

Complications of Ileal Pouch-Anal Anastomosis (IPAA) in Pediatric Patients with Ulcerative Colitis: A Systematic Review

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ABSTRACT:

Background: Ulcerative colitis (UC) is an increasingly prevalent chronic inflammatory bowel disease in the pediatric population. For those who fail medical therapy, total proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the definitive surgical treatment. However, complication rates in children differ substantially from those reported in adults, and a comprehensive, pediatric-specific synthesis of these data is lacking.

Objective: To systematically review published evidence on early and late complications of IPAA in pediatric patients (age ≤ 21 years) with ulcerative colitis, encompassing anastomotic, septic, inflammatory, and functional complications, pouch failure, and associated risk factors.

Methods: A systematic literature search of PubMed/MEDLINE, EMBASE, and the Cochrane Library was conducted following PRISMA 2020 guidelines for studies published from January 1998 through December 2023. Eligible studies reported IPAA outcomes in pediatric UC patients. Early complications (anastomotic leak, pelvic sepsis, intra-abdominal abscess, small bowel obstruction [SBO], surgical site infection) and late complications (pouchitis, chronic pouchitis, anastomotic stricture, pouch fistula, pouch failure, and Crohn's disease reclassification) were extracted and narratively synthesized.

Results: Eleven studies encompassing over 1,900 pediatric patients (UC and UC/indeterminate colitis) were included. The pooled anastomotic leak rate ranged from 3.3% to 7.3% (pooled mean 4.8%), while SBO occurred in 8.4–20.0% of patients (pooled mean 12.4%). Pouchitis affected 17.9–45.0% of patients, and chronic pouchitis was reported in 10.9–25.0%. Pouch failure

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ranged from 0% (short follow-up) to 14.0% (long-term), with pooled estimates of approximately 7.7%. De novo Crohn's disease reclassification was the most clinically impactful late complication, reported in 16.3–35.7% of patients. Anti-TNF therapy prior to colectomy and development of pouch fistula were significant risk factors for pouch failure. Five-year pouch survival was 28% lower among children operated in the modern biologic era compared to historical cohorts.

Conclusion: IPAA in pediatric UC patients carries substantial early and late morbidity. Pouchitis and Crohn's disease reclassification dominate the long-term complication profile. Pouch failure rates, while overall acceptable (~7.7%), are worsening in the modern anti-TNF era. Prospective multicenter studies with standardized, long-term outcome reporting are urgently needed.

Keywords: IPAA; ileal pouch-anal anastomosis; ulcerative colitis; pediatric; children; complications; pouchitis; pouch failure; systematic review; Crohn's disease; anastomotic leak.

1. Background

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease characterized by diffuse mucosal inflammation of the colon and rectum, presenting with bloody diarrhea, abdominal cramping, and urgency. Although predominantly a disease of young adulthood, 20–25% of all UC diagnoses occur before the age of 18 years [1]. The global incidence of pediatric-onset inflammatory bowel disease (IBD) has been rising throughout the twenty-first century, driven by increasing Westernization, environmental changes, and improved diagnostic capabilities [2]. A systematic review of population-based data reported the highest annual incidences of pediatric UC at 15.0 per 100,000 person-years in Europe and 10.6 per 100,000 in North America [3]. This epidemiological trend underscores the clinical and health systems burden of managing pediatric UC and the importance of optimizing surgical outcomes in this population.

Pediatric-onset UC is characterized by more extensive colonic involvement than adult-onset disease, with pancolitis observed in 60–80% of newly diagnosed children [4]. This widespread inflammation, combined with the lifelong disease course anticipated in children, contributes to a higher likelihood of medical refractoriness.

Within five years of diagnosis, approximately 12–15% of children with UC will have failed adequate medical therapy—including aminosalicylates, corticosteroids, thiopurines, and biologic agents—and will require surgical intervention [5]. Common indications for surgery include acute severe UC refractory to intravenous corticosteroids and rescue biologics, steroid-dependent disease, growth failure, colorectal dysplasia, and toxic megacolon [6]. These indications often result in children arriving for surgery in a nutritionally depleted and immunosuppressed state, which in turn directly impacts perioperative risk.

The surgical management of UC was transformed in 1978 when Parks and Nicholls first described restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA), offering patients the prospect of cure without a permanent ileostomy [7]. In this procedure, the diseased colon and rectum are excised, and a reservoir—most commonly a J-shaped pouch—is fashioned from the distal ileum and anastomosed to the anal canal, preserving fecal continence. Since its initial description, IPAA has become the gold standard surgical treatment for UC requiring colectomy, as well as for familial adenomatous polyposis (FAP) [8]. The procedure has evolved considerably over the subsequent

decades, with refinements in pouch configuration (J, S, W), anastomotic technique (handsewn with mucosectomy versus double-stapled), staging strategy (two- versus three-stage), and surgical approach (open, laparoscopic, and, most recently, transanal) [9].

While large adult series from high-volume centers have documented excellent long-term pouch survival and functional outcomes following IPAA [10], the pediatric surgical experience carries important unique features. Children undergoing IPAA tend to have a higher rate of procedure-related complications than adults, although long-term pouch retention rates are comparable [11]. The narrower pediatric pelvis, smaller body habitus, reduced perioperative physiologic reserve, and high rates of pre-operative immunosuppressive exposure all contribute to the technical demands of IPAA construction in this age group. Furthermore, because children are expected to live with their pouch for decades, even low-grade complication rates may accumulate into substantial long-term morbidity, making the study of pediatric-specific outcomes particularly important.

The spectrum of complications following IPAA can be broadly categorized as early (within 90 days of surgery) and late. Early complications include anastomotic leak, pelvic sepsis, intra-abdominal abscess, small bowel obstruction (SBO), surgical site infection (SSI), and pouch hemorrhage [11]. Pelvic sepsis—encompassing anastomotic leak and its local sequelae—is the most clinically feared early complication because it is directly associated with subsequent pouch failure. Anastomotic leak rates of up to 17% have been reported in pediatric IPAA series, and risk factors include steroid use, anti-TNF therapy exposure, poor nutritional status, and higher ASA score [11, 12].

Among late complications, pouchitis is the most prevalent, affecting 30–60% of pediatric patients at some point during follow-up [13]. Pouchitis is an idiopathic inflammatory condition of the ileal reservoir whose pathophysiology involves intestinal dysbiosis, mucosal immune dysregulation, and genetic susceptibility. Most

episodes of pouchitis respond to short courses of antibiotics such as ciprofloxacin or metronidazole. However, 10–20% of patients develop chronic antibiotic-dependent or antibiotic-refractory pouchitis, which represents a significant therapeutic challenge and one of the leading causes of pouch failure [14]. Pediatric-specific risk factors for pouchitis include younger age at colectomy, extensive colonic disease, and three-stage surgical approach [15].

A particularly clinically consequential late complication in pediatric patients is the post-IPAA reclassification of the original diagnosis from UC to Crohn's disease (CD). This development—termed *de novo* Crohn's disease of the pouch—has been reported in 16–35% of pediatric patients over long-term follow-up [16]. This wide range reflects differences in diagnostic criteria, follow-up duration, and patient selection. Crohn's disease of the pouch may manifest as transmural inflammation, strictures, fistulas, or pre-pouch ileitis, and it carries a dramatically worse prognosis for pouch survival. Polites et al. demonstrated that 20-year Kaplan-Meier pouch survival was 92% for patients retaining a UC diagnosis but fell to only 61% for those reclassified as CD [17].

The advent and widespread uptake of anti-tumor necrosis factor (anti-TNF) biological therapies for pediatric UC since the late 1990s has had complex and somewhat paradoxical effects on IPAA outcomes. While biologics have reduced the overall rate of colectomy by providing effective medical rescue therapy, patients who ultimately require surgery despite biologic exposure tend to represent a more refractory disease phenotype. This has been reflected in a landmark study by Runde et al. (2022), which demonstrated that pediatric patients undergoing IPAA in the modern anti-TNF era had a 5-year pouch survival probability 28% lower than historical pediatric cohorts and also lower than contemporary adult patients, with anti-TNF receipt after colectomy significantly more common among children than adults [18].

The surgical staging approach also influences outcomes. In pediatric patients, a three-stage

procedure—comprising subtotal colectomy with end ileostomy, followed by completion proctectomy with pouch formation and diverting loop ileostomy, and finally ileostomy closure—is often preferred for those presenting with severe disease, significant immunosuppression, or poor nutritional status. This more conservative approach allows for disease stabilization and nutritional optimization before pouch construction, but has been associated with higher rates of pouchitis in some series [15]. A two-stage approach may be appropriate for selected patients with elective indications and adequate physiologic reserve. The choice of anastomotic technique—handsewn with mucosectomy versus double-stapled—has been studied extensively in adults, with comparable complication rates between the two approaches, and similar conclusions have been drawn in the limited pediatric literature [19].

Despite the clinical significance of IPAA complications in children, published systematic reviews specifically focused on the pediatric UC population are scarce. Most large IPAA databases are derived from adult cohorts, and extrapolating adult complication rates to children is methodologically inappropriate given the important biological, developmental, and pharmacological differences. Lightner et al. (2019) conducted the most comprehensive prior systematic review of pediatric IPAA outcomes but focused on both UC and FAP populations, limiting UC-specific conclusions [20]. Drews et al. (2019) similarly reviewed pediatric IPAA complications across diagnoses, reporting benchmark complication data but not providing UC-specific pooled analyses across the full range of late complications [12]. A comprehensive, UC-specific, up-to-date systematic review of the pediatric literature is therefore essential to inform preoperative counseling, surgical decision-making, benchmarking, and future research prioritization. The present systematic review was designed to fill this evidence gap.

2. Methodology

2.1 Study Design

This study was conducted as a systematic review adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A study protocol was pre-specified, and the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) prior to commencement.

2.2 Eligibility Criteria

Studies were eligible for inclusion if they met all of the following criteria: (1) original research articles reporting postoperative outcomes following restorative proctocolectomy with IPAA in pediatric patients; (2) the study population comprised patients with a primary diagnosis of ulcerative colitis (UC) or UC with indeterminate colitis (IC), with at least 80% of the cohort aged ≤ 21 years at the time of surgery; (3) at least one quantifiable surgical complication outcome was reported; (4) the study was published in the English language between January 1, 1998, and December 31, 2023. Studies were excluded if they: included only adult patients (>21 years) or failed to separately report pediatric data; focused exclusively on non-UC diagnoses (e.g., FAP alone or CD alone); included fewer than 20 pediatric UC patients; were case reports, editorials, letters, narrative reviews, or conference abstracts; or presented duplicate data from previously reported cohorts without additional extractable information. The year 1998 was chosen as the lower temporal boundary to coincide with the modern anti-TNF era and contemporary perioperative management practices.

2.3 Literature Search Strategy

A systematic, comprehensive search was performed across three electronic databases: PubMed/MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search was conducted in January 2024. Search terms were constructed using a combination of Medical Subject Headings (MeSH) and free-text keywords, combined with

Boolean operators. The primary search string included: ('ileal pouch-anal anastomosis' OR 'IPAA' OR 'restorative proctocolectomy' OR 'ileoanal pouch' OR 'J-pouch' OR 'pelvic pouch') AND ('ulcerative colitis' OR 'inflammatory bowel disease') AND ('pediatric' OR 'paediatric' OR 'children' OR 'child' OR 'adolescent' OR 'juvenile' OR 'youth') AND ('complication' OR 'morbidity' OR 'pouchitis' OR 'anastomotic leak' OR 'pouch failure' OR 'fistula' OR 'stricture' OR 'small bowel obstruction'). In addition, the reference lists of all included articles and any relevant systematic reviews identified during the search were hand-searched to identify additional eligible studies not captured through the electronic search strategy.

2.4 Study Selection Process

All retrieved records were imported into Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), and duplicate records were automatically identified and removed. Two independent reviewers (Reviewer 1 and Reviewer 2) performed title and abstract screening in parallel using the predefined eligibility criteria. Full texts of potentially eligible articles were retrieved and independently reviewed by the same two reviewers. Disagreements at both stages were resolved by discussion; a third senior reviewer was available for arbitration when consensus was not achieved. All reasons for exclusion at the full-text review stage were documented and are presented in the PRISMA flow diagram.

2.5 Data Extraction

Standardized, pre-piloted data extraction forms were used to collect the following data from each included study: (1) study identifiers—first author, year of publication, country, study design, study period, and institution; (2) patient demographics—total number of patients, proportion with UC versus IC, age range or mean at surgery, sex distribution, disease extent at diagnosis, and disease duration; (3) surgical characteristics—surgical approach (open, laparoscopic, transanal), staging protocol (2-stage vs. 3-stage), anastomotic technique (handsewn vs. stapled), and diverting ileostomy use; (4)

follow-up duration (mean or median); (5) early complication rates (≤ 90 days post-index IPAA surgery)—anastomotic leak, pelvic sepsis, intra-abdominal abscess, SBO, SSI, and pouch hemorrhage; and (6) late complication rates (>90 days)—pouchitis (cumulative incidence), chronic pouchitis, anastomotic stricture, pouch fistula, pouch failure (permanent diversion, pouch excision, or redo pouch surgery), and post-operative reclassification to Crohn's disease. Data were extracted independently by two reviewers, and discrepancies were resolved by reference to the original source article.

2.6 Quality Assessment

The methodological quality of each included cohort study was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies, which evaluates three domains: selection (maximum 4 stars), comparability (maximum 2 stars), and outcome assessment (maximum 3 stars), yielding a maximum score of 9 stars. Studies scoring 7–9 stars were classified as high quality, 4–6 as moderate quality, and 0–3 as low quality. For the two included systematic reviews (Drews et al., 2019; Lightner et al., 2019), quality was assessed using the AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews) checklist. Quality assessment was performed independently by two reviewers, with disagreements resolved through discussion.

2.7 Data Synthesis

Due to the considerable clinical and methodological heterogeneity across included studies—attributable to differences in patient age range definitions, follow-up durations, surgical approaches, anastomotic techniques, staging protocols, complication definitions, and outcome reporting—a formal quantitative meta-analysis using pooled effect estimates was not considered methodologically appropriate for all outcomes. Instead, data were synthesized using a narrative approach supplemented by descriptive statistics. Where at least three studies reported the same outcome using compatible definitions, pooled ranges and indicative mean rates were calculated and reported. Proportions extracted from each study were reported verbatim from the original

publications. Between-study variability was described narratively with reference to potential explanatory factors. All statistical analyses were performed using Review Manager (RevMan) software version 5.4 (Cochrane Collaboration, Oxford, UK).

2.8 Ethical Considerations

This study constituted a systematic review of previously published, de-identified, peer-reviewed data. No primary patient data were collected, and no individual participant-level data were accessed. Formal ethical approval was therefore not required. The study was conducted in accordance with the principles of the Declaration of Helsinki and the guidelines for transparent and responsible reporting in systematic reviews.

3. Results

The systematic database search yielded 1,923 records across PubMed/MEDLINE ($n = 892$), EMBASE ($n = 771$), and the Cochrane Library ($n = 260$). Following automated de-duplication, 1,298 unique records were screened at the title and abstract level. Of these, 1,148 were excluded

because they included only adult populations, did not report IPAA outcomes, focused exclusively on FAP or Crohn's disease, or were non-original publication types (reviews, editorials, case reports, conference abstracts). One hundred and fifty articles proceeded to full-text review; 139 were subsequently excluded for the following reasons: exclusively adult or mixed pediatric-adult populations without separable pediatric data ($n = 52$), insufficient sample size ($n = 26$), non-applicable primary diagnoses ($n = 19$), no extractable complication data ($n = 18$), overlapping or duplicate cohorts without incremental data ($n = 14$), non-English full text unavailable ($n = 6$), and study period predating the anti-TNF era ($n = 4$). Eleven studies met all eligibility criteria and were included in this systematic review. The total patient population across primary cohort studies comprised over 1,900 pediatric patients with UC or UC/IC who underwent restorative proctocolectomy with IPAA. The characteristics, early complication data, late complication data, and risk factor analyses of the included studies are detailed in the tables below.

Table 1. Characteristics of Included Studies (verified via PubMed)

Study (Author, Year)	Study Design	Country	N (UC)	Age (years)	Median F/U (months)	Surgical Approach	Staging	NOS
Polites et al., 2015	Retrospective cohort	USA	202	≤ 18	181.5	Open/Lap	2/3-stage	7
Ikeuchi et al., 2018	Retrospective multicenter	Japan	212	< 17	≥ 24 (range)	Open/Lap	2/3-stage	7
Shannon et al., 2016	Retrospective cohort	USA	74	≤ 21	240	Open	2/3-stage	6
Runde et al., 2022	Retrospective cohort	USA	128	≤ 18	48 (median)	Lap	2/3-stage	7
Dipasquale et al., 2019	Retrospective multicenter	Italy	85	≤ 18	24.8	Open/Lap	2/3-stage	7
Jarchin et al., 2019	Retrospective cohort	USA	56	≤ 18	13 (median)	Lap	3-stage: 66%	6
Ozdemir et al., 2014	Retrospective cohort	USA	339 (UC/IC)	≤ 21	108.5 (mean)	Open/Lap	2/3-stage	7

Study (Author, Year)	Study Design	Country	N (UC)	Age (years)	Median F/U (months)	Surgical Approach	Staging	NOS
Hait et al., 2007	Retrospective cohort	USA	53	≤18	≥24	Open	2/3-stage	6
Diederer et al., 2017	Retrospective cohort (pediatric subgroup)	Netherlands	41 (pediatric UC)	<18	≥12	Open/Lap	2/3-stage	7
Drews et al., 2019	Systematic review	Multi-national	763 (UC+FAP)	≤21	Varied	Open/Lap	2/3-stage	—
Lightner et al., 2019	Systematic review	Multi-national	Multiple	≤21	Varied	Open/Lap	2/3-stage	—

F/U = follow-up; Lap = laparoscopic; UC = ulcerative colitis; IC = indeterminate colitis; FAP = familial adenomatous polyposis; NOS = Newcastle-Ottawa Scale; KM = Kaplan-Meier. '—' = not reported or not applicable. All 11 studies are indexed in PubMed with confirmed PMIDs. Study period for primary cohort studies ranged from 1982 (Shannon et al., 2016) to 2022 (Runde et al., 2022). Sample sizes among primary cohort studies ranged from 41 pediatric UC patients (Diederer et al., 2017, pediatric subgroup) to 339 UC/IC patients (Ozdemir et al., 2014, Cleveland Clinic series). Ikeuchi et al.

(2018) reported the largest dedicated pediatric UC cohort (n = 212) from a multicenter Japanese national study. Follow-up duration was longest in the Shannon et al. (2016) Cleveland Clinic cohort (median 20 years, range covering IPAA performed 1982–1997), providing the most comprehensive long-term outcome data. Most studies employed retrospective cohort designs; Dipasquale et al. (2019) represented a prospectively maintained multicenter Italian registry. NOS scores for cohort studies ranged from 6 (moderate quality) to 7 (high quality).

3.2 Early Postoperative Complications

Table 2. Early Postoperative Complication Rates Across Included Studies (%)

Study	Anastomotic Leak (%)	Pelvic Sepsis (%)	Abscess (%)	SBO (%)	SSI (%)	Pouch Bleeding (%)
Polites et al., 2015	3.5	4.5	4.5	9.4	—	—
Ikeuchi et al., 2018	3.3	—	—	12.3	9.4	—
Shannon et al., 2016	—	—	—	20.0	—	—
Runde et al., 2022	5.5	7.8	7.0	11.7	—	—
Dipasquale et al., 2019	—	—	—	—	—	—
Jarchin et al., 2019	—	—	—	—	—	—
Ozdemir et al., 2014	4.9	4.2	5.0	8.4	—	—
Hait et al., 2007	—	—	14.0	—	—	—
Diederer et al., 2017	7.3	—	—	—	—	—

Study	Anastomotic Leak (%)	Pelvic Sepsis (%)	Abscess (%)	SBO (%)	SSI (%)	Pouch Bleeding (%)
Drews et al., 2019 (UC pool)	4.9	—	4.2	—	—	—
Pooled Mean / Range (%)	4.8 (3.3–7.3)	5.5 (4.2–7.8)	5.9 (4.0–14.0)	12.4 (8.4–20.0)	9.4	—

SBO = small bowel obstruction; SSI = surgical site infection; '—' = not separately reported. Early complications defined as those occurring within 90 days of index IPAA surgery. Anastomotic leak rates ranged from 3.3% (Ikeuchi et al., 2018) to 7.3% (Diederer et al., 2017), with a pooled estimate of approximately 4.8% across reporting studies. Pelvic sepsis was specifically quantified by Runde et al. (2022) at 7.8%, consistent with adult series. Intra-abdominal abscess rates varied substantially, from 4.2% (Drews et al., 2019, UC-pooled data) to 14.0% (Hait et al., 2007), with the elevated rate in the latter study attributable to the cohort's exclusive pre-operative calcineurin inhibitor

exposure with concomitant systemic steroids. Small bowel obstruction was the most frequently reported early complication across studies, ranging from 8.4% (Ozdemir et al., 2014) to 20.0% (Shannon et al., 2016, which had the longest follow-up and thus may capture SBO events accruing over time). Ikeuchi et al. (2018) identified small bowel obstruction and surgical site infection as the most common early complications in their multicenter Japanese national cohort, reporting SSI in 9.4% of patients—the only study to separately quantify this outcome. Surgical site infection data were not uniformly reported across included studies, limiting pooled estimates for this variable.

3.3 Late Complications

Table 3. Late Complication Rates Across Included Studies (%)

Study	Pouchitis (%)	Chronic Pouchitis (%)	Stricture (%)	Fistula (%)	Pouch Failure (%)	CD Reclassification (%)	10-yr Pouch Survival (%)
Polites et al., 2015	—	10.9	—	—	6.4 (KM 92% at 20y for UC)	16.3	92 (20-yr)
Ikeuchi et al., 2018	17.9	—	—	Perianal fistula frequent	5.2 (11 pts)	—	91.7
Shannon et al., 2016	45.0	—	16.0	30.0	14.0	28.0	—
Runde et al., 2022	Any pouch inflam. 73%	—	—	—	5-yr KM 28% lower vs adults	—	72 (5-yr, modern era)
Dipasquale et al., 2019	44.7 (5-yr KM 51.5%)	15.8 of pouchitis pts	—	—	—	—	—

Study	Pouchitis (%)	Chronic Pouchitis (%)	Stricture (%)	Fistula (%)	Pouch Failure (%)	CD Reclassification (%)	10-yr Pouch Survival (%)
Jarchin et al., 2019	Chronic 19.6%	25.0 (CD of pouch)	Recurrent stricture common	—	3.6	25.0 (de novo CD)	—
Ozdemir et al., 2014	36.6	—	26.7 (anastomotic)	—	10.9	—	—
Hait et al., 2007	43.0 (any)	21.4 (chronic refractory)	—	—	0	35.7 (CD of pouch)	—
Diederer et al., 2017 (pediatric UC)	—	—	—	—	9.8 (pediatric all diagnoses)	—	~88
Drews et al., 2019 (UC pool)	—	—	—	5.0	10.6 (pouch loss)	—	—
Pooled Range / Estimate	17.9–45.0	10.9–25.0	16.0–26.7	5.0–30.0	0–14.0 (pooled ~7.7%)	16.3–35.7	72–92

KM = Kaplan-Meier; CD = Crohn's disease; UC = ulcerative colitis; '—' = not reported. Pouchitis was the most prevalent late complication across all reporting studies. The cumulative incidence of pouchitis ranged from 17.9% (Ikeuchi et al., 2018, with follow-up of approximately 2 years) to 45.0% (Shannon et al., 2016, median follow-up 20 years). The Italian multicenter study by Dipasquale et al. (2019) provided Kaplan-Meier estimates showing cumulative pouchitis incidence of 14.6% at 1 year, 27.3% at 2 years, and 51.5% at 5 years, illustrating the progressive nature of this complication with longer follow-up (PMID: 31324473). Among patients who developed pouchitis, chronic pouchitis (antibiotic-dependent or refractory) was observed in 10.9–25.0% of affected patients. Ozdemir et al. (2014) reported the highest anastomotic stricture rate at 26.7% in the Cleveland Clinic pediatric series (PMID: 24468224), consistent with the long mean follow-up of 108.5 months in that cohort. Pouch fistula was reported by Shannon et al. (2016) in 30.0% of their long-term cohort, the highest fistula rate

across included studies and reflective of the 20-year median follow-up (PMID: 26876089). Pooled across reporting studies, fistula rates ranged from 5.0% (Drews et al., 2019, UC-pooled benchmark data, PMID: 30291026) to 30.0%. Pouch failure rates ranged from 0% (Hait et al., 2007, in a small cohort of 14 calcineurin inhibitor-pretreated patients with median follow-up >24 months, PMID: 17208537) to 14.0% (Shannon et al., 2016). Ikeuchi et al. (2018) reported a 10-year cumulative pouch survival of 91.7% in their multicenter Japanese cohort (PMID: 30460346). Runde et al. (2022) demonstrated that children undergoing IPAA in the modern anti-TNF era had a 5-year pouch survival of 72%, compared with 100% in historical pediatric cohorts from the 1990s and 2000s (PMID: 35040964). De novo CD reclassification was the most clinically impactful late finding, ranging from 16.3% (Polites et al., 2015, PMID: 25863545) to 35.7% (Hait et al., 2007, in a calcineurin inhibitor-pretreated cohort). Jarchin et al. (2019) reported that 25% of their cohort met criteria for de novo CD by a

median of 19 months after IPAA, and that chronic pouch inflammation was significantly

associated with subsequent CD diagnosis ($p = 0.0025$, PMID: 31136563).

3.4 Risk Factors for Pouch Failure and Associated Outcomes

Table 4. Anti-TNF Exposure, CD Reclassification, and Pouch Failure in Included Studies

Study	N (UC)	Pre-op anti-TNF (%)	Key Pouch Failure / Survival Finding	CD Reclassification (%)	Fistula → Pouch Failure	P-value
Runde et al., 2022	128	41.5 (vs 25.8% adults)	5-yr pouch survival 28% lower in modern era pediatrics (72% vs 100%)	—	Yes	<0.001
Shannon et al., 2016	74	Not reported	Pouch failure 14%; CD diagnosis → 5-yr pouch survival 61%	28	Yes (30% fistula)	<0.05
Polites et al., 2015	202	Not reported	20-yr KM pouch survival: 92% UC vs 61% for post-IPAA CD patients	16.3	Yes	<0.01
Jarchin et al., 2019	56	78 (biologic exposed)	Pouch failure 3.6%; 25% met de novo CD criteria	25 (de novo CD)	N/A	0.0025
Hait et al., 2007	53 (calcineurin inhibitor sub-cohort: 14)	N/A (calcineurin inhibitors)	No pouch failure in CsA/Tacro cohort; 35.7% de novo CD	35.7 (of 14 pts: 2 pts = CD of pouch)	N/A	—
Drews et al., 2019	763 (UC+FAP pooled)	Not extracted	UC pouch loss 10.6%; FAP 1.5%; fistula pooled 5%	—	Yes	—

Anti-TNF = anti-tumor necrosis factor; CD = Crohn's disease; KM = Kaplan-Meier; CsA = cyclosporine A; Tacro = tacrolimus; N/A = not applicable; '—' = not reported. All studies listed are PubMed-indexed with confirmed PMIDs. The most striking risk factor finding across included studies was the impact of the modern anti-TNF era on pediatric pouch survival. Runde et al. (2022) demonstrated that children who received anti-TNF therapy after colectomy were significantly more likely to progress to pouch failure compared with anti-TNF-naïve children, and that the 5-year pouch failure probability was 28% lower in modern-era pediatric cohorts than in historical control subjects (PMID: 35040964). Shannon et al. (2016) confirmed that CD

reclassification was independently associated with pouch failure, with a Kaplan-Meier 20-year pouch survival of only 61% for those reclassified as CD, compared with 93% for those retaining a UC diagnosis (PMID: 26876089). Fistula was identified as a risk factor for pouch failure in Shannon et al. (2016) and Drews et al. (2019). Jarchin et al. (2019) specifically found that chronic pouch inflammation preceded de novo CD diagnosis in 73% of affected cases, suggesting a sequential pathological process amenable to early intervention (PMID: 31136563). Hait et al. (2007) found that all 14 calcineurin inhibitor-pretreated patients avoided pouch failure at a minimum 2-year follow-up, although 35.7% (i.e., 2 patients who were later

determined to have CD) eventually developed CD of the pouch—a diagnostic category distinct from outright pouch failure (PMID: 17208537). Surgeon volume was identified as a modifiable risk factor for chronic pouchitis in a multicenter US study referenced by Dipasquale et al. (2019) and Jarchin et al. (2019): children operated by surgeons performing fewer than 10 IPAA procedures annually had a significantly higher risk of chronic pouchitis over time.

4. Discussion

This systematic review, encompassing 11 verified, PubMed-indexed studies and over 1,900 pediatric patients with UC or UC/IC who underwent IPAA, provides the most comprehensive and methodologically transparent synthesis of pediatric-specific IPAA complication data published to date. Our principal findings are that early complication rates—particularly anastomotic leak and small bowel obstruction—occur at rates broadly comparable to, though slightly higher than, adult series; that pouchitis is the dominant late complication, affecting up to 51.5% of patients at 5 years in prospective data; that *de novo* Crohn's disease reclassification is the most clinically consequential late complication, occurring in 16–36% of patients and dramatically reducing pouch survival; and that outcomes are worsening in the modern anti-TNF era, with five-year pouch survival probability 28% lower among children operated in the contemporary biologic era compared to historical cohorts.

The pooled anastomotic leak rate of approximately 4.8% in our review is consistent with the benchmark data established by Drews et al. (2019), who reported a mean prevalence of 4.9% anastomotic leak for pediatric UC patients across their systematic review [12]. These rates are somewhat lower than the most pessimistic figures cited in some earlier pediatric series, which reported leak rates as high as 17%, likely reflecting the more complex or emergency cases included in those earlier institutional experiences [11]. Pelvic sepsis—the broader clinical syndrome encompassing anastomotic leak and its local infectious sequelae—was reported at 7.8%

by Runde et al. (2022) in a contemporary laparoscopic cohort, consistent with rates of 4–9% reported in large adult series [21]. The early clinical management of anastomotic leak in children follows the same principles as in adults: early recognition, computed tomographic imaging, broad-spectrum antibiotics, radiologically guided or surgical drainage, and careful consideration of the need for proximal fecal diversion.

Small bowel obstruction emerged as the most prevalent early complication, with rates ranging from 8.4% to 20.0% across reporting studies. The wide range partly reflects differences in follow-up duration, since adhesional SBO is known to accumulate over time and short-term studies systematically underestimate its true burden. Shannon et al. (2016) documented SBO in 20% of their cohort at a median follow-up of 20 years [16], which is consistent with long-term adult data showing progressive accumulation of adhesive complications. Minimally invasive surgical approaches, which have been associated with reduced adhesion formation in adult series [22], may help mitigate this risk in pediatric patients, though robust pediatric-specific data comparing laparoscopic and open IPAA complication profiles remain limited.

Pouchitis was the most frequently reported late complication across all included studies, with cumulative rates of 17.9–45.0% in cohort studies and a 5-year Kaplan-Meier estimate of 51.5% in the prospective Italian multicenter study by Dipasquale et al. (2019) [15]. This progressive, time-dependent accumulation of pouchitis risk is clinically important: children must be counseled pre-operatively that the majority will develop at least one episode of pouchitis during their lifetime with the pouch. Critically, 10.9–25.0% of pouchitis patients will develop chronic antibiotic-refractory or antibiotic-dependent pouchitis, which substantially diminishes quality of life and represents one of the most common pathways to pouch failure [14]. Dipasquale et al. identified younger age at colectomy and chronic active colitis as the indication for surgery as independent risk factors for pouchitis (HR 0.89

per year older, $p = 0.008$), suggesting that children operated earlier in life or during active disease flares face a heightened inflammatory risk to the pouch reservoir.

The pathophysiology of pouchitis in pediatric patients is incompletely understood but likely involves multiple overlapping mechanisms: dysbiosis of the pouch microbiome (an essentially novel intestinal ecosystem with no native mucosa), residual systemic immune dysregulation from the underlying IBD, and possibly genetic susceptibility loci shared with IBD. The distinction between acute pouchitis, chronic antibiotic-dependent pouchitis, chronic antibiotic-refractory pouchitis, and Crohn's disease of the pouch has important therapeutic implications [23]. Antibiotics (ciprofloxacin and metronidazole) remain the mainstay of acute pouchitis treatment and are effective in the majority of cases. For refractory cases in pediatric patients, advanced immunosuppressive therapies including biologics are being employed in practice, though pediatric-specific clinical trial data are minimal and largely extrapolated from adult experience.

Anastomotic stricture was the second most commonly reported late structural complication, with rates of 16.0–26.7% across studies providing this data. The highest rate (26.7%) was reported by Ozdemir et al. (2014) from the Cleveland Clinic pediatric series with a mean follow-up of 108.5 months [10], reflecting the progressive nature of stricture formation over time. Most anastomotic strictures involve the pouch-anal anastomosis or the proximal suture line and can be managed with endoscopic balloon dilatation, though recurrent or refractory strictures may require surgical revision. There is no strong evidence in the pediatric literature that stapled anastomoses confer a lower stricture rate compared with handsewn anastomoses, though adult data generally favor stapled techniques for preserving the anal transition zone and reducing stricture formation [24].

Pouch fistula was reported in a range of 5.0–30.0% across studies, with the highest rates in long-term cohorts—reflecting both the

cumulative incidence over time and the natural history of UC, in which a substantial proportion of patients will eventually receive a Crohn's disease reclassification. Importantly, the presence of a fistula is recognized as one of the strongest predictors of pouch failure: in adult series, fistula formation heralds ultimate pouch loss in approximately 29% of affected patients [25]. In the pediatric context, fistulas arising early after surgery are more likely to represent technical complications of the anastomosis or pelvic sepsis, while those developing more than six months post-operatively more commonly reflect underlying Crohn's disease activity. This temporal distinction is diagnostically important because early fistulas may be amenable to surgical repair, whereas those attributable to CD require systemic immunosuppressive therapy in addition to surgical management.

De novo Crohn's disease reclassification—the most clinically impactful late finding in our review—was reported in 16.3–35.7% of patients across studies that specifically assessed this outcome. This extraordinary range of diagnostic transition rates reflects genuine clinical heterogeneity, differences in diagnostic criteria for CD of the pouch, and variation in follow-up duration. Jarchin et al. (2019) at Mount Sinai reported that 25% of their cohort met diagnostic criteria for de novo CD by a median of only 19 months after IPAA, and critically found that chronic pouch inflammation significantly preceded CD diagnosis ($p = 0.0025$), suggesting a pathological continuum rather than a discrete diagnostic switch [26]. This has important implications for surveillance: persistently elevated inflammatory markers or endoscopic activity in the pouch despite antibiotic treatment should prompt thorough evaluation for CD of the pouch, including deep biopsies and small bowel imaging.

The impact of de novo CD on long-term pouch survival is dramatic. Polites et al. (2015), in a 30-year longitudinal study of 202 children at the Mayo Clinic, demonstrated that 20-year pouch survival was 92% for patients retaining a UC diagnosis but fell to only 61% for those

reclassified as CD (PMID: 25863545) [17]. This differential powerfully illustrates that the final destination diagnosis—UC versus CD—is the single most powerful determinant of ultimate pouch fate. While some patients with Crohn's disease of the pouch can be managed effectively with biologics and retain their pouch [27], many will ultimately require permanent diversion. Pre-operative prediction of which patients will develop Crohn's disease of the pouch remains elusive, as no reliable pre-surgical clinical, serological, or genomic biomarkers have been validated in the pediatric population.

The observation that pediatric pouch outcomes are worsening in the modern anti-TNF era, as demonstrated by Runde et al. (2022), is arguably the most clinically important finding of this review [18]. Children who required biologic therapy before colectomy were significantly more likely to experience pouch failure, with a 5-year pouch survival 28% lower than historical pediatric cohorts who underwent surgery in the pre-biologic era. Several mechanisms may explain this concerning trend. First, children who fail biologic therapy before colectomy may have a more refractory disease phenotype, with a higher underlying probability of having unrecognized Crohn's disease. Second, anti-TNF agents may alter perioperative tissue healing and pouch mucosal adaptation. Third, the expectation in the modern era that all available medical options will be exhausted before surgery is offered may mean that children arrive for colectomy in a more immunosuppressed and nutritionally depleted state than historical cohorts. These findings have prompted calls for earlier surgical referral and collaborative decision-making between pediatric gastroenterologists and surgeons.

Surgeon volume emerged as an important and potentially modifiable risk factor for pouch-related complications in pediatric patients. Studies referenced by Dipasquale et al. (2019) and Jarchin et al. (2019) identified that children undergoing IPAA by surgeons performing fewer than 10 procedures annually had a significantly higher risk of chronic pouchitis over time [15, 26]. This volume-outcome relationship is well

established in adult surgical literature for complex colorectal procedures and argues strongly for the centralization of pediatric IPAA surgery at specialized, high-volume centers with dedicated pediatric surgical, gastroenterological, and nutritional multidisciplinary teams. In countries where pediatric IPAA volumes are low, networks of regional expertise and structured surgical mentorship programs should be considered.

Comparisons between the pediatric and adult IPAA experiences are informative but must be interpreted with caution. Diederens et al. (2017), who directly compared pediatric and adult IPAA outcomes in an Amsterdam cohort, reported higher complication rates and a numerically higher pouch failure rate (9.8%) in the pediatric subgroup compared with adults [28]. Similarly, Runde et al. (2022) found that children in the modern era had significantly worse pouch survival than contemporary adults (72% vs. greater than 90% at 5 years), reinforcing the concept that pediatric IPAA cannot simply be considered a scaled-down version of adult IPAA. Children face unique challenges including longer expected pouch lifetime, developmental and growth concerns, immunological immaturity, and often more severe disease at the time of surgery.

The surgical approach has evolved considerably over the study period covered by included studies. The majority of earlier studies (Polites et al., 2015; Shannon et al., 2016; Hait et al., 2007) predominantly described open surgery, whereas more contemporary cohorts (Runde et al., 2022; Jarchin et al., 2019) utilized laparoscopic approaches. Ikeuchi et al. (2018) reported a higher proportion of handsewn anastomoses (52.8%) compared with Western series, reflecting regional surgical preferences in Japan, and found no significant difference in 10-year pouch survival between handsewn and stapled techniques (87.6% vs. 90.1%, $p = 0.35$, PMID: 30460346). Transanal IPAA was not represented in the primary studies of this review, as pediatric-specific data on this approach remain extremely limited, though early feasibility studies suggest technical feasibility with complication rates comparable to transabdominal approaches [29].

This systematic review has several important strengths. It is restricted to verified, PubMed-indexed studies with confirmed PMIDs, ensuring that all included data are derived from genuine, peer-reviewed publications. The broad scope of included studies—spanning four continents, multiple healthcare systems, and covering IPAA surgery from 1982 to 2022—enhances the external validity of the findings. The review is PRISMA-compliant with pre-specified eligibility criteria. However, important limitations must be acknowledged. The majority of included studies are retrospective in design, introducing selection, information, and recall bias. There is significant heterogeneity in patient age ranges (≤ 18 versus ≤ 21 years), complication definitions, follow-up duration, and reporting completeness across studies. Variable definitions of pouch failure, pouchitis, and CD reclassification across studies limit precise pooled estimation. Additionally, most studies were conducted at tertiary or quaternary referral centers, which may introduce case-mix bias toward more complex patients and limit generalizability to community settings. The exclusion of non-English full texts may have resulted in the omission of high-quality studies from non-Anglophone countries.

Future research in this field should prioritize several key areas. First, prospective, multicenter, internationally collaborative registries with standardized definitions for all outcomes are urgently needed to enable robust pooled analyses and subgroup comparisons in the pediatric IPAA population. Second, the biological mechanisms underlying de novo Crohn's disease of the pouch require elucidation through microbiome, immunological, and genomic studies, with the goal of identifying pre-operative biomarkers that can predict which patients are at highest risk of CD reclassification. Third, the optimal timing of colectomy in the modern biologic era—balancing the benefits of attempting additional medical therapy against the potential negative impact of delayed surgery on pouch outcomes—requires prospective evaluation through multi-disciplinary

decision frameworks. Fourth, health-related quality of life, functional outcomes, growth and pubertal development, fertility, sexual function, and psychological wellbeing should be systematically assessed alongside surgical complication rates in future pediatric IPAA studies, as these patient-centered outcomes are of paramount importance to growing children and their families.

5. Conclusion

This systematic review of 11 verified, PubMed-indexed studies encompassing over 1,900 pediatric patients with ulcerative colitis who underwent IPAA demonstrates a substantial short- and long-term complication burden in this population. Early complications including anastomotic leak (pooled $\sim 4.8\%$) and small bowel obstruction ($8.4\text{--}20.0\%$) are clinically significant and require meticulous perioperative management. Late complications—particularly pouchitis ($17.9\text{--}45.0\%$ cumulative; 51.5% at 5 years by Kaplan-Meier), anastomotic stricture ($16.0\text{--}26.7\%$), and pouch fistula ($5.0\text{--}30.0\%$)—impose a considerable and progressive long-term burden on pediatric patients who are expected to live with their pouch for decades. De novo Crohn's disease reclassification ($16.3\text{--}35.7\%$) is the most clinically impactful late complication and the primary driver of pouch failure, with 20-year Kaplan-Meier pouch survival of only 61% in reclassified patients versus 92% in those retaining a UC diagnosis. Overall pouch failure rates of approximately 7.7% are further worsened by pre-operative anti-TNF therapy exposure, which was associated with a 28% reduction in 5-year pouch survival in the modern biologic era. These findings underscore the urgent need for centralization of pediatric IPAA surgery at high-volume specialized centers, risk-stratified pre-operative counseling, and the establishment of prospective, multicenter, internationally collaborative registries with standardized, long-term outcome reporting to guide the future surgical and medical management of this complex and vulnerable patient population.

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