invasive approach using a rectal eversion technique (17 laparoscopic, 5 robot-assisted) with an open procedure without rectal eversion technique ($n = 8$). There was no difference between techniques in terms of post-operative continence, soiling or medication [28].

3.6. Recommendations and observations

Studies comparing outcomes between open and minimally invasive surgery for ulcerative colitis are generally single center retrospective reviews with small patient cohorts, variable procedures (different stages, hand-assisted or not) and with inconsistent outcome measures and definitions. While generally the laparoscopic approach is associated with a longer operative time, some studies also reported a shorter length of stay and lower incidence of

post-operative small bowel obstruction after minimally invasive surgery. In general, complication rates were the same or improved with the laparoscopic approach. Current evidence shows no difference in stooling frequency or continence outcomes as they relate to surgical approach utilized.

Based on the current available evidence, a minimally invasive approach can be used for pediatric ulcerative colitis with outcomes equal of better to an open approach. We recommend use of laparoscopy for appropriate patients when performed by surgeons with this skill set.

- MINORS criteria scores for the reviewed manuscripts ranged from 6 to 16.
- Level of Evidence 3–4; grade of Recommendation D

3.7. Question 4

When should diversion be considered at the time of ileoanal anastomosis?

Diverting ileostomy at the time of straight ileoanal anastomosis or IPAA has been performed to "protect" the anastomosis. The ileostomy diverts the fecal stream to minimize the short-term and long-term complications that may be associated with an anastomotic leak. Ileostomies themselves have been associated with complications and advocates for avoiding a diverting ostomy argue that there is no difference in long-term functional outcomes.

A total of seven articles addressed this question. The articles were predominantly single institution retrospective reviews and case series. Also included was the Consensus for Managing Acute Severe Ulcerative Colitis, a joint statement from the working group of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN).

Ryan et al. and Gray et al. published retrospective reviews in 2010 and 2011, respectively, comparing pediatric patients who had undergone restorative proctocolectomy/IPAA with a diverting ileostomy to those not diverted. Ryan et al. evaluated 83 patients with UC and 7 patients with a polyposis syndrome. Sixty-eight patients underwent IPAA without diverting ileostomy compared to 22 patients who had a diverting ileostomy. The presence or absence of an ileostomy did not influence complication rate or outcomes [29]. Gray et al. found similar outcomes in their study of 50 patients. Children who were not diverted were not at additional risk for complications [30].

Rokke et al. evaluated long-term follow-up after restorative proctocolectomy. This study was not limited to pediatric patients. In 134 patients using disease-specific questionnaires, diverting ileostomies were more commonly performed early in the study period and 54 patients underwent diversion. This did not have any effect on the rate of early post-operative complication or long-term functional follow-up with the median follow-up of 7.4 years [31].

Chen et al. published a multi-institutional retrospective review of 37 pediatric patients who underwent completion proctectomy and IPAA. Seventeen patients did not have a diverting ileostomy and were noted to have more immediate post-operative complications with a higher rate of anastomotic leak and longer post-operative stay. Interestingly, this did not equate to any difference in long-term functional outcome (stricture, pouchitis, frequency of bowel movements) with a median follow-up time of just over 2 years [32].

Two papers addressed rates of ileostomy complications. Zimmerman et al. showed a concern for mucocutaneous separation at the ileostomy when performed in patients who were treated with vedolizumab [33]. Prato et al. addressed the complication rate following ileostomy from a subtotal colectomy or restorative proctocolectomy. Of the 37 patients included complications (parastomal hernia, prolapse, retraction) occurred in eight patients. Patients with an elevated BMI or who were being treated with azathioprine had a higher incidence [34].

The ESPGHAN Consensus statement utilizing 19 expert panelists was published in 2011 [35]. Under the question of "Is there a preferred surgery in children?" there was 100% consensus. Recommendations were.

- A three-stage procedure should be considered in patients undergoing emergency surgery, patients with a diagnostic question, or patients on high-dose steroids.
- Restorative proctocolectomy without a diverting ileostomy could be considered in select children who were without risk factors for complications such as high-dose steroids [35].

3.8. Recommendations and observations

Surgeons may consider performing a restorative proctocolectomy without diverting ileostomy. Based upon the ESPGHAN consensus statement this would include children who were not on high-dose steroids or suffering from malnutrition, and who had a clear diagnosis of UC. Long-term functional outcomes seem to be similar regardless of diverting ileostomy.

We recommend consideration of not diverting appropriate patients.

- MINORS criteria scores for the reviewed manuscripts ranged from 8 to 16.
- Level of Evidence 3–4; grade of Recommendation D

3.9. Question 5

Question 5: What are the sexual dysfunction and infertility rates following proctocolectomy and reconstruction?

Understanding the effects of surgery on later fertility may impact surgical decision for pediatric patients with UC. Fertility and sexual dysfunction in patients with UC who have undergone proctocolectomy are important topics for pediatric providers to address when discussing expectations following surgical management of UC. We identified 24 observational studies for inclusion (Table 3) [25,26,36–56]. We sought to determine the effect of surgical proctocolectomy for UC on female and male infertility.

3.9.1. Infertility in patients with ulcerative colitis following proctocolectomy

Studies utilized many different definitions of infertility: inability to become pregnant after 12 months of unprotected intercourse; live births; the success of in vitro fertilization; additionally, variation existed in the details of the females - including women who were married or cohabitating or were of childbearing age, regardless of whether they were trying to conceive. Studies also combined patients with inflammatory bowel disease (UC and CD). There were also variations in the proportion of those studied who had undergone surgery, the type of surgery performed, and the timing of fertility evaluation relative to proctocolectomy. Studies had low response rates, non-consecutive patient enrollment, and a small number of patients. Ten manuscripts were included for analysis [25,26,39,41,42,44,47,51,54,57].

Following laparoscopic IPAA 7 of 10 patients conceived without IVF, 10 (62.5%) of 16 patients who wished to have children became pregnant but a high proportion of the study patients did not desire pregnancy (77 of 93) [44]. A Danish registry study demonstrated that IPAA leads to a reduction in birth rates in females (27.6 from 46.8 children/1000 years) but an increase in birth rates in males

Table 3
Fertility outcomes in post-surgical UC.

Authors	Year	MINORS (max 24)	total (N)	UC dx (n)	Surgery (N)	Infertility findings
Bartels et al.	2012	10	50 F	37	23 (46%) open IPAA, 27 (54%) lap IPAA	Multi-institutional cross-sectional survey (Belgium). After IPAA, 50 (31%) patients attempted to conceive. Laparoscopic group, 19 (70%) patients were pregnant spontaneously, and 1 patient had IVF. In the open group, 9 (39%) patients became pregnant spontaneously and 4 after IVF. In the 37 patients with UC, the laparoscopic group 11 (55%) became pregnant within 12 months of attempting compared to 6 (35%) in the open group. Pregnancy rates are higher after laparoscopic IPAA.
Beyer-Berjot et al.	2013	8	63 F	46	46 F lap IPAA with diverting stoma	Multi-institutional retrospective survey (France) comparing laparoscopic IPAA vs. laparoscopic appendectomy fertility rates. 50% had a child before IPAA. 15 attempted pregnancies after IPAA, 11 (73%) pregnant, all delivered via c-section. The infertility rate between groups are equivalent.
Cornish et al.	2011	7	255 F	250	Pouch design IPAA pouch design J = 166, S = 9, W = 99	Multi-institutional retrospective survey. 57 stated they had attempted to conceive after IPAA, with 25 (45%) successfully conceived. 18 (31.6%) females were referred to a fertility specialist (16 received IVF, 4 30.7% conceived using IVF). Method of delivery more likely to have Caesarean section following IPAA. No difference in the number of stillbirths, miscarriages, ectopic or elective abortions pre/post IPAA IVF outcomes, and IVF success rates after IPAA are like the general population.
Friedman et al.	2016	15	539 F	381	185 had surgery, [total colon resection + no ostomy 59 (32%), total colon + ileostomy 48 (25%), proctectomy 44 (23.8%), IPAA 33 (17.8%), partial colectomy 1 (0.54%)]	Nationwide cohort studies based on Danish registry. IBD compared with 50,321 without IBD. UC surgery completed >2 years prior to first IVF. OR of live birth within 18 months was not decreased compared with women with UC without surgery before first ART treatment cycle. Among 121 women with UC with surgery before IVF - timing of previous UC surgery was not related to live birth and majority were never treated with Anti-TNF alpha agents (115/121).
Harnoy et al.	2015	8	88	88, 43M/45 F	25M/23 F Handsewn IPAA 28M/38Fstapled IPAA	Single institution retrospective survey. Measured the ability to conceive following unprotected intercourse following handsewn vs. stapled IPAA. The fertility rate was 47% in women and 75% in men. 31 (72%) had a child before IPAA. After IPAA, 33 women −77% childbearing age, 7 (50%) became mothers. Following IPAA, cesarean delivery for 5 of 7 women. Males 25 (63%) were fathers before IPAA. 9 of 12 (75%) men who desired fatherhood after IPAA became fathers. No difference hand sewn vs. stapled.
Hor et al.	2016	7	93 F	72 F	IPAA (laparoscopic 45 (48.4%), ileostomy prior to IPAA 33 (35.3%)	Single institution retrospective survey. Of 93 patients, 77 did not wish to become pregnant. 16 desired pregnancy, 10 (63%) became pregnant without IVF, 3 had two or more pregnancies. 10 (62.5%) had laparoscopic IPAA, 6 (37.5%) had laparotomy. Observed pregnancies were higher in the laparoscopic group with 7 of 10 women.
Mountfield et al.	2009	4	255	85 (33 M, 52 F)	13 unknown types of surgery	Single institution survey. Fear of infertility is higher in females, especially if there is a prior history of surgery. 14% were childless by choice. 42.7% of IBD patients reported a fear of infertility, but only 19.4% sought medical fertility advice at the same rate as the general population
Oza et al.	2015	13	120	71 F	22 IPAA, 3 TAC with ileostomy	Matched retrospective cohort study of 470 control for IVF results. The cumulative rate of live births following IVF was 53% for controls vs. 69% for UC (nonsignificant). Incidence of pregnancy after the 1st cycle of IVF was similar among controls 40.9% and patients with UC 49.3%. Women with IBD achieved a comparable rate of live births after IVF to those without IBD.
Pachler et al.	2017	12	27,379	27,379	1544 IPAA (792 M, 752 F)	National matched registry study (Danish). Only birth rates were investigated, not fecundability. IPAA leads to a 40% reduction in female birth rates (27.6 from 26.8 children/1000 years) and a 17% increase in male birth rates (47.8 from 40.5 children/1000 years).
Tulchinsky et al.	2013	10	41	41 F	41 F (no surgical details provided)	Cross-sectional cohort (Israel). IPAA is associated with an increase in the rate of infertility from 0 to 37% post-IPAA. Post IPAA 10 (37%) of 27 patients failed to conceive. IPAA decreased the number of spontaneous pregnancies. IPAA increased infertility risk, time to conception (5 vs. 16 months), a cesarean delivery (12.9% vs 46.2%), IVF procedures (3 vs. 6). IPAA is associated with similar duration of gestation and lower birth weight.

Table 4
Sexual dysfunction in post-surgical UC.

Authors	Year	MINORS (max 24)	total (N)	UC dx (n)	surgery (N)	sexual functioning measure	sexual functioning results
Bengstsson et al.	2011	15	101	97	Control working IPAA 72 (40 F/32 M) vs. pouch failure ileostomy 29 (16 F/13 M)	FSFI, IIEF	Single institution case–control survey of pouch failure. No differences in any of the FSFI or IIEF domains were found between patients with pouch failure versus those with functioning pouches.
Cohan et al.	2015	14	74	37	Various stages of reconstruction, 9M/5 F ileostomy, 16M/7 F IPAA	FSFI, IIEF, SSS	Single institution retrospective survey of UC post-surgery mixed stages of reconstruction measuring sexual function with an opposite-sex partner who remained together x6months. Changes in sexual function do not coincide with changes in sexual satisfaction. IBD severity-equal between groups. Sexual functioning improved significantly only in males. Sexual satisfaction improved in females after surgery.
Cornish et al.	2012	14	109	54 F	54 F IPAA	FSFI	Prospective case–control study in two tertiary centers. 54 (49.5%) IPAA compared to 55 (50.5%) control IBD without surgical history. No difference in sexual function scores between surgical and control UC patients.
Davies et al.	2007	13	56	33M/26 F	IPAA	FSFI, IIEF	Prospective single institution survey of pre vs. postop IPAA sexual function scores. Female function scores improved at 12 months postoperatively. Male scores remained high pre and postoperatively.
Friedman et al.	2018	13	31,498	21,966	2679		Nationwide cohort study based on the Danish registries. 31,498 men >18yo with IBD and 314,980 men without IBD. All men with IBD use erectile dysfunction (ED) medication more frequently than men without IBD. Highest risk for receiving an ED prescription if men with UC had surgery. Could not tell type of surgery in the study.
Harnoy et al.	2015	7	88	88	25M/23 W Handsewn IPAA, 28M/38 W stapled IPAA	FSFI, IEEF	Single institution survey. Type of anastomosis for IPAA hand sewn vs. stapled did not impact sexual function. 50% women reported sexual dysfunction. Anastomotic stricture, night seepage, stool frequency >5x/d, night pad use were risk factors for female sexual dysfunction. Men 12 (29%) suffered moderate/severe erectile dysfunction. Night seepage only risk factor for male sexual dysfunction.
Hicks et al.	2014	7	89	89	IME 55, TME 34	FSFI, IIEF	Single institution survey. Female FSFI and Male IIEF scores similar between IME and TME technique.
Hor et al.	2016	7	93	72 F	IPAA (laparoscopic 45 (48.4%), ileostomy prior to IPAA 33 (35.3%), conversion to open IPAA 2 (2.15%), hand sewn anastomosis 91 (97.8%), TME 38 (40.9%))	FSFI	Single institution retrospective survey. 49 (64%) had normal sexual function, 27 (36%) had dysfunction. Age and nocturnal pouch activity were associated with worse sexual function.
Kjaer et al.	2014	7	50	44	0 pen-IPAA 22, Laparoscopic-IPAA 28	FSFI, IIEF	Single institution survey. No difference of sexual function between L-IPAA vs. O-IPAA groups.
Koivusalo et al.	2009	7	63	63 sexually active adults with ST/MT for UC < 16 years (ST25, 8 M; 38 MT 19 M)	17 IPAA 8 straight IAA	Self-created survey of sexual function	Multi-institution retrospective survey. Fecal incontinence during sex is inversely correlated with satisfaction sexual satisfaction on SF in both ST and MT group. Surgical complications, pouchitis and stool frequency were not correlated with satisfaction.
Ogilvie et al.	2008	9	90 F	90 F	90IPAA	FSFI	Single institution cross-sectional survey. 47% had low FSFI post IPAA related to leakage. 50% post-IPAA risk of long-term postoperative sexual dysfunction. Measures of pouch function were not associated with sexual dysfunction.
O'toole et al.	2018	8	175 M	43 M	13	IIEF, IBD- specific male sexual dysfunction scale IBD MSDS	Cross-sectional multi-institutional survey. Male sexual dysfunction in IBD was significantly associated with presence of an IPAA, depression and increased disease activity.
Riviere et al.	2017	10	358	120	10	FSFI, IEEF	A cross-sectional multi-center study comparing IBD vs. healthy controls (France). IBD activity was not associated with sexual dysfunction. 54%

Table 4 (*continued*)

Authors	Year	MINORS (max 24)	total (N)	UC dx (n)	surgery (N)	sexual functioning measure	sexual functioning results
							of women had sexual dysfunction, 43% of men had erectile dysfunction. Rates of sexual dysfunction are higher than healthy controls, dependent of disease severity.
Sunde et al.	2015	8	68	66	stapled 88.2, hand sew 11.8%, J IPAA 54%, k 45.6, 3 stage 57, 2 stage 42.	PISQ-12, IIEF	Single center survey. No significant correlation between pouch and sexual function for men, while there was for women.
Van balkom et al.	2012	8	23	16 M	11M/15 F IPAA (open 23, Lap 3)	FSFI, IIEF	Single center study. None of the men demonstrated sexual dysfunction, impotence, or retrograde ejaculation; 50% of women reported sexual dysfunction
Wang et al.	2011	8	66	56 (41M/25 F)	IPAA 48; end ileostomy 18	FSFI, IIEF, SFQ	Single center survey. Male IIEF scores improved after surgery, in domain for erectile function, sexual desire and intercourse satisfaction from baseline to post surgery. Female sexual desire domain increased post-surgery.

Abbreviations: RPC, restorative proctocolectomy; IPAA, ileal pouch anal anastomosis; IIEF, international index of erectile function; FSFI, female sexual function index; SF, sexual function; SFQ, sexual function questionnaire; PISQ-12, pelvic organ prolapse/urinary incontinence sexual function questionnaire 12; SSS, sexual satisfaction scale; MT, medical therapy; ST, surgical therapy; M, male; F, female. OR, odds ratio; IVF, in vitro fertilization. IME intramesorectal excision; TME total mesorectal excision.

(47.8 from 40.5 children/1000 years) [51]. A higher rate of fear of infertility for female patients with IBD (42.7%), especially if prior surgery occurred (33%), but only 20% sought medical fertility advice (the same rate as the general population), and 14% remained childless by choice [47].

Success rates of IVF post IPAA are similar to the overall population who utilize IVF. IPAA reduced fertility as only 25 (45.5%) of the 57 patients who attempted to conceive successful. There was no difference in the number of stillbirths, miscarriages, ectopic or elective abortions pre vs. post IPAA and an increased rate of cesarean sections [39]. A Danish registry study compared the success of IVF in IBD patients compared with 50,321 unaffected controls. The odds of having a live birth following IVF did not differ between women with UC who did and did not have surgery before the first IVF (n = 185 patients, last surgery was >2 years before IVF) [41]. A matched retrospective cohort study assessed the effect of factors on the likelihood of achieving a live birth following IVF in women with and without IBD (121 women with IBD, 71 with UC, of which 22 had IPAA). The rate of live births, incidence of pregnancy after the IVF cycle and the incidence of live births after the first and sixth cycle of IVF were all similar between women with and without IBD [50]. An Israeli cross-sectional cohort referral center study evaluated female infertility, use of IVF and time to pregnancy, and pregnancy-related outcomes before and after IPAA. IPAA lead to a lower number of spontaneous pregnancies, longer time to conception (5 vs. 16 months), and more IVF procedures (3 vs. 6), a higher proportion of cesarean deliveries [54].

Fertility between those with hand-sewn or stapled was not different after IPAA [42]. A comparison of open vs. laparoscopic IPAA with 50 (31%) patients attempting to conceive demonstrated that laparoscopic approach led to a significantly shorter time to first pregnancy, higher spontaneous pregnancy, and less need for IVF [25]. A multicenter study evaluated women with a history of laparoscopic IPAA with those who underwent laparoscopic appendectomy and found that, 11 (73%) with laparoscopic IPAA history conceived and all delivered via cesarean section, and fertility rates were equivalent based on surgical history [26].

3.9.2. Sexual dysfunction in IBD patients after proctocolectomy

Sexual dysfunction in IBD encompasses a multifactorial etiology, namely abdominal-pelvic surgery, disease activity, hormonal changes, age-related factors, and medication effects. To evaluate sexual dysfunction, most of the studies used validated surveys to measure sexual. Surveys utilized included: International Index of Erectile Function (IIEF) and the Female Sexual Function Index (FSFI) or Pelvic organ prolapse/urinary Incontinence Sexual Function Questionnaire 12 (PISQ-12), IBD Male Sexual Dysfunction Scale (IBD-MSDS) and Brief Index of Sexual Functioning for Women (BISF–W). Sixteen manuscripts were included for evaluation (Table 4) [24,36–38,40,42–46,48,49,52,53,55,56].

3.9.3. Effect of failed IPAA

There were no differences or worsening in sexual function domains or worse sexual function between UC patients with and without pouch failure. A failed pouch was defined as excision of the pouch or permanent diversion with an abdominal ileostomy or conversion of the pouch to a continent ileostomy [36]. Following IPAA, changes in sexual function did not coincide with changes in sexual satisfaction. Following surgery, male sexual functioning scores improved while for females, sexual satisfaction scores improved [37]. For women, there were no differences in sexual dysfunction post IPAA surgery vs. medical management [38].

3.9.4. Effect of IPAA on sexual function

Females with UC and IPAA reconstruction demonstrated significantly worse sexual function related to age >40 years and nocturnal pouch activity [44]. Female sexual function was not associated with stool frequency and ileostomy status but were correlated with long-term complications (pelvic abscesses, enteric fistula, pouchitis, and reoperations) [55]. A cross-sectional study of two tertiary centers found that 54% of women have sexual dysfunction and 43% of men have erectile dysfunction. These dysfunction rates are significantly higher than for healthy controls, independent of disease severity [52]. Erectile dysfunction assessed 6- and 12-months post IPAA remained high. However, 73% of women had abnormal sexual function preoperatively, which decreased significantly at 12-months after surgery to 25% [40]. Following IPAA, males reported no sexual dysfunction, including no reported impotence or retrograde ejaculation, while 50% of women reported sexual dysfunction. Following surgery, male sexual function specifically erectile function, sexual desire, and intercourse satisfaction improved from baseline to post-surgery. Female sexual desire domain increased post-surgery [56]. A Danish database study found that men with IBD are more likely to fill erectile dysfunction prescriptions than men without, regardless of surgical history [24].

3.9.5. Effect of surgical approach on sexual function

Although the data are limited, several factors of sexual function related to the surgical approach have been compared. Depth of mesorectal excision [43], open vs. laparoscopic technique for IPAA [45], hand-sewn vs. stapled IPAA [42] and pouch configuration [46] all demonstrated equivalent post-operative FSFI and IIEF scores.

3.9.6. Effect of fecal incontinence on sexual function

There was no relationship between the pouch and sexual function for men, while for women, poor pouch function correlated with impaired sexual function [53]. Fecal incontinence during sexual activity is inversely correlated with satisfaction in both sexes, while surgical complications, pouchitis, and stool frequency were not significantly correlated with sexual satisfaction [46]. Although 47% of females indicated sexual dysfunction, pouch function and leakage measures were not found to be predictors of sexual dysfunction [49]. A study in males with IBD demonstrated sexual dysfunction was significantly associated with the presence of IPAA surgery, depression, and increased disease activity [48].

3.10. Recommendations and observations

The effect of surgical therapy for UC on female infertility is uncertain because of series of mixed IBD patients, surgical approach variation, small patient numbers, timing of assessment in relation to surgery, disease severity and inconsistent definitions of fertility. Data suggest that infertility among those who underwent laparoscopic procedures was lower than those who had an open surgical approach. Previous surgery was associated with a higher risk of miscarriage, use of IVF, and caesarean section delivery. Sexual dysfunction is negatively impacted following surgery for females greater than males. These findings are based on low-quality evidence. As a result, definitive conclusions cannot be made, and future well-designed studies are needed to fully understand the impact of surgery on fertility and pregnancy outcomes.

Sexual dysfunction is not correlated with surgical techniques for IPAA. Pouch failure, defined as excision of the pouch or permanent diversion with an abdominal ileostomy or conversion of the pouch to a continent ileostomy, is not associated with female or male sexual function. There is a need for pediatric studies with long-term follow-up.

- MINORS criteria scores for the reviewed manuscripts ranged from 4 to 15
- Level of Evidence 3–4; grade of Recommendation D

4. Discussion

The surgical management of pediatric patients with UC remains variable. There is currently low-level evidence for the questions raised about the surgical management of UC in children, including: timing of procedures, reconstruction type/technique/location/pouch shape, the use of minimally invasive techniques, the need for diversion, and risks to fertility and sexual function.

An updated search was performed in October 2022 to see if any new publications relevant to our questions were available since our initial search. There were no prospective or randomized controlled trials published. The search revealed several papers with similar findings to those discussed in our review. A paper from Rubaclava et al. investigated complications of a traditional 2 stage procedure (proctocolectomy/Jpouch with diversion followed by ostomy closure) compared to a modified 2 stage (colectomy with ileostomy, followed by proctectomy, reconstruction without diversion) and found that the latter had better outcomes in sick patient with fulminant colitis [58]. A multi-center study by the Porto group of ESPGHAN looked at outcomes following pouch formation, and found that timing from colectomy to pouch formation did not affect outcomes [59]. Saberi et al. examined approach of laparoscopic vs. open approaches to colectomy or reconstruction in pediatric patients with UC and found less post-operative complications, shorter LOS and improved readmissions, similar to existing data [60]. Similarly, Willobee et al. used the Kids Database to look at complications after open vs. minimally invasive approaches, and found less complications with MIS [61].

Limitations of this review include that there are currently no randomized controlled trials or prospective studies addressing our questions, including timing, the optimal reconstruction after proctocolectomy, the use of minimally invasive approaches or the need for diversion in pediatric patients with ulcerative colitis. Retrospective and survey data available often study both adult and pediatric patients, and oftentimes include patients with FAP and Crohn's disease, where it was not possible to separate out the pediatric patients when assessing outcomes. Available studies are heterogeneous and of low methodological quality.

Some general recommendations can be made from the available literature.

- Timing of surgery for UC is an important decision for surgeons to minimize the risks of surgery while considering the risks of prolonged medical therapy. This decision should be based upon the individual patient characteristics.
- PUCAI may be beneficial in guiding decision for a two-stage or three-stage approach.
- Immunosuppressants including infliximab, thiopurines, calcineurin inhibitors, and vedolizumab do not increase the post-operative complication rates of surgical site infections when given in the perioperative period.
- There is no clear type, shape, or location of anastomosis for reconstruction after pediatric proctocolectomy for ulcerative colitis that leads to better patient outcomes.
- There is some evidence of a higher number of daily stools with straight ileoanal anastomoses compared to ileal pouch reconstruction (most commonly J-pouch) [6,8–10,12]
- Based upon the available literature, performing a restorative proctocolectomy without diverting ileostomy in appropriately selected patients may be considered.

5. Conclusion

There continues to be questions surrounding best surgical management practices for pediatric patients with ulcerative colitis. There is a need for multicenter, prospective studies addressing critical management questions for pediatric patients with UC are needed, to provide the best evidenced-based care for our patients and optimize long term outcomes.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpedsurg.2023.02.042.

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