

# Stapled Anastomosis Versus Hand-Sewn Anastomosis With Mucosectomy for Ileal Pouch-Anal Anastomosis: A Systematic Review and Meta-analysis of Postoperative Outcomes, Functional Outcomes, and Oncological Safety

Cancer Control  
Volume 31: 1–14  
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DOI: 10.1177/10732748241236338  
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## Abstract

**Purpose:** This systematic review and meta-analysis aimed to compare outcomes between stapled ileal pouch-anal anastomosis (IPAA) and hand-sewn IPAA with mucosectomy in cases of ulcerative colitis and familial adenomatous polyposis.

**Methods:** This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines 2020 and AMSTAR 2 (Assessing the methodological quality of systematic reviews) guidelines. We included randomized clinical trials (RCTs) and controlled clinical trials (CCTs). Subgroup analysis was performed according to the indication for surgery.

**Results:** The bibliographic research yielded 31 trials: 3 RCTs, 5 prospective clinical trials, and 24 CCTs including 8872 patients: 4871 patients in the stapled group and 4038 in the hand-sewn group. Regarding postoperative outcomes, the stapled group had a lower rate of anastomotic stricture, small bowel obstruction, and ileal pouch failure. There were no differences between the 2 groups in terms of operative time, anastomotic leak, pelvic sepsis, pouchitis, or hospital stay. For functional outcomes, the stapled group was associated with greater outcomes in terms of seepage per day and by night, pad use, night incontinence, resting pressure, and squeeze pressure. There were no differences in stool Frequency per 24h, stool frequency at night, anti-diarrheal medication, sexual impotence, or length of the high-pressure zone. There was no difference between the 2 groups in terms of dysplasia and neoplasia.

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Data Availability Statement included at the end of the article

**Conclusions:** Compared to hand-sewn anastomosis, stapled ileoanal anastomosis leads to a large reduction in anastomotic stricture, small bowel obstruction, ileal pouch failure, seepage by day and night, pad use, and night incontinence. This may ensure a higher resting pressure and squeeze pressure in manometry evaluation.

**Protocol Registration:** The protocol was registered at PROSPERO under CRD 42022379880.

### Keywords

stapled anastomosis, hand-sewn anastomosis, ileal pouch-anal anastomosis, postoperative outcomes, functional results, oncological outcomes

Received November 26, 2023. Received revised January 30, 2024. Accepted for publication February 6, 2024.

## Introduction

Ileal-pouch anal anastomosis (IPAA) is primarily employed in the treatment of ulcerative colitis (UC) and familial adenomatous polyposis (FAP).<sup>1</sup> Since its initial description by Parks et al in 1978,<sup>2</sup> the procedure has undergone several technical modifications. Restorative proctocolectomy is also referred to as IPAA or pelvic pouch. This procedure can be performed in 1, 2, or 3 stages.<sup>3</sup> The rectal stump can be replaced with a “J,” “W,” or “S” or S pouch. The most recent modification involves preserving the anal transitional zone and using a stapled device for IPAA. Subsequently, 2 types of IPAA have been suggested: 1 involving mucosectomy of the rectal stump followed by a hand-sewn IPAA, and the other utilizing a stapled IPAA without mucosectomy. Since both UC and FAP are mucosal diseases, mucosectomy allows for removal of the diseased colon and rectal mucosa.<sup>4</sup> In the case of stapled anastomosis, it is essential to preserve the anal transitional zone, in contrast to traditional hand-sewn anastomosis.<sup>5</sup> This approach offers the advantage of being quicker with less manipulation of the anal canal.<sup>6</sup> The choice between these 2 techniques remains controversial. In the case of hand-sewn anastomosis, mucosectomy necessitates manipulation of the anal canal, increasing the risk of sphincter damage and alterations in anal sphincter pressure.<sup>6</sup> In the case of stapled anastomosis, mucosectomy is not performed, as it is based on the rationale that the mucosa of the anal transitional zone has rich sensory innervation, which plays a role in anal sphincter function, distinguishing between flatus and stool and contributing to the maintenance of the anorectal inhibitory reflex. However, proponents of hand-sewn anastomosis with mucosectomy emphasize the risk of residual inflamed mucosa affecting short-term outcomes and the risk of dysplasia and cancer affecting long-term outcomes and oncological safety. Many studies have compared these data,<sup>7,8</sup> but their results have been controversial, underscoring the importance of this systematic review and meta-analysis.

The purpose of this systematic review and meta-analysis is to compare the outcomes of stapled IPAA vs hand-sewn IPAA in patients undergoing restorative proctocolectomy for UC

and FAP in terms of postoperative outcomes, functional outcomes, and oncological safety.

## Methods

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines 2020<sup>1</sup> and AMSTAR 2 (Assessing the methodological quality of systematic reviews) guidelines.<sup>2</sup> The protocol was registered at PROSPERO under CRD 42022379880.

### Electronics Searches

We conducted bibliographic research on January 30, 2023, using the following sources: The National Library of Medicine through PubMed, Cochrane database, and Google Scholar. The Keywords used were “proctocolectomy,” “ileal pouch-anal anastomosis,” “ulcerative colitis,” “restorative proctocolectomy,” “pelvic pouch,” “functional outcomes,” “stool frequency,” “seepage,” “pad usage,” “incontinence,” “quality of life,” “dysplasia,” “inflammation,” “dysplasia,” “anastomosis,” “complications,” “morbidity,” “mortality,” “anastomotic leak,” “pelvic sepsis,” “anastomotic stricture,” “pouch related stricture,” “small bowel obstruction,” “pouchitis,” “anorectal physiology,” “impotence,” “meta-analysis,” “review,” “controlled clinical trial” and “randomized clinical trial.” We manually checked the reference lists of the relevant reviews for additional citations.

### Inclusion and Exclusion Criteria

We retained randomized and controlled clinical trials, irrespective of their publication status or language, including adult patients who underwent IPAA using a stapled anastomosis or handsewn anastomosis with mucosectomy. Only articles published in peer-reviewed journals were included in this study.

## Outcomes Measures

The primary outcome was postoperative findings. We assessed the postoperative complications during the follow-up period. The secondary outcomes were the functional and oncological outcomes.

## Data Extraction

Two authors extracted the data independently, and senior authors settled the disparities after discussion.

## Assessment of Studies Quality and Risk of Bias Assessment

Two authors independently appraised all the studies that met the selection criteria. Concerning quality assessment, CCTs and RCTs were assessed according to the methodological index of non-randomized studies (MINORS)<sup>3</sup> and Consolidated Standards of Reporting Trials (CONSORT) statement,<sup>4</sup> respectively. We excluded all studies with a MINORS or CONSORT statement inferior to 13. For the risk of bias in the RCTs, we used the Cochrane tool for bias assessment to assess the risk of bias in randomized trials (ROB2).<sup>5</sup> We evaluated bias in 5 distinct domains (randomization process, deviations from intended interventions, bias in the measurement of outcome, bias to missing outcome data, bias in selecting the reported results, and overall bias). Within each domain, 1 or more signaling questions led to judgments of “low risk of bias,” “some concerns,” or “high risk of bias” high risk of bias. The Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias in CCTs.<sup>6</sup>

## Data analysis

The analysis of continuous data was performed using the statistical software Review Manager 5.3.5, developed by the Cochrane Collaboration, specifically for conducting meta-analyses.<sup>7</sup> If the mean and standard deviation (SD) values were not directly available, they were inferred from the median and interquartile range (IR) using the estimation method proposed by Hozo et al.<sup>8</sup> For instances in which the sample size exceeded 25, it was assumed that the median and mean values were equivalent. Furthermore, for sample sizes below 70, the SD was approximated by dividing the IR by 4, and for those above 70, by dividing the IR by 7.

## Evaluating Study Heterogeneity

The examination of heterogeneity in the studies involved a three-pronged approach: Application of the Cochrane Q-test (Chi<sup>2</sup> test), analysis of Tau<sup>2</sup> (true effect variance), and calculation of a 95% predictive interval to gauge the extent of heterogeneity,<sup>9</sup> utilizing the Comprehensive Meta-analysis software for predictive interval determination. Employing

funnel plots for visual heterogeneity analysis.<sup>10</sup> Sensitivity checks were conducted through subgroup analyses, where relevant.<sup>11</sup> In scenarios where significant heterogeneity was detected, particularly in studies grouped under Ulcerative Colitis (UC) and Familial Adenomatous Polyposis (FAP), a detailed subgroup analysis was undertaken, segregating studies focused solely on UC or FAP from those encompassing both conditions.

## Synthesizing study findings

Two researchers independently evaluated the evidence related to primary outcomes using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology.<sup>12</sup> This included the consideration of study limitations, consistency of effect, accuracy, relevance, and potential publication bias. The certainty of the evidence was categorized as high, moderate, low, or very low. Enhancements to evidence strength were considered under circumstances of significant effect, dose-response correlation, or plausible confounding. The assessment followed the procedures outlined in sections 8.5 and 8.7 and chapters 11 and 12 of the Cochrane Handbook for Systematic Reviews of Interventions. The GRADEpro GDT software facilitated the preparation of the Summary of Findings tables, with detailed rationales for any downgrading or upgrading decisions provided in the footnotes.

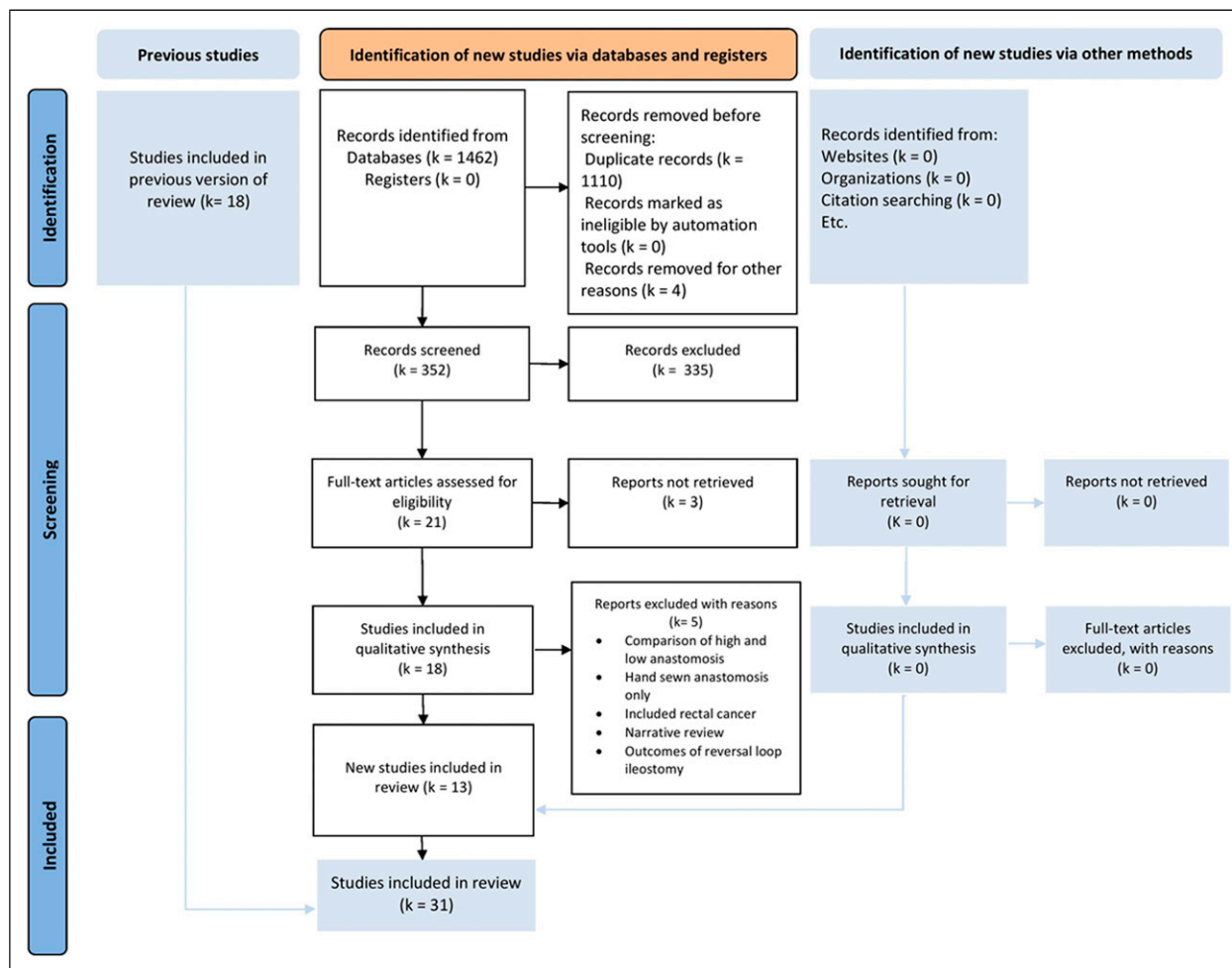
## Determining the Magnitude of Effects for Meta-Analysis

The RevMan 5.4 software, provided by the Cochrane Collaboration, was utilized.<sup>7</sup> The mean difference (MD) was chosen as a measure of continuous data. In the case of binary outcomes, odds ratios (OR) and 95% confidence intervals (95% CI) were calculated. A random-effects model was used for these calculations, with a significance threshold of .05.

## Results

### Bibliographic Research

The bibliographic research yielded 36 trials (Figure 1). Five studies were excluded for the following reasons<sup>13-16</sup>: 1 study included patients undergoing stapled anastomosis and compared high with low anastomosis,<sup>13</sup> 1 study included only patients undergoing a hand-sewn anastomosis,<sup>14</sup> 1 study included patients with rectal cancer,<sup>15</sup> 1 study compared the outcomes of the reversal loop ileostomy,<sup>16</sup> and 1 study was a narrative review.<sup>17</sup> We then retained 31 trials<sup>18-48</sup>: 3 RCTs,<sup>39,40,44</sup> 5 prospective clinical trials,<sup>19-23</sup> and 24 CCTs.<sup>18,24-38,41-43,45-48</sup> The demographic data of the studies are summarized in Table 1. These studies included 8872 patients, 4871 patients in the stapled group, and



**Figure 1.** PRISMA flow-diagram of the bibliographic research.

4038 hand-sewn group, and were published between 1991 and 2022.

**Operative Time.** Operative time was reported in 6 studies. It was estimated in 472 patients (178 in the stapled group and 293 in the hand-sewn group). There was no significant difference between the 2 groups (MD = -12.59; IC95% [-49.24, 24.07];  $P = .5$ ). There was a high heterogeneity among the studies.

**Anastomosis Leak.** Anastomotic leaks were reported in 14 studies. It was reported in 62 of 1372 patients in the stapled group and 123 of 1522 patients in the handsewn group. There was no significant difference between the 2 groups (OR = .84; IC95% [.58, 1.21];  $P = .34$ ).

**Pelvic Sepsis.** Pelvic sepsis was reported in 17 studies. It was estimated in 7526 patients, occurring in 560 of 4047 patients in the stapled group and 293 of 3479 patients in the hand-sewn group. There was no significant difference between the 2 groups (OR = .85; IC95% [.60, 1.19];  $P = .34$ ). There was little heterogeneity among these studies.

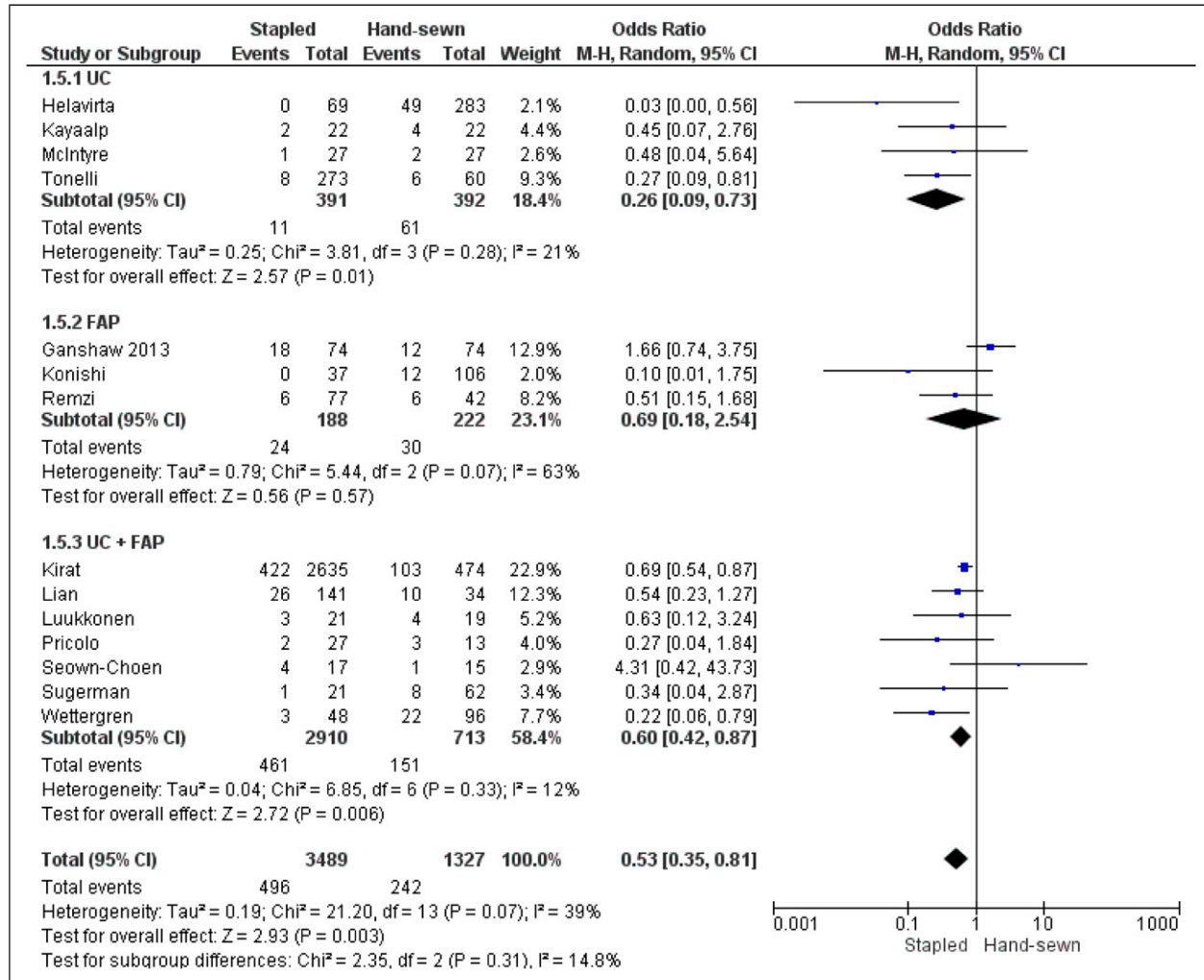
**Pouchitis.** Pouchitis was reported in 11 studies. It was estimated in 4108 patients, occurring in 1133 of 3087 patients in the stapled group and 384 of 1021 patients in the hand-sewn group. There was no significant difference between the 2 groups (OR = .59; IC95% [.35, 1.01];  $P = .05$ ). There was little heterogeneity among these studies.

**Anastomotic Stricture.** The Anastomotic structure was reported in 15 studies (Figure 2). It was estimated in 4816 patients, occurring in 496 of 3489 patients in the stapled group and 242 of 1327 patients in the hand-sewn group. There was a lower rate of anastomotic strictures in the stapled group (OR = .53; IC95% [.35, .81];  $P = .003$ ). There was little heterogeneity among the studies (Tau<sup>2</sup> = .19 (I<sup>2</sup> = 39%).). In the UC and UC + FAP subgroup analyses, we found a significantly lower rate of anastomotic stricture in the stapled group than in the hand-sewn group (OR = .26; IC95% [.09, .73];  $P = .01$ ) and (OR = .60; IC95% [.42, .87];  $P = .006$ ), respectively. For the FAP subgroup, there was no difference between the 2 groups (OR, .69; IC95% [.18, 2.54];  $P = .57$ ).

**Table 1.** List of the Retained Studies.

Nbre of Study	Author	Journal	Type of Study	Year of Publication	Study Period	N	Indications				Sex (M/F)		Age			BMI (Kg/m <sup>2</sup> )	Pouch (l/s)	Laparoscopic Approach	Protective Loop	Follow-Up (years)				
							SA	HA	FAP	UC	IC/CD	SA	HA	SA	HA						SA	HA		
1	Alsukhni	Colon rect dis	Retro comp	2010	1981-2009	81	59	22	22	81	41/18	14/8	44	43.5	-	-	-	-	5	9.5				
2	Araki	Kurume med	Retro/pros	1998	1990-1997	37	29	8	21	16	3/5	17/12	29.3	28.9	-	-	-	-	-	-				
3	Bednarz (NF)	HGE	Retro comp	2005	1994-2003	71	56	15	9	62	-	-	-	-	-	-	-	-	-	-				
4	Cohen	An. Of surg	Retro comp	1992	1982-1992	483	158	325	24	437	90/68	170/147	32.5	31.9	-	102/223	155/3	87	325	2	4.9			
5	Fukui (mano)	Colorectal dis	Retro comp	2022	2016-2020	32	14	18	3	29	12/2	12/6	51	49	-	-	-	-	-	-	-			
6	Fukushima	Surgery today	Retro comp	2000	1986-1998	210	146	64	197	13	102/108	40/34	35	31.5	-	100/0	110/0	66	22	-	-			
7	Ganeshaw 2013	Colorectal dis	Pros comp	2013	1984-2006	148	74	74	148	-	40/34	40/34	28	28.5	22.8	23.1	74/0	42	2	71	74	2.4	11.4	
8	Ganeshaw 2015 (RRM)	Arch of surg	Retro comp	2015	2005-2009	100	50	50	100	-	26/24	25/25	28.5	29.3	-	50/0	50/0	32	10	-	3.7	12.1		
9	Gecim	Col rect dis	Retro comp	1999	1981-1997	1457	99	1358	153	1304	762/695	-	-	-	-	99/0	1358/0	-	99	1358	-	-		
10	Gemlo (pouch)	Am. J. of surgery	Retro comp	1995	1980-1992	297	80	157	15	282	139/158	-	-	-	-	68/229	-	-	-	-	5.8	-		
11	Gozzetti	Am. J. of surg	Retro comp	1994	1985-1992	88	48	40	0	88	-	-	33.6	28.5	-	-	-	48	40	-	-	-	-	
12	Helavirta	Sc. J. of surg	Retro comp	2016	1985-2009	352	69	283	-	352	-	25/23	-	-	69/0	283/0	-	-	-	-	-	-	-	
13	Harnoy	J. Of surg res	Retro comp	2015	1996-2011	88	40	48	-	88	18/22	-	-	-	-	-	-	-	-	-	-	-	-	
14	Ishii	Int. Surj	Retro comp	2015	1988-2010	91	59	32	-	91	37/22	14/18	32.2	45.7	-	-	-	-	-	-	-	7.7	7.6	
15	Kayaalp	Am. J. of surgery	Retro comp	2003	1992-2000	44	22	22	-	44	14/8	13/9	32	32	26	25	22/0	-	-	18	20	-	-	
16	Kirat	Surgery	Retro comp	2009	1983-2007	3019	2635	474	191	2222	606	1476/1159	339/267	38.1	37.1	25.6	24.4	242/1212	310/162	-	2270	468	6.4	10.3
17	Konishi	Ann GE surg	Retro comp	2017	2000-2012	143	37	106	143	-	19/18	53/63	31	30	-	-	22	48	22	69	3.4	4.33		
18	Lian	Col rect dis	Retro comp	2009	-	175	141	34	9	107	59	99/42	22/12	41.4	35.7	27.3	25.2	131/110	25/9	-	121	34	6	7.7
19	Luukkonen	Arch of surg	Pros radom	1993	1990-1991	40	21	19	1	39	10/11	10/9	38.8	36	-	-	-	-	2	1	-	-	-	-
20	McIntyre	Col rect dis	Pros comp	1994	1990-1991	54	27	27	-	54	14/13	14/13	37	37	-	27/0	27/0	-	-	-	-	-	-	-
21	Pricolo	Col rect dis	Pros comp	1996	1993-1995	40	27	13	9	31	11/16	9/4	36	40	-	27/0	13/0	-	-	-	-	-	-	-
22	Reilly	An. Of surg	Pros radom	1997	1992-1994	32	17	15	-	32	9/8	9/6	-	-	-	-	-	-	17	15	-	-	-	-
23	Remzi	Col rect dis	Retro comp	2001	1983-1999	119	77	42	119	-	43/34	23/19	-	-	-	-	-	-	37	42	4.4	8.3	-	-
24	Saigusa	Surgery today	Retro comp	2000	1996-1996	32	20	12	18	14	14/6	8/4	33.9	32.7	-	-	-	-	-	-	-	-	-	-
25	Scotte (NF)	HGE	Retro comp	1998	1984-1996	68	33	35	-	68	37/33	-	-	-	-	33/0	35/0	-	23	35	-	-	-	-
26	Seow-choen	Br.J.Surg	Pros radom	1991	1988-1989	32	17	15	5	27	8/9	10/5	-	-	-	-	-	-	17	15	-	-	-	-
27	Silvestri	Surgery	Retro comp	2008	1987-2007	294	66	228	-	294	-	-	-	24.1	25.8	-	-	-	34	77	4.4	4.3	-	-
28	Sugerman	An. Of surg	Retro comp	1991	1982-1990	83	21	62	2	81	-	-	-	-	-	21/0	44/18	-	21	62	-	-	-	-
29	Tonelli	ANZ surg	Pros comp	2016	1984-2011	333	273	60	-	333	157/116	35/25	39.6	36.5	-	262/11	21/39	-	164	57	9.5	15.2	-	-
30	Wettergren	Eu j of surg	Retro comp	1993	1983-1991	144	48	96	144	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
31	Ziv	Am. J. of surg	Retro comp	1996	1983-1992	692	454	238	-	692	213/241	109/129	35	34	-	279/175	148/90	-	407	236	1.7	3.9	-	-

Nbre: number; retro: retrospective; comp: comparative; pros: prospective; Random: randomized; Ni: total number of patients; SA: stapled anastomosis; HA: hand-sewn anastomosis; Mi: male; F: female; FAP: familial adenomatous polyposis, UC: ulcerative colitis; IC: indeterminate colitis; CD: crohn disease.



**Figure 2.** Forest plot of anastomotic stricture.

**Small Bowel Obstruction.** Small-bowel obstruction was reported in 12 studies. It was estimated in 4524 patients, occurring in 572 of 3367 patients in the stapled group and 203 of 1157 patients in the hand-sewn group. The stapled group had a lower rate of small bowel obstruction (OR = .79; IC95% [.65, .97];  $P = .02$ ).

**Ileal Pouch Failure.** Ileal pouch failure was reported in ten studies. It was estimated in 5110 patients, occurring in 135 of 3825 patients in the stapled group and 99 of 1285 patients in the hand-sewn group. A lower rate of ileal pouch failure was observed in the stapled group (OR = .32; IC95% [.23, .43];  $P < .00001$ ).

**Hospital Stay.** Hospital stay was reported in 4 studies. It was estimated in 3447 patients: 2875 in the stapled group and 572 in the hand-sewn group. There was no significant difference between the 2 groups (MD = .51; IC95% [-1.94, 2.97];  $P = .59$ ). There was a low heterogeneity among the studies.

**Stool Frequency Per 24h.** The stool frequency per 24h was reported in 14 studies. It was estimated that there were 4445 patients: 3347 in the stapled group and 1098 in the hand-sewn group. There was no significant difference between the 2 groups (MD = .14; IC95% [-.29, .56];  $P = .53$ ). There was little heterogeneity among these studies.

**Stool Frequency at Night.** Stool frequency at night was reported in 7 studies. It was estimated in 3808 patients: 3093 in the stapled group and 715 in the hand-sewn group. There was no significant difference between the 2 groups (OR = .05; IC95% [-.41, .50];  $P = .84$ ). There was little heterogeneity among these studies. In the UC + FAP subgroup analysis, we found a significantly lower rate of stool frequency in the handsewn group than in the stapled group (OR = .3; IC95% [.15, .45];  $P < .0001$ ). For the UC and FAP subgroups, there were no differences between the 2 groups (OR = .01; IC95% [-.88, .89];  $P = .99$ ) and (OR = -.10; IC95% [-.71, .51];  $P = .75$ ), respectively.

**Seepage by Day.** Seepage by Day was reported in 4 studies. It was estimated in 3356 patients: occurring in 441 of 2787 patients in the stapled group and 173 of 569 patients in the hand-sewn group. There was a lower rate of seepage per day in the stapled group (OR = .41; IC95% [.25, .66];  $P = .0003$ ). There was little heterogeneity among these studies.

**Seepage by night.** Seepage by night was reported in 5 studies. It was estimated in 3345 patients: occurring in 765 of 2789 patients in the stapled group and 270 of 556 patients in the hand-sewn group. There was a lower rate of seepage at night in the stapled group (OR, .38; IC95% [.20, .72];  $P = .003$ ). There was little heterogeneity among these studies.

**Pad Use.** The Use of a pad was reported in 8 studies. It was estimated in 3504 patients, occurring in 429 of 2864 patients in the stapled group and 196 of 640 patients in the hand-sewn group. There was a lower pad use rate in the stapled group (OR = .42; IC95% [.30, .60];  $P < .00001$ ).

**Pad Use Per day.** The use of pads per day was reported in 4 studies. It was estimated in 3559 patients: occurring in 399 of 2807 patients in the stapled group and 204 of 752 patients in the hand-sewn group. There was a lower rate of daily pad use in the stapled group (OR = .36; IC95% [.27, .49];  $P < .00001$ ).

**Pad Use Per Night.** The use of pads per night was reported in 3 studies. It was estimated in 3522 patients, occurring in 486 of 2778 patients in the stapled group and 290 of 744 patients in the hand-sewn group. There was a lower rate of overnight pad use in the stapled group (OR = .29; IC95% [.24, .35];  $P < .00001$ ).

**Night Incontinence.** Night incontinence was reported in 12 of the studies. It was estimated in 4217 patients, occurring in 130 of 3250 patients in the stapled group and 196 of 967 patients in the hand-sewn group. There was a lower rate of night incontinence in the stapled group (OR, .37; IC95% [.27, .51];  $P < .00001$ ).

**Antidiarrheal Medication.** Antidiarrheal medication was reported in 6 studies. It was estimated in 581 patients, occurring in 43 patients out of 201 in the stapled group and 131 380 patients in the hand-sewn group. There was no significant difference between the 2 groups (OR = .62; IC95% [.32, 1.21];  $P = .16$ ). There was little heterogeneity among these studies.

**Sexual Impotence.** Sexual impotence was reported in 6 studies. It was estimated in 3432 patients, occurring in 346 of 2818 patients in the stapled group and 97 of 614 patients in the hand-sewn group. There was no significant difference between the 2 groups (OR = .70; IC95% [.30, 1.65];  $P = .41$ ). There was little heterogeneity among these studies.

**Resting Pressure.** Resting pressure was reported in 7 studies. It was estimated that there were 293 patients: 166 in the stapled group and 127 in the hand-sewn group. There was a greater value of resting pressure associated with the stapled group (MD = 14.74; IC95% [9.58, 19.9];  $P < .00001$ ). Moderate heterogeneity was observed among the studies.

**Squeeze Pressure.** The squeeze pressure was reported in 6 studies. It was estimated in 261 patients (146 in the stapled group and 115 in the hand-sewn group). There was a greater value of squeeze pressure in the stapled group (MD = 21.78; IC95% [5.67, 7.88];  $P = .008$ ). Significant heterogeneity was observed among the studies.

**Length of the High-Pressure Zone.** The length of the high-pressure zone has been reported in 5 studies. It was estimated that there were 229 patients: 135 in the stapled group and 94 in the hand-sewn group. There was no significant difference between the 2 groups (MD = .27; IC95% [−.06, .60];  $P = .11$ ). There was little heterogeneity among these studies.

**Dysplasia.** Dysplasia was reported in 3 studies. It was estimated in 300 patients, occurring in 69 of 186 patients in the stapled group and 28 of 114 patients in the hand-sewn group. There was no difference between the 2 groups (OR, 1.62; IC95% [.73, 3.58];  $P = .24$ ). There was little heterogeneity among these studies.

**Neoplasia.** Neoplasia was reported in 3 studies. It was estimated in 300 patients, occurring in 20 of 186 patients in the stapled group and 10 of 114 patients in the hand-sewn group. There was no difference between the 2 groups in terms of neoplasia (OR, .63; IC95% [.24, 1063];  $P = .34$ ).

**Quality Assessment of the Included Studies and Reporting of the Effects of Stapled Ileoanal Anastomosis.** The quality assessment and risk of bias are presented in [Table 2](#). The results of the pooled analyses are presented in [Table 3](#). A Summary of the evidence is presented in [Table 4](#). This review shows that stapled ileoanal anastomosis is superior to hand-sewn anastomosis.

- This leads to a large reduction in anastomotic stricture, small bowel obstruction, ileal pouch failure, seepage by day and night, pad use, and night incontinence.
- It may ensure a higher resting pressure and squeeze pressure in the manometry evaluation.
- We do not know if it leads to additional anastomotic leak, pelvic sepsis, pouchitis, sexual dysfunction, antidiarrheal medication, length of high-pressure zone, operative time, hospital stay, stool frequency, dysplasia, and neoplasia because the evidence is very uncertain.

Table 2. Quality Assessment and Risk of Bias in the Retained Studies.

Nbre of Study	Author	Type of Studies	CONSORT MINORS	Newcastle-Ottawa Scale	Randomization Process	Deviations from Intended Interventions	Cochrane Risk of Bias 2			
							Bias in Measurement of Outcome	Bias to Missing Outcome data	Bias in Selecting the Reported results	Overall Bias
1	Alsukhni	Retro comp	22	*****	-	-	-	-	-	-
2	Araki	Retro/pros	18	****	-	-	-	-	-	-
3	Bednarz	Retro comp	17	****	-	-	-	-	-	-
4	Cohen	Retro comp	22	*****	-	-	-	-	-	-
5	Fukui	Retro comp	18	****	-	-	-	-	-	-
6	Fukushima	Retro comp	18	****	-	-	-	-	-	-
7	Ganshaw 2013	Pros comp	22	*****	-	-	-	-	-	-
8	Ganshaw 2015	Retro comp	21	*****	-	-	-	-	-	-
9	Gecim	Retro comp	18	***	-	-	-	-	-	-
10	Gemlo	Retro comp	18	****	-	-	-	-	-	-
11	Gozetti	Retro comp	16	****	-	-	-	-	-	-
12	Helavirta	Retro comp	22	****	-	-	-	-	-	-
13	Harnoy	Retro comp	20	****	-	-	-	-	-	-
14	Ishii	Retro comp	16	***	-	-	-	-	-	-
15	Kayaalp	Retro comp	22	****	-	-	-	-	-	-
16	Kirat	Retro comp	22	****	-	-	-	-	-	-
17	Konishi	Retro comp	20	****	-	-	-	-	-	-
18	Lian	Retro comp	18	****	-	-	-	-	-	-
19	Luukkonen	Pros random	25	-	Low risk	Some concerns	Some concerns	Low risk	Low risk	Some concerns

(continued)



**Table 2.** (continued)

Nbre of Study	Author	Type of Studies	CONSORT	MINORS	Newcastle-Ottawa Scale	Randomization Process	Deviations from Intended Interventions	Cochrane Risk of Bias 2			
								Bias in Measurement of Outcome	Bias to Missing Outcome data	Bias in Selecting the Reported results	Overall Bias
20	McIntyre	Prosp comp	18	-	*****	-	-	-	-	-	-
21	Pricolo	Pros comp	22	-	*****	-	-	-	-	-	-
22	Reilly	Pros random	-	27	-	Low risk	Some concerns	Low risk	Low risk	Some concerns	
23	Remzi	Retro comp	22	-	*****	-	-	-	-	-	-
24	Saigusa	Retro comp	18	-	****	-	-	-	-	-	-
25	Scotte	Retro comp	16	-	***	-	-	-	-	-	-
26	Seow-choen	Pros random	-	25	-	Low risk	Some concerns	Low risk	Low risk	Some concerns	
27	Silvestri	Retro comp	18	-	*****	-	-	-	-	-	-
28	Sugerman	Retro comp	16	-	****	-	-	-	-	-	-
29	Tonelli	Pros comp	22	-	*****	-	-	-	-	-	-
30	Wettergren	Retro comp	18	-	*****	-	-	-	-	-	-
31	Ziv	Retro comp	18	-	*****	-	-	-	-	-	-

Nbre: number; CONSORT: Consolidated Standards of Reporting Trials; MINORS: methodological index of non-randomized studies; retro: retrospective; comp: comparative; pros: prospective; Random: randomized.

**Table 3.** Outcomes of the Pooled Analysis.

Outcomes	Nbr of Studies	Nbr of patients	Stapled	Hand-Sewn	OR/MD	95% IC	P	I <sup>2</sup> (%)	Tau <sup>2</sup>
<b>Postoperative Outcomes</b>									
Operative time	6	472	178	293	-12.59	-49.24,24.07	0.5	91	1829.9
Hospital stay	4	3447	2875	572	.51	-1.94, 2.97	.68	92	4.85
Anastomotic leak	14	2894	62/1372	123/1522	.84	.58, 1.21	.34	0	0
Pelvic sepsis	17	7526	560/4047	293/3479	.85	.60, 1.19	.34	31	.12
Pouch fistula	13	2535	81/1223	49/1312	1.24	.62, 2.50	.54	46	.63
Pouchitis	11	4108	1133/3087	384/1021	.59	.35, 1.01	.05	66	.39
Anastomotic stricture	15	4816	496/3489	242/1327	.53	.35, .81	.003	39	.19
Small bowel obstruction	12	4524	572/3367	203/1157	.79	.65, .97	.02	0	0
Ileal pouch failure	10	5110	123/3825	99/1285	.32	.23-.43	.001	0	0
<b>Functional outcomes</b>									
Stool frequency per 24h	14	4445	3347	1098	.14	-.29, .56	.53	63	.32
Stool frequency at night	7	3808	3093	715	.05	-.41, .50	.84	96	.28
Seepage day	4	3356	441/2787	173/569	.41	.25, .66	.0003	32	.09
Seepage night	5	3345	765/2789	270/556	.38	.20, .72	.003	50	.23
Pad use	8	3504	429/2864	196/640	.42	.30, .60	<.00001	11	.04
Pad use day	4	3559	399/2807	204/752	.36	.27, .49	<.00001	5	.01
Pad use night	3	3522	486/2778	290/744	.29	.24, .35	<.00001	0	0
Antidiarrheal medication	6	581	43/201	131/380	.62	.32, 1.21	.16	39	.26
Night incontinence	12	4217	130/3250	196/967	.37	.27, .51	<.00001	11	.04
Sexual impotence	6	3432	346/2818	97/614	.70	.30, 1.65	.41	61	.55
Resting pressure (mmHg)	7	293	166	127	14.74	9.58, 19.90	<.00001	67	29.25
Squeeze pressure (mmHg)	6	261	146	115	21.78	5.67,3 7.88	.008	86	305.1
Length of high pressure zone (cm)	5	229	135	94	.27	-.06, .60	.11	51	.07
<b>Oncological outcomes</b>									
Dysplasia	3	300	69/186	28/114	1.62	.73, 3.58	.24	47	.23
Neoplasia	3	300	20/186	10/114	.63	.24, 1.63	.34	0	0

## Discussion

This systematic review and meta-analysis concluded that the stapled group had better outcomes than the hand-sewn group in terms of anastomotic stricture, small bowel obstruction, ileal pouch failure, seepage by day and night, pad use, night incontinence, resting pressure, and squeeze pressure in the manometry evaluation. It was also concluded that there were no differences between the 2 groups in terms of anastomotic leak, pelvic sepsis, pouchitis, sexual dysfunction, antidiarrheal medication, length of high-pressure zone, operative time, hospital stay, stool frequency, dysplasia, and neoplasia.

Operative time is a critical factor in evaluating surgical techniques. Our systematic review and meta-analysis found no significant difference in operative time between stapled and hand-sewn ileal pouch-anal anastomosis (IPAA) procedures.<sup>1-6</sup> This aligns with the results of 4 of the 6 studies we reviewed. The heterogeneity in these studies may be attributed to the lack of standardized measurement tools and limited data on the surgeon's experience. Additionally, most studies were retrospective and lacked clear patient allocation information. Anastomotic leaks, particularly in the lower gastrointestinal tract, are a significant concern (56). Our study revealed a lower relative incidence of anastomotic leak in the stapled group

than in the hand-sewn group,<sup>7-11</sup> which may be attributed to the tension-free anastomosis with stapling. Hand suturing resulted in a lower anastomosis placement relative to the dentate line, potentially leading to ischemia and anastomotic stricture. However, subgroup analysis showed no difference between the 2 techniques in studies involving familial adenomatous polyposis (FAP) patients,<sup>27,44,48</sup> likely due to the limited number of studies and heterogeneity in the definition of strictures at the IPAA. The higher use of diverting stomas in the hand-sewn group may also have contributed to this heterogeneity. In addition, several factors that were not assessed in our study affected the outcomes. Many patients undergoing intestinal surgery are elderly, and vascularization tends to decrease with advancing age, often due to atherosclerosis. Unfortunately, low cardiac output was a common occurrence, particularly in 'fragile' patients who frequently required at least 1 day of intensive care or were managed in the wards. These patients were often classified by anesthesiologists as ASA class 3. Low cardiac output can lead to a temporary reduction in intestinal blood flow, a condition known as Non-occlusive Mesenteric Ischemia (NOMI).<sup>49</sup> This may contribute to anastomotic dehiscence, irrespective of whether anastomosis is performed manually or mechanically.<sup>49</sup>

**Table 4.** Summary of Findings Table.

Outcomes	No of participants Follow-Up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated Absolute Effects	
				Risk with Stapled	Risk Difference with Hand-Sewn
Anastomotic leak	2894 (14 studies)	⊕⊕⊕○ Moderate	OR .84 (.58 to 1.21)	0 per 1000	0 fewer per 1000 (0 fewer to 0 fewer)
Pelvic sepsis	7526 (17 studies)	⊕⊕⊕○ Moderate	OR .85 (.60 to 1.19)	84 per 1000	12 fewer per 1000 (32 fewer to 14 more)
Pouch related fistula	2535 (13 studies)	⊕⊕⊕○ Moderate	OR 1.24 (.62 to 2.50)	37 per 1000	9 more per 1000 (14 fewer to 51 more)
Ileal pouch failure	5110 (10 studies)	⊕⊕⊕⊕ High	OR .32 (.23 to .43)	77 per 1000	51 fewer per 1000 (58 fewer to 42 more)
Pochitis	4108 (11 studies)	⊕⊕⊕○ Moderate	OR .59 (.35 to 1.01)	376 per 1000	114 fewer per 1000 (202 fewer to 2 more)
Anastomotic stricture	4816 (14 studies)	⊕⊕⊕⊕ High	OR .53 (.35 to .81)	182 per 1000	77 fewer per 1000 (110 fewer to 29 fewer)
Small bowel obstruction	4524 (12 studies)	⊕⊕⊕⊕ High	OR .79 (.65 to .97)	175 per 1000	32 fewer per 1000 (54 fewer to 4 fewer)
Dysplasia	300 (3 studies)	⊕○○○ Very low <sup>a</sup>	OR 1.62 (.73 to 3.58)	246 per 1000	100 more per 1000 (54 fewer to 293 more)
Neoplasia	300 (3 studies)	⊕○○○ Very low <sup>a</sup>	OR .63 (.24 to 1.63)	88 per 1000	31 fewer per 1000 (65 fewer to 48 more)
Seepage day	3356 (4 studies)	⊕⊕⊕⊕ High	OR .41 (.25 to .66)	304 per 1000	152 fewer per 1000 (206 fewer to 80 fewer)
Seepage night	3345 (5 studies)	⊕⊕⊕○ Moderate	OR .38 (.20 to .72)	486 per 1000	222 fewer per 1000 (327 fewer to 81 fewer)
Pad use	3504 (8 studies)	⊕⊕⊕⊕ High	OR .42 (.30 to .60)	306 per 1000	150 fewer per 1000 (189 fewer to 97 fewer)
Pad use day	3559 (4 studies)	⊕⊕⊕⊕ High	OR .36 (.27 to .49)	271 per 1000	153 fewer per 1000 (180 fewer to 117 fewer)
Pad use night	3522 (3 studies)	⊕⊕⊕○ Moderate	OR .29 (.24 to .35)	390 per 1000	233 fewer per 1000 (257 fewer to 207 fewer)
Night incontinence	4217 (12 studies)	⊕⊕⊕⊕ High	OR .37 (.27 to .51)	203 per 1000	117 fewer per 1000 (138 fewer to 88 fewer)
Sexual dysfunction	3432 (6 studies)	⊕⊕○○ Low	OR .70 (.30 to 1.65)	158 per 1000	42 fewer per 1000 (105 fewer to 78 more)
Antidiarrhea medication	581 (6 studies)	⊕○○○ Very low <sup>a</sup>	OR .62 (.32 to 1.21)	345 per 1000	99 fewer per 1000 (201 fewer to 44 more)
Resting pressure	293 (7 studies)	⊕⊕○○ Low <sup>a,b</sup>	-	-	MD 14.74 higher (9.58 higher to 19.9 higher)
Squeeze pressure	261 (6 studies)	⊕⊕○○ Low <sup>a,b</sup>	-	-	MD 21.78 higher (5.67 higher to 37.88 higher)
Length of high pressure zone	229 (5 studies)	⊕○○○ Very low <sup>a</sup>	-	-	MD .27 higher (.06 lower to .6 higher)
Operative time	471 (6 studies)	⊕○○○ Very low <sup>a,b</sup>	-	-	MD 12.59 lower (49.24 lower to 24.07 higher)
Hospital stay	3447 (4 studies)	⊕○○○ Very low <sup>a,b</sup>	-	-	MD .51 higher (1.94 lower to 2.97 higher)
Stool frequency	4445 (14 studies)	⊕⊕○○ Low	-	-	MD .14 higher (.29 lower to .56 higher)
Stool frequency by night	3808 (7 studies)	⊕⊕○○ Low	-	-	MD .05 higher (.41 lower to .5 higher)

\***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI**: Confidence interval; **MD**: mean difference; **OR**: odds ratio.

**GRADE Working group grades of evidence****High certainty**: We are very confident that the true effect lies close to that of the estimate of the effect.**Moderate certainty**: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.**Low certainty**: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.**Very low certainty**: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Explanations.

<sup>a</sup>Small sample size of the included patients.

<sup>b</sup>Existing of a heterogeneity among the different studies.

Regarding small bowel obstruction,<sup>12-23</sup> our study, which included data from 12 studies, demonstrated a lower rate of small bowel obstruction in the stapled group. Ileal pouch failure and pouchitis can lead to complications and revision surgery. Our findings were consistent with those of Kirat et al.,<sup>43</sup> who identified the type of anastomosis as a risk factor for pouchitis. However, the significance of these findings remains uncertain. Ileoanal anastomosis modifies anatomy and has functional consequences, including seepage per day and night incontinence.<sup>24-26</sup> Our study indicated a lower rate of daily seepage in the stapled group. Patients in the stapled group also used fewer pads (29, 46, 47, 51). Antidiarrheal medication use did not differ significantly between the 2 techniques (29, 42, 48, 52, 53). Six studies evaluated sexual impotence (29, 40, 42, 43, 48, 52), and the results were in line with Kirat et al's findings, suggesting that sexual function may be more affected by proctectomy and pelvic nerve damage than by IPAA type. However, further research using validated questionnaires is needed to reduce the subjectivity in assessing this outcome. Functional factors, such as stool frequency, consistency, urgency, and incontinence, were considered, but these remain subjective measures. Manometry measures, including resting pressure, squeeze pressure, and the length of the high-pressure zone, were analyzed in 7 studies.<sup>1,26,38,46,47,49</sup> Our findings favored the stapled technique, potentially due to better sphincter and perianal nervous system preservation. Residual rectal mucosa is a concern in patients with UC and FAP after IPAA due to the risk of colorectal cancer.<sup>35</sup> Mucosectomy for UC aims to eliminate mucosal inflammation and the risk of malignant transformation. Hand-sewn anastomosis with mucosectomy may be more challenging, but offers a definitive cure. For patients with FAP, residual rectal mucosa can lead to polyposis, dysplasia, and neoplasms (63). Our study found no significant difference in dysplasia rates between stapled and hand-sewn anastomoses.<sup>31,35,48</sup> The risk of cancer recurrence after mucosectomy was noted, possibly because of incomplete rectal mucosa removal. A portion of patients in the hand-sewn group had remnant rectal mucosa. Mucosectomy can reduce the risk, but does not entirely eliminate it.

Our study had several limitations. Owing to the reduced number of RCTs, the lack of some outcomes, and the lack of suitable follow-up. We did not assess other outcomes, such as cuffitis, in the UC population because they were not reported in the majority of studies. We included additional CCTs with a risk of selection bias and low-to-moderate heterogeneity between the studies, highlighting the need for additional RCTs on this topic. However, the quality of evidence is limited. We assessed the risk of bias using different tools. Therefore, our findings should be cautiously interpreted. Making firm conclusions for dealing with rectal cancer or dysplasia is challenging, given the small number of studies conducted to date. In addition, for several studies, the follow-up was limited and did not provide strong recommendations in terms of oncological safety. Additional long-term data in the context

of standardized surveillance protocols may provide better answers. In addition, there may be concerns about introducing bias by including UC and FAP. These 2 diseases have different clinical presentations, etiology, preoperative treatment, development of pathology, and recurrence or development of cancer. To alleviate this issue, we performed a subgroup analysis of patients with UC and FAP, when possible.

## Conclusions

In conclusion, both anastomoses had advantages and disadvantages. Additional RCTs with larger sample sizes and longer follow-up periods seem to be mandatory for a greater placement of stapled IPAA in the therapeutic armature of UC and PAF to investigate which patients need stapled or handsewn IPAA.

## Author Contributions

Mohamed Ali Chaouch, Mohammad Iqbal Hussain, Amine Gouader, Bassem Krimi and Alessandro Mazzotta wrote the main manuscript text and Adriano Carneiro Da Costa, Niccolo Puttricciani and Hani Oweira checked the statistical analysis. All authors reviewed the manuscript and validate the final version of the manuscript.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Ethical Statement

### Ethical Approval

This research involves Human participants. It is a retrospective analysis of published cases and did not require informed consent. Ethics approval and consent to participate were not applicable in this review.

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## Data Availability Statement

All data generated or analyzed during this study are included in this published article.

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