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Modified two-stage restorative proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis: a systematic review and meta-analysis of observational research

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Abstract

Purpose: Restorative proctocolectomy(RPC) is performed for patients with refractory ulcerative colitis(UC). This operation is performed in 2 or 3-stages and involves forming a diverting loop ileostomy thought to protect patients from complications related to anastomotic leak. However, some advocate for a modified 2-stage approach, consisting of subtotal colectomy followed by completion proctectomy and ileal pouch anal anastomosis without diverting ileostomy. We present a systematic review and meta-analysis comparing postoperative complication rates between modified 2-stage and traditional RPC with ileal pouch anal anastomosis.

Methods: Records were sourced from PubMed/Embase databases. Studies comparing postoperative complications following RPC for ulcerative colitis(UC) were selected according to PRISMA guidelines comparing modified 2-stage(exposure), classic 2-stage, and 3-stage approaches(comparators). The primary outcome measure was safety as measured by postoperative complication rates. We employed random-effects meta-analysis.

Results: We included ten observational studies including 1727 patients(38% modified 2-stage). Among pediatric patients, modified 2-stage approaches had higher rates of anastomotic leak than 3-stage approaches($p=0.03$). Among adult cohorts with lower preoperative biologic use rates, modified 2-stage approaches had lower leak rates than classic 2-stage approaches($p<0.001$).

Conclusions: The modified 2-stage approach may be safe for adult patients who otherwise require a 3-stage approach while reducing costs and length of stay. Pediatric patients may benefit

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from lower leak rates when receiving 3-stage compared to modified 2-stage approaches, especially when on biologics. The modified 2-stage approach may be safer than the classic 2-stage approach for adult patients with lower biologic exposure.

Keywords

ulcerative colitis; restorative proctocolectomy ileal pouch anal anastomosis; outcomes; systematic review; meta-analysis

Introduction:

Background

Ulcerative colitis(UC) affects over one million patients in the United States alone.[1,2] Despite advances in medical management of UC, surgery remains the only curative modality for the disease. Estimates show between 8.7 and 17% of UC patients need surgery within 10 years of diagnosis.[3] This rate is higher among pediatric patients, with 15 to 20% requiring colectomy within five years of diagnosis.[4] For refractory UC, restorative proctocolectomy with ileal pouch-anal anastomosis(RPC-IPAA) is performed to resect the colon and rectum while preserving fecal continence.[5]

Several staged approaches to completing a RPC-IPAA exist.[6] The 2-stage approach consists of 1) a proctocolectomy with IPAA and formation of a temporary loop ileostomy, followed six to eight weeks later with 2) ileostomy reversal to restore continuity.[7] In theory, creation of the loop ileostomy should protect the newly formed IPAA from complications in UC patients who are often ill while taking immunosuppressive therapy to manage their disease, ultimately reducing the risk of infectious complications and anastomotic leak.[8] For UC patients with severe disease, malnutrition, and/or requiring high-doses of corticosteroids, a 3-stage RPC-IPAA is often performed.[6] This consists of a 1) subtotal colectomy with end ileostomy, 2) completion proctectomy with IPAA and loop ileostomy, and 3) stoma closure.[9-11] Proponents of the 3-stage approach argue delaying formation of the critical IPAA until the second procedure allows more time for patients to recover from the sequelae of severe UC and to wean immunosuppressive therapy.[6]

Despite the popularity of 2 and 3-stage RPC-IPAA, some have offered evidence that loop ileostomy and increased staging are unnecessary in selected UC patients.[7,12] Loop ileostomy formation and closure confer morbidity of its own, including small bowel obstruction(SBO) and dehydration.[13] Adding to this controversy is the modified 2-stage approach, which consists of a 1) subtotal colectomy(STC) with end ileostomy followed by 2) undiverted completion proctectomy and IPAA. This approach treats the presenting UC with STC and allows the patient time to recover prior to performing the IPAA. Thus, patients are theorized to have lower rates of anastomotic leak than if the pouch was performed at the initial procedure.[6] While this method shows some promise in the literature, many surgeons are slow to adopt modified 2-stage IPAA due to limited data to support one approach versus another.[11,12]

There is no clear consensus on assigning UC patients to the RPC-IPAA approach that best fits their disease. Most operative decision-making surrounding RPC-IPAA is dependent on surgeon and/or institutional experience. Elucidating the outcomes associated with each approach is critical to providing surgeons and their patients the best-informed operative decisions and is the rationale of our study.

Aim/Objectives:

We present a systematic review with meta-analysis of observational studies comparing (A)Patients: Pediatric or adult patients with UC, (B)Exposure: undergoing modified 2-stage RPC-IPAA, or (C)Comparator: classic 2- or 3-stage RPC-IPAA, and (D)Outcomes: reporting post-operative complication rates with both procedures. We aimed to compare the safety profiles of modified 2-stage RPC-IPAA compared to classic 2-stage and 3-stage approaches. We hypothesized that the modified 2-stage approach has comparable safety to these approaches, in combined and separate comparisons.

Materials and Methods:

Review Protocol

We did not use a registered review protocol. We used Preferred Reporting Items for Systematic Reviews and Meta-Analyses(PRISMA) reporting guidelines.[14]

Eligibility

We included randomized controlled trials or comparative cohort studies in (A)Patients: Pediatric or adult patients with UC, (B)Exposure: undergoing modified 2-stage RPC-IPAA, or (C)Comparator: classic 2- or 3-stage RPC-IPAA, and (D)Outcomes: reporting post-operative complication rates with both procedures as listed below. We excluded cross-sectional studies and studies performed in patients with Crohn’s disease. No language or time restrictions were applied.

Sources, Search, and Study Selection

We conducted a comprehensive search of PubMed and Embase from inception to March 28, 2020. We then hand-searched references of included articles for additional records. The detailed strategy listing is reported in Appendix A. Two study investigators (WYL and SE) independently reviewed the title and abstract of studies identified in the search to exclude studies that did not address the research question of interest based on pre-specified inclusion and exclusion criteria. The full text of the remaining articles was examined. Conflicts in study selection at this stage were resolved by consensus, referring to the original article, in consultation with a third investigator(SS). Non-English records were translated using Google translate and preliminary data from unpublished trials were sourced from ClinicalTrials.gov if applicable.

Data Extraction and Items

Data on patient population studied, intervention cohort and sample size, comparison cohort and sample size(if applicable), outcome measures, covariate(s) if used, study type, years

studied, and number of centers were abstracted by two authors independently(WYL and SE) and discrepancies were resolved by consensus, referring to the original article, in consultation with a third reviewer(SS). If available, we noted the biologic use reported by each study, defined as the percentage(%) of patients reported to be taking biologics in each study cohort.

Outcomes

Primary comparison was performed between modified 2-stage RPC-IPAA and traditional(classic 2 and 3-stage) RPC-IPAA. Our secondary comparison was modified 2-stage versus classic 2-stage or 3-stage RPC-IPAA in separate subgroup analyses. The primary outcome measures were safety, measured by postoperative rates of anastomotic leak, wound infection, pelvic sepsis, pneumonia, pouchitis, stricture formation, hernia, ileus/small bowel obstruction(SBO), stoma-related complications, or deep venous thrombosis(DVT). We chose these outcomes because they were either specific to the operations performed or clinically relevant during a patient's postoperative course. Secondary outcomes were return to surgery or readmission within 30 days, hospital length of stay(HLOS), and hospital cost(HC). Data were selected for clinical relevance and availability in the literature.

Risk of Bias within Studies

Risk of bias(RoB) was assessed for each included record according to the Methodological index for non-randomized studies(MINORS) criteria.[15] Records were given scores of zero through two for 12 criteria of bias assessment. The ideal global score is 24 for comparative studies and 16 for non-comparative studies.

Risk of bias across studies

Due to the small sample of records available for our review, assessment of RoB across studies was limited to qualitative review of the records included in meta-analysis.

Summary Measures

For meta-analysis, dichotomous and continuous outcomes were reported as pooled odds ratios and mean differences, respectively. Imputation of mean and standard deviation (SD) was performed as needed using previously validated methods.[16,17]

Statistical Analysis

Analysis was performed on pooled statistics from comparative records and forest plots were generated using Review Manager 5(The Cochrane Collaboration, 2019, London, UK). Pooled odds ratios(OR) and mean differences(MD) were generated using Mantel-Haenszel and inverse-variance tests, respectively, using a random-effects model. For outcomes with no events, pooled risk differences were generated. Statistical heterogeneity was assessed using the I^2 statistic with a $I^2 \geq 50\%$ considered to be substantial heterogeneity.

Additional analyses

We stratified our meta-analysis by pediatric versus adult cases and by records comparing modified with classic 2-stage RPC-IPAA versus records comparing modified 2-stage with 3-stage approaches. Between-study sources of heterogeneity were investigated using subgroup analyses by stratifying original estimates according to study characteristics (as described above). In this analysis, a p-value for differences between subgroups of <0.10 was considered statistically significant.

We performed separate meta-analyses of adjusted risk ratios(RR) using a generic inverse variance random-effects model for studies that reported outcomes adjusted for differences in baseline characteristics.

Results

Study Selection

Our search yielded 38 records comparing modified 2-stage with traditional RPC-IPAA performed for UC patients. Four duplicates were removed, and 34 records underwent full-text and abstract screening for eligibility. We excluded 24 records, with reasons detailed in Appendix B.[18-27,12,28-32,7,11,33-38] This included studies that compared RPC-IPAA staged approaches but did not stratify by our intervention of interest(i.e. modified 2-stage approach). Because of this, these studies could not be included in meta-analysis. The remaining ten records were included in meta-analysis.(Fig. 1)

Study Characteristics and Individual Results

Characteristics of the ten records included for meta-analysis included 13 centers and 1727 patients.[6,39,3,40,41,4,42-44](Table 1) Four pediatric studies encompassed 146(8.5%) cases.[41,4,44,43] 656(38%) and 1071(62%) subjects underwent modified 2-stage and traditional RPC-IPAA, respectively. Among traditional cases, 777(73%) and 294(27%) cases were classic 2-stage and 3-stage RPC-IPAA, respectively. Reported mean age of patients undergoing surgery ranged between 12.5 and 43 years. Two records were found to have possible patient sample overlap and were not included in pooled analyses together.[6,39] Of the ten studies included in our review, seven(70%) reported significant differences in preoperative characteristics among their cohorts.[6,39,3,40,42,45,43] Two records did not stratify baseline characteristics(i.e. age and sex) by RPC-IPAA staged approach; however, they did stratify their outcomes analysis by our intervention of interest.[42,45] While all included records included patients receiving RPC-IPAA for UC, two studies(20%) further stratified indication for RPC-IPAA as toxic megacolon, acute bleeding, dysplasia, or carcinoma.[45,3] Four studies(40%) stated that they included urgent cases in their cohorts. [45,42,6,40,43]

Risk of Bias within Studies

The range of RoB scores in records included in meta-analysis was 16-18.[6,39,3,40,41,4,11] (Appendix C)

Primary analysis outcomes

Rates of anastomotic leak, wound infections, pneumonia, pouchitis, stricture formation, ileus/SBO, and DVT were comparable between modified 2-stage and traditional RPC-IPAA (Fig. 2A-E, G-H). Hernia formation rates were significantly higher in the modified 2-stage group (OR=9.82,95%CI(1.78,54.30),I^2=0%) (Fig.2F). Pelvic sepsis was analyzed in two studies that likely had subject pool overlap; both reported comparable pelvic sepsis rates between modified 2 stage and traditional RPC-IPAA.[6,39] One study reported stoma-related complication rates and found no significant difference between the four RPC-IPAA staged approaches.[6]

Rates of hospital readmissions, reoperation, and HLOS related to IPAA were comparable between modified 2-stage and traditional RPC-IPAA.(Fig.3) One study not included in meta-analysis due to possible subject overlap found no difference in HLOS or HC related to IPAA between modified 2-stage and traditional RPC-IPAA.[6] However, a subsequent study by the same authors found reduced HC associated with modified 2-stage RPC-IPAA cases.[39] We did not perform meta-analysis of HC due to possible subject overlap between the two studies.

Adjusted meta-analyses

Most(6/7,86%) studies reporting differences in baseline characteristics between modified 2-stage and traditional RPC-IPAA performed adjusted analysis of select outcomes.(Table 1) Two of these studies performed adjusted analysis of postoperative anastomotic leak rates comparing modified with classic 2-stage procedures.[40,3] Our pooled adjusted analysis found no difference in adjusted anastomotic leak rates (RR=0.48,95%CI(0.12,1.92),I^2=69%).(Fig.4) One study not included in quantitative analysis reported no association between staged approach and anastomotic leak rates after adjustment, though they did not report numeric results.[45] The remaining three studies reporting adjusted outcomes found that staged approach did not predict complication incidence, HLOS, or SBO.[42,6,39] One study found that 3-stage approaches were predictors of higher HC.[6]

Risk of Bias Across Studies

Due to the small sample of records in our study, we were limited to qualitative assessments of potential RoB across studies. 2 of the 8 records (25%) reported no difference in adverse outcomes between modified 2-stage and traditional RPC-IPAA.[4,40] There was also heterogenous inclusion of outcomes across all studies; whether this can be attributed to selective reporting is unclear. We performed additional sensitivity analyses to mitigate uncertainty surrounding possible bias across studies.

Sensitivity analysis

We found substantial heterogeneity for meta-analyses of anastomotic leak rates, DVT, HLOS, and reoperation rate.(Figs.2A,2H,3B,&3C)

Limiting meta-analysis of anastomotic leak rates to pediatric patients receiving modified 2-stage versus 3-stage RPC-IPAA reduced heterogeneity to I^2=0. In the same analysis, we

found that pediatric patients receiving modified 2-stage RPC-IPAA had significantly higher rates of postoperative anastomotic leak compared to 3-stage RPC-IPAA(OR=4.54,95%CI(1.13,18.3),I^2=0%).(Fig.5A) We also found that, among both pediatric and adult patients, limiting meta-analysis of anastomotic leak rate to 3-stage comparison groups reduced heterogeneity to I^2<50%, with no differences in leak rates between the two groups.(Fig.5B) Among the records using classic 2-stage RPC-IPAA as the main comparator, we found that one study reporting relatively high rates of preoperative biologic use(>20%) contributed to remaining heterogeneity.[40] After excluding this study, we found that adults undergoing modified 2-stage RPC-IPAA had lower risk of anastomotic leak compared to their classic 2-stage counterparts(OR=0.33,95%CI(0.19,0.56),I^2=1%). (Fig.5C)

Despite heterogeneity among two studies reporting DVT rates, both concluded that DVT rates were comparable between modified 2-stage and traditional RPC-IPAA.[6,3]

Heterogeneity dropped to I^2=0% for HLOS when one pediatric study reporting preoperative biologic use >40% in its cohort was removed.[43] Pooled analysis of remaining studies showed that the modified 2-stage approach was associated with shorter HLOS(MD= −1.97,95%CI(−2.93,−1.01),I^2=0%).(Fig.5D)

All studies reporting reoperation rates were focused on pediatric patients.[43,44,41] One study that compared modified 2-stage to classic 2-stage RPC-IPAA rather than 3-stage RPC-IPAA was the largest source of heterogeneity.[44] After removal, meta-analysis of the two pediatric studies comparing modified 2-stage with 3-stage RPC-IPAA still found no difference in reoperation rates.(Fig.5E)

Discussion

Summary of Evidence

Based on ten studies, reporting on 1727 patients, most complication rates were comparable between modified 2-stage and traditional approaches to RPC-IPAA among both adult and pediatric populations. However, we found a striking difference in anastomotic leak rates when stratifying our analysis by adult and pediatric populations. Among pediatric patients receiving index subtotal colectomy, we found that those who received an eventual modified 2-stage RPC-IPAA were four times more likely than their 3-stage counterparts to have a postoperative diagnosis of anastomotic leak. This suggests that the temporary diverting stoma performed in 3-stage cases may offer some measurable protection against leak among pediatric patients.

Conversely, there was no difference in leak rates between adult patients receiving modified 2-stage versus 3-stage RPC-IPAA, thus suggesting that the 3-stage approach may be overutilized among adult patients. This trend held even in meta-analysis of adjusted leak rates. Strikingly, adult patients in studies with biologic use <20% were at *lower* risk of anastomotic leak when receiving modified compared to classic 2-stage RPC-IPAA. This suggests that delaying IPAA formation itself may have more utility than temporary diversion in preventing anastomotic leak. While evidence suggests that preoperative biologic use in

itself does not confer increased postoperative complication rate, biologic use may be considered a surrogate marker for pre-operative UC severity in these cases.[46,47]

Heterogeneity in anastomotic leak meta-analysis could be attributed to biologic use; indeed, the study driving increased leak rates in meta-analysis of pediatric patients receiving modified 2-stage approaches reported biologic use >40%,[43] compared to <10% in the other two studies.[4,41] We also found this trend among comparisons of adult modified versus classic 2-stage procedures, where inclusion of one study reporting biologic use >20% appeared to make leak rates comparable between the two groups.[40] Despite this, the increased leak rate among pediatric patients compared to adult patients is unclear: this may be due to smaller sample sizes seen in pediatric studies and/or variations in how symptomatic leaks are reported among different studies.[48] It may also demonstrate a difference between how adult and pediatric patients manifest the sequelae of severe UC, keeping in mind that often times pediatric patients do have a more severe phenotype at baseline or it could reflect a difference in how surgeons perceive the fitness of a pediatric versus an adult patient to proceed with restoration of continence.[4]

While anastomotic leaks are a worrisome complication following RPC-IPAA, sepsis secondary to leak is arguably the more feared outcome. Two studies with likely sample overlap reported no differences in sepsis among adult patients receiving modified 2-stage versus traditional RPC-IPAA.[6,39]

Like anastomotic leak, analysis of HLOS was also sensitive to biologic use. This is likely because HLOS is a marker of postoperative complication profile, which may reasonably be worse among patients with high immunosuppression who may also have been exposed to a more severe disease burden.[8] We found that pediatric cohorts with <40% biologic use receiving modified 2-stage approaches had significantly lower HLOS than 3-stage cases. This is likely because relatively healthy UC patients receiving modified 2-stage RPC-IPAA require only two hospital stays instead of three needed for 3-stage procedures

We also found an increased hernia rate among modified 2-stage RPC-IPAA compared to traditional procedures. Of the two studies that reported hernia rates, one suggested that the observed hernia rate differences have been due to a small sample of modified 2-stage patients in their cohort.[6] The second study reported one ventral hernia in their modified 2-stage RPC-IPAA attributed to complications relating to the closed stoma site following end ileostomy takedown.[4] Like the first study, this study also had relatively small modified 2-stage cohorts. A possible explanation for the small samples would be if the majority of cases were open; however, while the first study did not report open versus laparoscopic cases, the second reported that 88.5% of cases were laparoscopic.[4] Thus, the small sample of modified 2-stage RPC-IPAA in the first study may be due to the relative novelty of the approach at the time of publication.[6] The small sample seen in the second study may be due in part to the relative rarity of UC in a single pediatric center, despite increasing global incidence rates.[4,2,49-52]

Notably, there were no differences in wound infection, pneumonia, and DVT rates between modified 2-stage and traditional RPC-IPAA. This likely means that patients are receiving

similar standard postoperative recovery protocols regardless of staged approach for RPC-IPAA. Although the difference was not significant, we found that rates of ileus/SBO were lower in patients who did not receive loop ileostomy (i.e. modified 2-stage RPC-IPAA. This lends some credence to reports in the literature that associate loop ileostomy with greater rates of stoma-related complications, including SBO.[53-55] Pouchitis rates were also similar between modified 2-stage and traditional RPC-IPAA, suggesting that operative techniques for building the IPAA itself(e.g. anastomotic technique) are similar despite staged approaches.

Limitations

The limitations of evidence are: estimates are based on observational studies and not randomized controlled trials, selective reporting of outcomes in individual studies, and small number of patients and events, specifically for anastomotic leak. Currently, the modified 2-stage procedure is performed at limited centers with experience, and rates of complications with modified 2-stage IPAA may be higher when used in low-volume centers. Additionally, while most studies used a combination of clinical, radiologic, and intraoperative evidence, diagnostic criteria for anastomotic leak are not uniform and likely variable across studies, likely contributing to heterogeneity in pooled analysis despite stratification. And while leaks are an important outcome to consider following colorectal surgery, the paucity of data surrounding sepsis outcomes in our analysis limits applicability to clinical practice. Reassuringly, the lack of reported sepsis may represent the relative safety of RPC-IPAA regardless of staged approach. Although all included records focused on UC as a main indicator for RPC-IPAA, we also found heterogeneity in reporting for specific indications, such as toxic megacolon or dysplasia. Reporting on urgent versus elective operations was also variable. Additionally, not all studies stratified their cohorts by minimally invasive versus open approaches. All these factors may impact postoperative outcomes; due to the inherent reporting differences among the current literature, controlling for these factors proved difficult and limits our conclusions.

We relied on retrospective comparative cohort studies. Again, this is due to the relative lack of prospective evidence in the current literature; at the time of writing, no prospective studies comparing staged approaches to RPC-IPAA exist. Additionally, the relatively small samples available in single centers limit the power available to detect clinically relevant differences in outcomes. Alternatively, multicenter collaborations offer statistical power and more standardized extensive collection of IBD-specific preoperative data and outcomes than what is currently available. One such collaboration has already begun building an IBD-specific surgical database with promising initial results.[56, 57]

Conclusions

Despite these limitations, our study represents the most current review of available literature comparing RPC-IPAA staged approaches. We show that 3-staged approaches may be overutilized among healthier adult UC patients, leading to unnecessary costs, longer stays, and unjustified exposure to the risks surrounding diverting ileostomy formation. The modified 2-stage approach may be safer for these adult patients who would otherwise receive a 3-stage approach while reducing costs and HLOS. However, the 3-stage approach

appears safer than the modified 2-stage approach for pediatric patients, especially those on biologics. The modified 2-stage approach appears safer than the classic 2-staged approach for adult patients with less biologic exposure and better controlled disease. More importantly, we highlight the continued need for studies examining these complex procedures to provide the best evidence-based care for UC patients reliant on curative surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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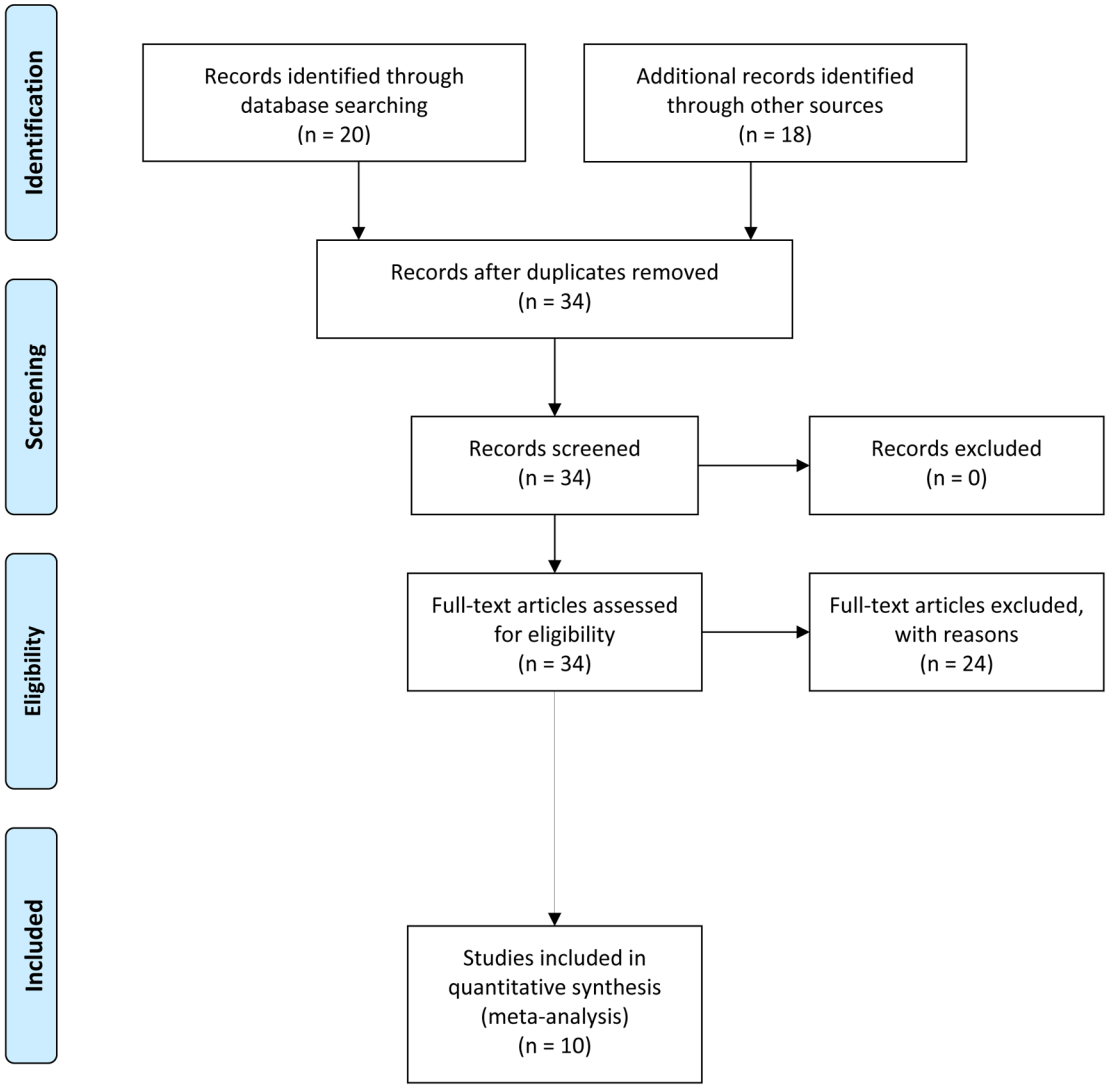
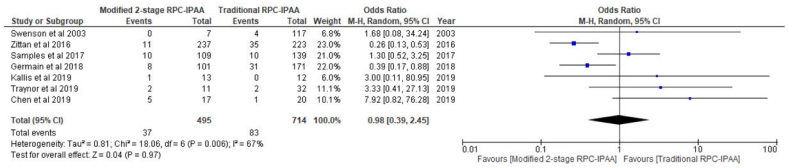
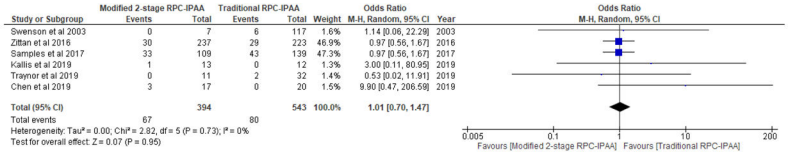


Figure 1:
PRISMA flow diagram summarizing record selection process.

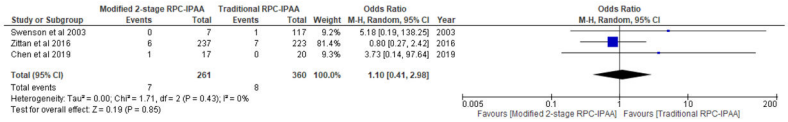
A) Anastomotic leak



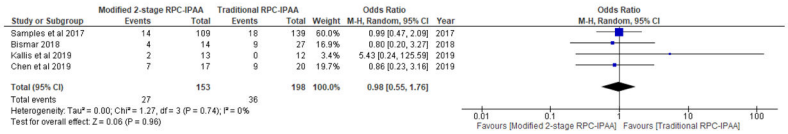
B) Wound infections



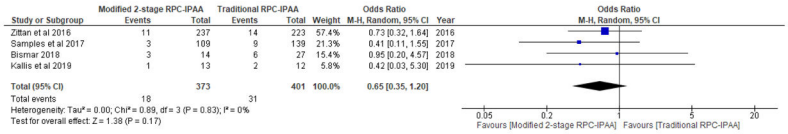
C) Pneumonia



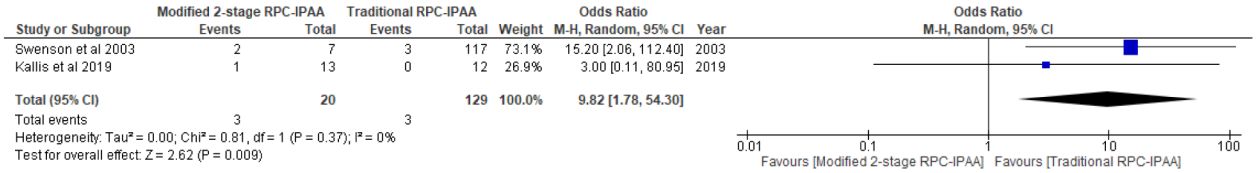
D) Pouchitis



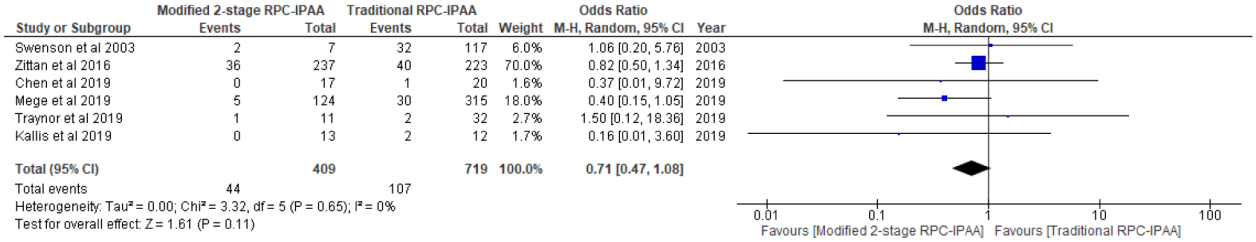
E) Stricture formation



F) Hernia formation



G) Ileus/SBO



H) DVT

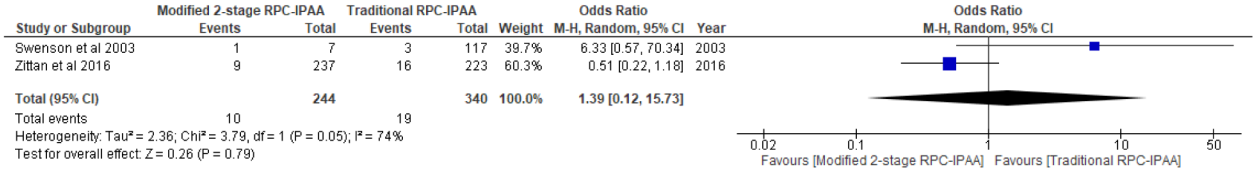
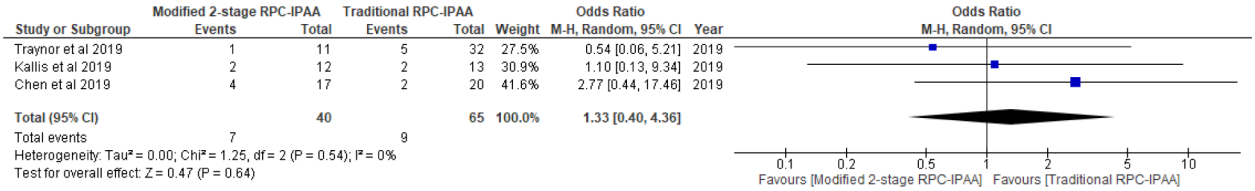


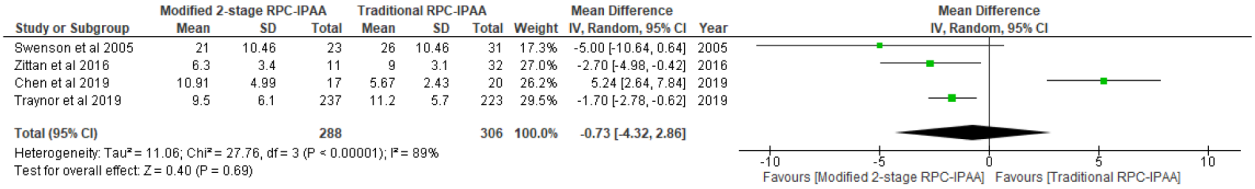
Figure 2:

Results of meta-analysis of primary outcome comparing modified 2 stage with traditional RPC-IPAA, i.e. rates of A) anastomotic leak, B) wound infections, C) pneumonia, D) pouchitis, E) stricture formation, F) hernia formation, G) ileus/SBO, and H) DVTs post-IPAA formation.

A) Postoperative hospital readmission



B) Cumulative HLOS related to IPAA (days)



C) Reoperations

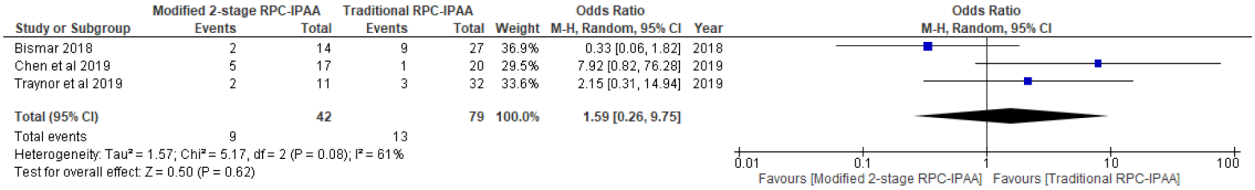


Figure 3:

Meta-analysis of secondary outcomes comparing modified 2-stage with traditional RPC-IPAA, i.e. A) postoperative hospital readmission rates and B) cumulative HLOS related to IPAA.

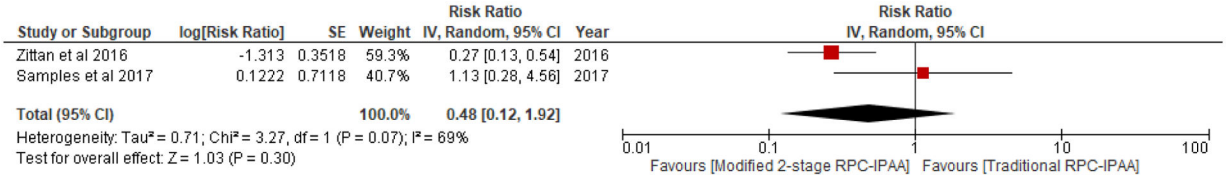
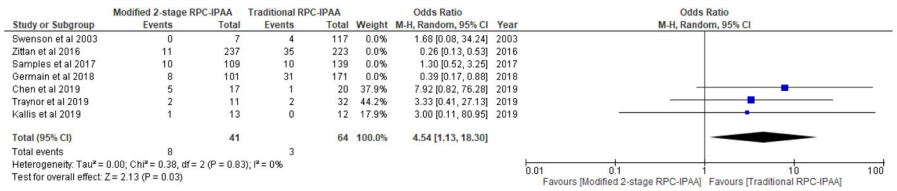


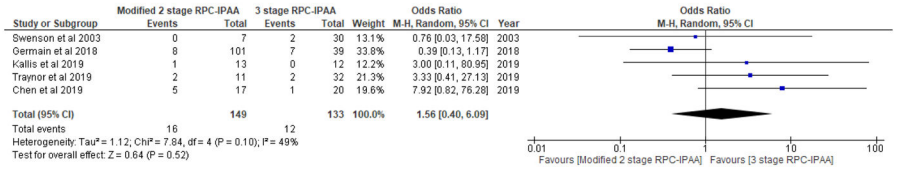
Figure 4:

Pooled comparisons of adjusted postoperative anastomotic leak rates in modified 2 stage vs. classic 2-stage RPC-IPAA

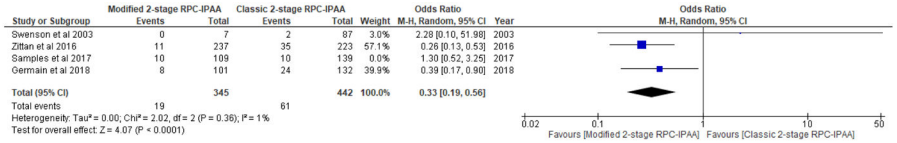
A) Anastomotic leak rates among pediatric patients receiving modified 2-stage vs 3-stage RPC-IPAA



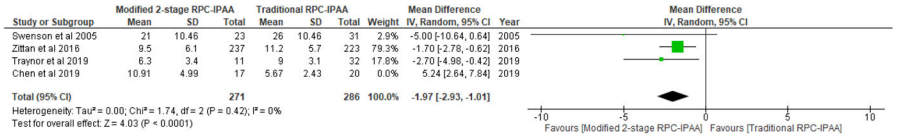
B) Anastomotic leak rates among all patients receiving modified 2-stage vs 3-stage RPC-IPAA



C) Anastomotic leak rates among adult patients receiving modified vs classic 2-stage RPC-IPAA reporting <20% biologic use



D) HLOS among modified 2-stage vs traditional RPC-IPAA reporting biologic burden <10%



E) Reoperation rate among pediatric patients receiving modified 2-stage vs 3-stage RPC-IPAA

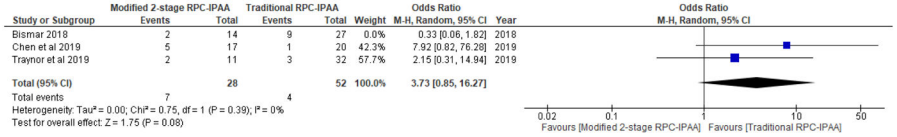


Figure 5:

Sensitivity and subgroup analysis encompassing meta-analysis of: anastomotic leak rates among A) pediatric patients receiving modified 2-stage vs. 3-stage RPC-IPAA, B) all patients who received modified 2-stage vs. 3-stage RPC-IPAA, and C) adult patients who received modified vs. classic 2-stage RPC-IPAA, D) HLOS among studies reporting <10% preoperative biologic use, and E) reoperation rates among pediatric patient receiving modified 2-stage vs 3-stage RPC-IPAA.

Table 1:

Summary of study characteristics of records included in meta-analysis.

Study	Study Design	Center(s)	Years studied	Population	Intervention/ Comparison Group(s) (n)	Age, years (mean/ median)	% Female	Outcome Measure(s)	Procedure before/after which baselines/ outcomes were collected	Covariate(s) and factor(s) used in adjusted analysis	Prin concl
Swenson et al, 2003	Retrospective cohort	1	1991-2001	All UC patients who underwent RPC-IPAA.	Classic 2-stage RPC-IPAA (87)	37.7	36.7	Pouchitis, pelvic/ abdominal sepsis, wound infection, PNA, anastomotic leak, intestinal obstruction, hernia, prolonged ileus, stoma complications, DVT, HLOS, HC, readmissions, overall complication rate	Index stage/ IPAA stage for complications, all stages for HLOS and cost	Age, steroid use, low HCT, weight loss prior to surgery, low serum albumin, high serum bilirubin, gender	For pa with s diseas two-s mod path appea have compli lower and a s length than tradit three path
					3-stage RPC-IPAA (30)	32.8	46.7				
					Modified 2-stage RPC-IPAA (7)	34.2	28.6				
Swenson et al, 2005	Retrospective cohort	1	1995-2003	All UC patients who underwent RPC-IPAA.	3-stage RPC-IPAA (31)	35.8	32.3	Pelvic sepsis, HLOS, HC, overall complication rate	Index stage/ IPAA stage	Low HCT, steroid use, age, ASA derivative use, duration of illness prior to surgery, 6-MP/AZA use before colectomy	Modi stage IPAA compa compl rates lower h co compar stage IPA
					Modified 2-stage RPC-IPAA (23)	33.9	39.1				
Zittan et al, 2016	Retrospective cohort	1	2002-2013	All UC patients who underwent RPC-IPAA	Classic 2-stage RPC-IPAA (223)	40	58.7	DVT, ileus/ SBO, wound infection, PNA, UTI, stricture, pouch fistula, pouch failure, intra-abdominal abscess, anastomotic leak, HLOS	Index stage/ IPAA stage	BMI, Gender, disease duration, steroid use, albumin, anti-TNF therapy, PSC	Signifi lower anasto leak a patien under modi stage IPA compa classic RPC-
					Modified 2-stage RCP-IPAA (237)	35.6	52.3				
Samples et al, 2017	Retrospective cohort	1	2003-2010	All UC patients who underwent RPC-IPAA	Classic 2-stage RPC-IPAA (139)	38	48.2	Anastomotic leak, stricture formation, pouchitis, wound infection	Index stage/ IPAA stage	Admission year, patient age, sex, race, smoking status, diabetes, dysplasia or cancer diagnosis, BMI,6-MP/ AZA, ASA derivative use, anti-TNF use, and steroid drug use	Modi stage IPAA i and ef approa compa outcom more U popul base BMI, s use, urgen opera
					Modified 2-stage RCP-IPAA (109)	38	45.9				

Study	Study Design	Center(s)	Years studied	Population	Intervention/ Comparison Group(s) (n)	Age, years (mean/ median)	% Female	Outcome Measure(s)	Procedure before/after which baselines/ outcomes were collected	Covariate(s) and factor(s) used in adjusted analysis	Prin conclu
Traynor et al, 2019	Retrospective cohort	1	2007-2017	Pediatric (<18 y.o.) UC patients undergoing RPC-IPAA	3-stage RPC-IPAA (32)	16	50	Anastomotic leak, time spent diverted, HLOS, readmission rates, 30-day max Clavien-Dindo complication score	IPAA stage/ IPAA stage + ileostomy reversal if applicable	Not performed	The m 2 stage IPAA r in fe hospita compa the 3- appro cohort sim base presen
					Modified 2-stage RCP-IPAA (11)	15	55				
Kallis et al, 2019	Retrospective cohort	1	2010-2018	Pediatric(5-21 y.o.) UC patients undergoing RPC-IPAA	3-stage RPC-IPAA (12)	14.2	42	Anastomotic leak, wound infection, bloody ostomy output, dehydration, pouchitis, anastomotic stricture, ventral hernia, SBO, pouch volvulus, postoperative diagnosis of Crohn's disease	Not specified/ index stage + IPAA stage	Not performed	Compl rates compa betw modi stage stage IPA cohort sim base presen
					Modified 2-stage RPC-IPAA (13)	12.5	34				
Mege et al, 2019	Retrospective Case-control	4	2005-2015	All consecutive patients undergoing laparoscopic IPAA for IBD	SBO during follow up (41)	43	42	SBO (case control study)	Index stage/ Index stage + IPAA stage	Surgical procedure (RPC vs STC), ileus, stoma complications, Dindo complication classification, incisional hernia	Modi stage I poten safer proce wi temp ileos with r to S incid
					No SBO (480)	42	54				
Germain et al, 2018	Retrospective comparison of non-contemporary cohorts	1	1995-2015	All UC patients who underwent RPC-IPAA (335)		30	41.2	Anastomotic leak, pelvic abscess, anastomotic stricture, pouchitis, SBO, pouch failure	Not specified/ IPAA stage or diverting ileostomy closure	Male gender, age, disease duration, smoking status, pouch creation at first surgery, laparoscopic approach, time period in which surgery occurred	Adopt modif stage IPA assoc wi decre anasto leakag
Bismar et al, 2018	Retrospective cohort	1	2004-2017	Pediatric (5-18 y.o.) UC patients undergoing RPC-IPAA	Classic 2-stage RPC-IPAA (27)	14	55.6	Appetite recovery, stool continence, need to antidiarrheal medication, anastomotic stricture requiring dilatation, pouchitis, reoperation	Index stage/all stages	Not performed	Outcor similar grou how modi stage IPAA red relian antidia
					Modified 2-stage RPC-IPAA (14)	14	35.7				

Study	Study Design	Center(s)	Years studied	Population	Intervention/ Comparison Group(s) (n)	Age, years (mean/ median)	% Female	Outcome Measure(s)	Procedure before/after which baselines/ outcomes were collected	Covariate(s) and factor(s) used in adjusted analysis	Prin conclu
					3-stage RPC-IPAA (20)	16	52.9	Length of stay, 30-day complication after IPAA, anastomotic leak, PNA, wound infection, UTI, portal vein thrombosis, SBO, bleeding requiring transfusion, 30-day postoperative CT scan, unplanned readmission, unplanned reoperation, duration of ileostomy, 30-day complication after ileostomy reversal, length of follow up			
Chen et al, 2019	Retrospective cohort	1	2008-2016	Pediatric (≤18 y.o.) UC patients undergoing RPC-IPAA	Modified 2-stage RCP-IPAA (17)	16	30		Index stage/ IPAA formation	Not performed	Patien dive ileos we signifi less lil ha imme postop compli compa undiv pati