Postoperative complications of colectomy and J-pouch with ileostomy versus without ileostomy in children with inflammatory bowel diseases: a systematic review and meta-analysis

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ABSTRACT

Background The efficacy of performing a restorative proctocolectomy and J-pouch ileal anal anastomosis without diverting ileostomy in children with inflammatory bowel disease has been a longstanding debate. A systematic review and meta-analysis is presented comparing the occurrence of postoperative complications in children who underwent either the pouch-anal anastomosis (IPAA) with ileostomy (diverted) versus the undiverted procedure.

Methods Records were sourced from CINAHL, CENTRAL, EMBASE and MEDLINE databases. Studies followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and compared postoperative complications in pediatric patients diagnosed with inflammatory diseases aged less than 18 years who underwent J-pouch with ileostomy versus without ileostomy. The primary outcome was the occurrence of postoperative leaks, and the secondary outcomes were presence of postoperative small bowel obstruction (SBO), pouchitis, stricture and fistula complications. A random-effects meta-analysis was used.

Results Twenty-three observational studies in the systematic review were included with 658 patients (83% diverted, 17% undiverted). Pooled estimates showed no difference in occurrence of leaks in children who underwent J-pouch/IPAA with ileostomy versus without (odds ratio (OR) 0.54, 95% confidence interval (CI) 0.17 to 1.64, I²=16%). There was no difference in the occurrence of SBO, pouchitis or strictures in children who underwent J-pouch/IPAA with ileostomy versus without (SBO: OR 2.27, 95% CI 0.52 to 9.92, I²=0%, pouchitis: OR 1.76, 95% CI 0.95 to 3.24, I²=0%, strictures: OR 2.72, 95% CI 0.44 to 16.69, I²=66%).

Conclusion The meta-analysis did not find differences in the occurrence of complications in pediatric patients who underwent the IPAA with ileostomy procedure versus without ileostomy.

INTRODUCTION

Inflammatory bowel disease (IBD) refers to a group of chronic, relapsing autoimmune diseases that result in chronic intestinal inflammation of both the small and large intestine. Affecting 1.5 million North Americans, the cause of this disease is not yet known but is proposed to occur as a result of inappropriate immune response to environmental factors as well as luminal and microbial antigens. Although the onset of this disease typically manifests during adulthood, children are increasingly being diagnosed with IBD.

Since 1978, the gold standard surgical treatment of ulcerative colitis (UC) is restorative proctocolectomy with ileal pouch-anal anastomosis (RP-IPAA), which can be performed via laparoscopic or open procedure, in one, two or three stages and constructed with an S-reservoir, a J-reservoir or a W-reservoir. Data from Widmar et al suggest that diversion does not prevent pouch excision and a need for long-term diversion after pouch leak in adult patients. Recently, Khalid et al demonstrated greater probability of anastomotic strictures (odd ratio (OR) 0.40; 95% confidence interval (CI) 0.26 to 0.62, p<0.0001) and pouch failures (OR 0.54 (0.36 to 0.82), p=0.003) in adult diverted than in non-diverted patients, although reoperation was more frequently required in non-diverted patients (OR 2.51 (1.12 to 5.59), p=0.02). Hence, results are still inconclusive, debatable and rarely focus on pediatric populations with consideration of numerous postoperative complications.

Systematic reviews investigating certain postoperative complications in children who undergo diverting ileostomy procedures versus not are lacking. Moreover, differences in short-term and long-term outcomes for pediatric patients who undergo IPAA are limited owing to constraints in study design.
and infrequency of IPAA in children. To address this gap, an investigation is needed comparing the frequency of postoperative complications between diverted versus undiverted IPAA procedures in a pediatric population aged less than 18 years diagnosed with IBD.

The objective of this systematic review and meta-analysis was to compare the frequency of postoperative complications in pediatric patients with IBD who have done IPAA with ileostomy (diverted) versus without ileostomy (undiverted). Secondary objectives included estimating the pooled frequency of these complications in the surgical groups.

METHODS

This review followed the Cochrane Methodology to identify and select the studies and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses to guide the reporting of this systematic review.

Search strategy and selection criteria

A systematic search for relevant studies published between 1946 and November 4, 2019 was performed using the following databases: CINAHL (1982 onwards), CENTRAL, EMBASE (1980 onwards) and MEDLINE (1996 onwards). Twenty-two studies were included after this initial search. An update was performed in July 2021 identifying three additional eligible studies. Searches were developed and conducted by a librarian experienced in systematic reviews, using a method designed to optimize term selection, and the MEDLINE search was peer reviewed by a second librarian before being translated for the other databases. Search strategies are presented in the online supplemental file 1. The study protocol has been registered in Open Science Framework (10.31219/osf.io/svuwm). All duplicate records were removed online, records retrieved by the electronic search were downloaded and imported into a Reference Manager—a citation database, and then were uploaded to a systematic review software Covidence (www.covidence.org) for title and abstract screening and full-text review. Four reviewers (IO, MK, NT, VG) screened at each study. The validated Methodological Index for Non-Randomized Studies (MINORS) criteria were used to assess the quality of the studies. Exclusion criteria

Studies were excluded if documented complications were not provided for the surgery performed or did not mention the primary endpoints of interest. Case studies, literature reviews, systematic reviews, editorials, letters to the editor, conference abstracts and commentaries were excluded, in addition to studies not written in English.

Data extraction and outcomes

Two authors (IO and NT) extracted patient frequencies using a predesigned and piloted data abstraction sheet in Excel V.14.7.7. The extracted information included study details (design, location of the study and sample size), patient demographics including age and gender, disease diagnosis, average or median follow-up, and surgical details including the procedure implemented.

The primary clinical outcome was the occurrence of anastomosis leaks. The secondary outcomes included the occurrence of small bowel obstruction, pouchitis, strictures and fistula (duodenal, enterovaginal or rectovaginal) at the designated follow-up period, as defined by the study author.

A diagnosis of stricture at the anastomosis was confirmed on examination and/or endoscopy, and anastomotic leak was defined as evidence of leak on imaging (such as pelvic fluid collection adjacent to the anastomosis) or at reoperation. Small bowel obstruction was defined by a contrast-enhanced X-ray or a CT result, demonstrating findings for obstruction, in tandem with abdominal pain, vomiting, abdominal distention, nausea, and/or decreased or absent flatus and/or stool. Late obstruction was defined as occurring after closure of the covering ileostomy. Rectovaginal fistula could have been detected on MRI, after restorative proctocolectomy. Pouchitis was primarily diagnosed clinically by symptoms of increased stool frequency, abdominal pain, and fecal incontinence and endoscopically confirmed, and was defined as inflammation in the pouch in a symptomatic patient who may have been prescribed antibiotics in the year prior to follow-up.

Assessment of risk of bias within studies

Two reviewers (NT and IO) independently reviewed each study. The validated Methodological Index for Non-Randomized Studies (MINORS) criteria were used to assess the quality of the studies. Items assessed included clearly stated aims, inclusion and representativeness of patients, reliable prospective data collection, appropriate and unbiased endpoints, sufficient follow-up period, follow-up loss, adequate study size calculation, contemporary groups (to address historical bias), baseline equivalence and adequate statistical analysis. Items 1 through 7 apply to non-comparative, while items 8 through 12 for comparative studies. Records were given scores of 0 through 2 for 12 criteria of bias assessment. The maximum (ideal) global score is 24 for comparative studies and is 16 for non-comparative studies.
Statistical analysis

All statistical analyses were performed using the R statistical programming language (V.4.0.3).17 Continuous valued variables were expressed as mean±SD, and categorical variables were expressed as numbers and percentages. Inter-rater reliability was assessed between reviewers in assessing quality of the studies using weighted kappa for each of the 12 items of the MINORS scale and using a two-way model, single rater intraclass correlation coefficients (ICCs) or the total MINORS score.18 Data were meta-analyzed using a random-effects model with R package ‘meta’.19 Pooled ORs were generated using Mantel-Haenszel test, using a random-effects model. If there were not enough studies (a minimum of two studies) to compare the two types of surgery, the proportion was pooled with a 95% CI for the complication for one type of surgical procedure using random effects. Statistical heterogeneity was determined using $I^2$ tests. $I^2$ is the proportion of total variation observed between studies attributable to differences between studies rather than sampling errors. High heterogeneity was defined as $I^2 >75%$.

RESULTS

Study selection

The initial search yielded 1080 studies of which 22 were originally included after full-text review. Two records were found to have patient overlap and thus were removed from the review before performing the update.20 21 After an update was performed, there were 23 total studies that met the inclusion criteria and were included in the systematic review. Seven of these studies were used in the meta-analysis9 11 22–26 (figure 1).

Study characteristics and individual results

Characteristics of the 23 studies with 658 patients can be found in online supplemental file 2, table S1. A total of 547 (83%) and 111 (17%) underwent IPAA with ileostomy or IPAA without ileostomy, respectively.

Of the 23 studies, the mean age of patients who underwent surgery ranged between 10.4 and 16.3 years. Based on the definition of IBD inclusion in each study, 714 (719, 99%) children presented with only clinically diagnosed UC (diagnosed via preoperative biopsies, histologic examinations of surgical specimens, endoscopy or a combined approach) or indeterminate colitis (5 of 719, 1%) diagnosed with indeterminate colitis discerned from a combination of standard laboratory tests, fecal markers of inflammation, serological biomarkers and gastrointestinal endoscopy with biopsies.21

There was wide variability in the percentage of females included (25%–90%). Across all studies, follow-up was at least 1 year. Of the 23 studies, 7 (32%) described conducting IPAA with ileostomy in one or two stages,20–22 27–30 8 (35%) in three stages,10 31–37 and 2 (9%) in one, two or three stages.26 38 The remaining six (26%) were not well defined.23–25 39–41

Of the seven studies quantifying our outcomes in the groups of IPAA with ileostomy versus without,9 11 22–26 four (67%) reported no significant differences in preoperative characteristics among their cohorts.22–25 Four (67%) stratified baseline characteristics, such as age, sex, duration of

Figure 1  Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 flow diagram for updated systematic reviews which included searches of databases and registers only.
illness before resection or immunosuppression at time of surgery.22–25 Indications for surgery included chronic anal pain and failure to achieve full continence (one study (17%))22 and acute presentation of UC refractory to medical intervention (one (17%)).20 One study (17%) included an urgent case in their cohort.22

Risk of bias across studies
Moderate agreement was achieved across the 12 items of the MINORS scale (weighted kappa 0.66, 95% CI 0.57 to 0.75 and when examining the total score for all included studies (ICC 0.68, (0.37 to 0.85)). MINORS scores for comparative studies (n=17) ranged from 17 to 20, with mean 17.4±1.5. MINORS scores for non-comparative studies (n=6) ranged from 8 to 12, with a mean of 10.1±1.5. The ideal global score is 16 for non-comparative studies and is 24 for comparative studies, which indicates fair study quality based on this definition.16 Please see online supplemental file 3 for the methodological appraisal of observational studies (online supplemental table S2).

Primary analysis outcome
Leaks
There were five comparative studies that reported on leaks.9 11 23 25 26 The pooled estimate showed no difference in postoperative risk of leaks among patients who underwent the J-pouch procedure as compared with patients with J-pouch without ileostomy (OR 0.54, 95% CI 0.17 to 1.64, I²=16%) (figure 2).

Secondary analysis outcomes
Small bowel obstruction
Three studies were included in the pooled meta-analysis for the complication of small bowel obstruction.9 25 25 The pooled estimate indicated no difference in the odds of small bowel obstruction in children with ileostomy versus without (OR 2.27, 95% CI 0.52 to 9.92, I²=0%) (figure 3A).

Pouchitis
There were six relevant studies included in the pooled meta-analysis.9 11 22–25 the pooled estimate suggested no difference in patients with J-pouch and ileostomy developing pouchitis compared with patients without ileostomy (OR 1.76, 95% CI 0.951 to 3.24, I²=0%) (figure 3B).

Strictures
There were two studies that reported on strictures in J-pouch with ileostomy versus without. The pooled estimate showed no difference in risk of strictures between patients with J-pouch with ileostomy versus without (OR 2.72; 95% CI 0.44 to 16.69, I²=66%) (figure 3C).

Fistula
None of the included studies compared the occurrence of fistula between the two surgery types; nor was fistula reported across the studies for pediatric patients without ileostomy. Therefore, the pooled prevalence of fistula in these patients was 2.0% (95% CI 0.0% to 4.0%, I²=0%) (figure 4).

DISCUSSION
This systematic review included 23 studies (658 patients), among which 7 studies quantified complications of interest between the J-pouch/IPAA with ileostomy procedure versus without. Results from the meta-analysis demonstrated that there is no difference in postoperative complications, specifically anastomotic leaks, when comparing pediatric patients with J-pouch with ileostomy versus patients with J-pouch without ileostomy. Avoiding a diverting ileostomy in select patients could be a safe alternative because there is no evidence of a protective benefit against leaks when using a diverting ileostomy. The majority of studies had small sample sizes, with CIs overlapping one, which reduces statistical confidence in the findings. In the adult literature, anastomotic leak rates range from 5% to 19%,42–44 and there seems to be a trend towards decreased clinically detectable leak rates in the diverted versus undiverted group.23 This finding does not align with previous literature reporting higher incidence of anastomotic leakage in the undiverted than diverted populations.42 45–48

No statistical difference was found in small bowel obstruction in diverted versus undiverted pediatric patients, which contrasts with prior literature. Although the target populations differ, one study of a clinical sample of adults showed significantly higher odds of small bowel obstruction in diverted patients (OR 5.05 (1.35 to 18.92)).

![Figure 2](http://wjps.bmj.com/)

**Figure 2**: Meta-analysis forest plot for leaks in diverted vs undiverted ileostomy groups.
than undiverted patients after adjusting for steroid use, age, length of follow-up, prior subtotal colectomy and primary preoperative diagnosis. Moreover, restorative proctocolectomy requires extensive bowel manipulation and pelvis dissection, and manipulating the small bowel for ileostomy might increase the incidence of clinically distinguished small bowel obstruction. Additionally, small bowel obstruction resulting from an abscess is a prevalent complication after proctocolectomy and ileo-anal anastomosis. The meta-analysis did not find evidence of increased odds of pouchitis in children who underwent J-pouch/IPAA with ileostomy versus without ileostomy, given that the CIs overlapped one due to small sample sizes. This finding suggests non-inferiority of the diverting ileostomy approach. Larger sample size studies are warranted. Pouchitis is the most prevalent long-term complication in patients who undergo IPAA. Sixty per cent of affected children suffer from recurrent episodes and 5%–10% can develop chronic pouchitis. Pouchitis can develop in 80% of adult patients after RP-IPAA, significantly impairing quality of life. Literature suggests similar pouchitis rates between diverted versus undiverted groups, likely due to comparable operative techniques for building the IPAA. In fact, Dolgin et al reported no significant difference between the J-pouch and ileostomy versus without ileostomy procedures, in terms of complications or functional outcomes and no patient developed a significant pouch complication in either group. Hence, the diverting stoma did not affect pouchitis occurrence, although one study suggests that creating a diverting ileostomy could avoid consequences of pouch leak or failure by enabling recovery of anal sphincter function. Pouchitis may occur more frequently in IPAA with

<table>
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<th>Study</th>
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<th>OR</th>
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<td>A) Small bowel obstruction</td>
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<td></td>
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<tr>
<td>Gray 2012</td>
<td>2</td>
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<td>[0.14; 19.07]</td>
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<td>[0.10; 70.49]</td>
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<tr>
<td>Rubalcava, 2021</td>
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<td>34</td>
<td>2.76</td>
<td>[0.30; 25.71]</td>
<td></td>
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<tr>
<td>Marlanda, 2020</td>
<td>0</td>
<td>7</td>
<td>1.17</td>
<td>[0.32; 4.32]</td>
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<td>Random effects model</td>
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<td>70</td>
<td>2.27</td>
<td>[0.52; 9.92]</td>
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<tr>
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| B) Pouchitis |           |              |            |         |               |
| Chen 2019    | 9         | 20           | 1.17       | [0.32; 4.32] |
| BismarB 2019 | 9         | 27           | 1.25       | [0.31; 5.11] |
| Rubalcava, 2021 | 26     | 34           | 1.77       | [0.50; 6.32] |
| Gray 2012    | 11        | 28           | 1.73       | [0.52; 5.77] |
| Marlanda, 2020 | 1        | 7            | 6.69       | [0.24; 187.28] |
| Dolgin 1999  | 5         | 14           | 8.33       | [0.84; 83.17] |
| Random effects model | 130    | 100          | 1.76       | [0.95; 3.24]  |
| Heterogeneity: $I^2=0\%$, $t^2=0$, p=0.70 |           |              |            |         |               |

| C) Stricture |           |              |            |         |               |
| BismarB 2019 | 6         | 27           | 1.05       | [0.22; 5.02] |
| Rubalcava, 2021 | 20     | 34           | 6.67       | [1.61; 27.63] |
| Random effects model | 61      | 31           | 2.72       | [0.44; 16.69] |
| Heterogeneity: $I^2=66\%$, $t^2=1.1300$, p=0.09 |           |              |            |         |               |

Figure 3 (A) Meta-analysis forest plot for secondary outcome complications in diverted vs undiverted ileostomy groups for small bowel obstruction. (B) Meta-analysis forest plot for secondary outcome complications in diverted vs undiverted ileostomy groups for pouchitis. (C) Meta-analysis forest plot for secondary outcome complications in diverted vs undiverted ileostomy groups for stricture.

Figure 4 Forest plot for the proportion of fistula complication in patients with J-pouch with ileostomy.
ileostomy patients owing to inflammatory stasis within the reservoir, particularly from larger reservoirs, which empty only partially during defecation.63

Among the two studies reporting strictures, the pooled estimate showed no difference in risk of strictures between patients with J-pouch with ileostomy versus without.9 22 Similarly, previous literature reports comparable frequencies in anastomotic strictures between undiverted versus diverted groups because pouch anastomosis leaks can resolve without significantly contributing to symptoms, resulting from dilatation treatment. Despite this, Gawad et al5 6 and other authors propose that residual, active disease at the ileoanal anastomosis site could still compromise healing, and the extent of inflammation in resected surgical specimens predicts pouch-related complications, such as anastomotic stricture and leaks post-IPAA.20 65

In this review, the percentage of fistula in pediatric patients who underwent J-pouch with ileostomy was low (at 2%). This aligns with previous literature indicating low prevalence of fistula in children with familial adenomatous polyposis (FAP) and UC postoperation for J-pouch.66 67

Limitations
Overall, the biggest limitations include: (1) lack of consistent outcome reporting; (2) lack of studies comparing the two surgical approaches for pooled analysis and (3) lack of data on other confounding risk factors (including age, body mass index (BMI), case urgency, nutritional status, etc). Addressing each of these concerns would enable direct comparison between the defined outcomes based on clinical factors. Second, the estimates collected in this systematic review are based on observational studies and not on randomized controlled trials. However, randomizing by surgery type is a difficult approach, and only one study has randomized by diversion.55 69 70 Lastly, surgeons may have a clinical preference towards undiverted surgery in patients who are ‘healthier’ (ie, lack of anastomosis tension, good pelvic dissection, nutritional status and decreased immunosuppressant doses)5 6 because an undiverted pouch can have more favorable preoperative and operative characteristics and because diversion does not always prevent pouch excision.5 6 25 69 70 This potential preference might explain why there were so few studies comparing the outcomes directly between IPAA diverted versus undiverted ileostomy procedures.

In conclusion, this meta-analysis suggests no difference in the number of anastomotic leaks, or in small bowel obstruction, pouchitis and stricture in IPAA with ileostomy versus no ileostomy. Future studies are encouraged to report short-term and long-term outcomes consistently for pouch surgery so that pooled analyses can be performed. In particular, a future investigation of leaks, strictures, long-term function, acute and chronic pouchitis, and level of intervention to control these complications, including antibiotics, immunotherapy or pouch excision, is warranted. If sample size permits, studies are encouraged to stratify their outcomes by diversion status as well as IBD type to identify specific differences in complications among children. Because the presence of intestinal occlusions could be highly correlated in IPAA with ileostomy from adhesions,34 71 capturing adhesions data in a subsequent review is recommended. Finally, standard preoperative health criteria for choosing undiverted or diverted procedures should be developed to optimize surgery selection for children with IBDs.

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Contributors
ID contributed to data curation, investigation, methodology, project administration, visualization, validation, writing (original draft) and writing (review and editing). NT contributed to investigation, validation and writing (review and editing). MK contributed to validation, visualization and writing (review and editing). VG contributed to validation and visualization. LH contributed to formal analysis, methodology, software, supervision, validation, visualization and writing (review and editing). AT contributed to formal analysis, methodology, software, supervision, validation, visualization and writing (review and editing). AN contributed to conceptualization, investigation, methodology, project administration, supervision, validation and writing (review and editing).

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Data are available upon reasonable request.

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REFERENCES


Hallgren KA. Computing interrater reliability for observational data: an overview and tutorial. Tutor Quant Methods Psychol 2012;8:23–34.


