

Endoscopic management of ileal pouch–anal anastomosis strictures: meta-analysis and systematic literature review

Parth Patel^a, Manav Patel^b, Mohamad Ayman Ebrahim^a, Priyadarshini Loganathan^c, Douglas G. Adler^d

Saint Joseph Hospital, Chicago; Smt. NHL Municipal Medical College, India; University of Texas health science center San Antonio; Center for Advanced Therapeutic Endoscopy at Porter Adventist Hospital, USA

Abstract

Background Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) is a common surgical procedure for ulcerative colitis and familial adenomatous polyposis. IPAA strictures are a known complication, often requiring surgical intervention. Endoscopic interventions offer a less invasive alternative, but their safety and efficacy remain uncertain.

Methods A comprehensive literature search was performed to identify pertinent studies. Outcomes assessed were technical success, clinical success (immediate and end of follow up), pouch failure rate and adverse events. Pooled estimates were calculated using random effects models with a 95% confidence interval.

Results A total of 607 patients from 9 studies were included. Technical success, defined as the ability to pass the endoscope through the stricture, was achieved in 97.4% of patients. Immediate clinical success, defined as symptom improvement post-intervention, was seen in 44.5% of patients. Clinical success at the end of follow up was observed in 81.7% of patients. However, 6.8% of patients experienced pouch failure and ultimately 14.5% required surgical intervention for refractory strictures or complications. Endoscopic intervention-related serious adverse events occurred in 3.9% of patients, including perforation and major post-procedural bleeding.

Conclusions Endoscopic interventions for IPAA strictures demonstrate high technical success rates, providing a less invasive option for managing this complication. While clinical success rates immediately post-procedure and at end of follow up are promising, a significant proportion of patients ultimately require surgical intervention for pouch failure or refractory strictures.

Keywords Ileal pouch–anal anastomosis, endoscopic balloon dilation, stricturotomy

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^aDepartment of Internal Medicine, Saint Joseph Hospital, Chicago (Parth Patel, Mohamad Ayman Ebrahim); ^bDepartment of Medicine, Smt. NHL Municipal Medical College, India (Manav Patel); ^cDepartment of Internal Medicine, University of Texas health science center San Antonio (Priyadarshini Loganathan); ^dDepartment of Gastroenterology, Center for Advanced Therapeutic Endoscopy at Porter Adventist Hospital (Douglas G. Adler)

Conflict of Interest: None

Correspondence to: Douglas G. Adler, MD, Center for Gastroenterology & Hepatology, Center for Advanced Therapeutic Endoscopy at Porter Adventist Hospital in Denver 80210, Colorado, USA, e-mail: dougraham2001@gmail.com

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Introduction

Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) is the procedure of choice for the management of ulcerative colitis (UC) that has proven refractory to medical therapy, UC with dysplastic/neoplastic transformation of intestinal mucosa and familial adenomatous polyposis [1]. IPAA improves the quality of life in UC patients by decreasing the symptom burden and avoiding the need for an end ileostomy [2].

Adverse events following IPAA include pouch leaks, pouch sinus formation, pouch strictures, pouchitis, cuffitis, pouch neoplasia and irritable pouch syndrome [3]. The reported incidence of strictures following IPAA ranges from 5-38%, with the most common stricture locations being the pouch outlet, followed by the pouch inlet, the afferent limb and the mid-pouch [4,5].

The surgical management of IPAA strictures includes several options, including pouch resection, strictureplasty, stapler resection, pouch revision and re-anastomosis,

depending on the stricture's location and severity, as well as the surgeon's experience [5]. While surgical treatments are effective, they are associated with significant morbidity [4,5]. Minimally invasive endoscopic interventions that have been used for other gastrointestinal tract strictures, such as balloon dilation, stricturotomy and stent placement, have been shown to be effective for IPAA strictures [4].

We conducted a meta-analysis of studies that analyzed the safety and efficacy of endoscopic interventions for the management of IPAA strictures.

Materials and methods

This study adhered to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) checklist to identify the safety and efficacy of endoscopic interventions for the management of IPAA strictures (Appendix A).

Search strategy

The literature was searched by 2 authors (PP, MP) for studies that focused on IPAA strictures, endoscopic balloon dilation, endoscopic management of IPAA strictures and related terms. Search strategies were created using a combination of keywords and standardized index terms. Searches were run on April 12, 2024, in Embase (n=448), Scopus (n=8), PubMed (n=204), and Cochrane (n=4). Full search strategies are provided in Appendix B.

The title and abstract of studies from the primary search were independently screened by 2 authors (PP and MP). Based on predetermined inclusion and exclusion criteria, studies that did not address our specific research question were excluded. The full texts of the initial screened-in articles were then reviewed for relevant information. Any discrepancy in article selection was resolved by mutual consensus, after discussion with the third co-author (MAE). Additional relevant articles were manually searched from the bibliographic section of the selected articles, as well as the systematic and narrative articles on the topic.

Study selection

For the purposes of this meta-analysis, we included studies that evaluated the efficacy and safety of different endoscopic techniques for the management of IPAA strictures. Studies that reported data specific to patients who underwent endoscopic management for IPAA strictures were included.

The exclusion criteria were as follows: (1) single patient case reports, review articles and editorials; (2) studies performed in the pediatric (<18 years) population; (3) non-English language studies; (4) non-human/animal studies; and (5) non-clinical laboratory studies.

Data abstraction and quality assessment

Two authors (PP and MP) independently abstracted data from the studies using a pre-approved standardized form. Quality assessment to ascertain the individual study risk-of-bias was carried out independently by 2 authors (MAE, PP) using the National Institute of Health (NIH) quality assessment tool for before–after (pre–post) studies with no control group (Supplementary Tables 1 and 2).

Outcomes assessed

Outcomes assessed were technical success, immediate clinical success, success at the end of the follow-up period, incidence of pouch failure and intervention-related adverse events, among patients with IPAA strictures undergoing endoscopic management.

Statistical analysis

Standard meta-analysis statistics were used, following the methods suggested by DerSimonian and Laird. The pooled efficacy rates with the corresponding 95% confidence interval (CI) were calculated by logit-transformation using a random-effects model. Heterogeneity between study-specific estimates was assessed using the Cochrane Q statistical test for heterogeneity and the I^2 statistics. Publication bias assessment was deferred as number of studies included in analysis were less than 10. All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 4 (BioStat, Englewood, NJ).

Results

Search results and population characteristics

The initial search yielded 664 references. After the removal of duplicates, a total of 346 studies, including full articles and abstracts, underwent formal title and abstract screening. A total of 9 studies, including 607 patients, were included based on our inclusion and exclusion criteria (Fig. 1).

A total of 607 patients (54% male, mean age 44.5±6.5 years) with IPAA strictures were included in the final analysis. The most common indication for IPAA was UC (97%). One or more strictures were present in each patient and the most common locations were pouch outlet (46%), followed by pouch inlet (33%), afferent limb (11%), and other (10%). Mean stricture length was 1.4±0.4 cm. Endoscopic interventions were performed with techniques including endoscopic balloon dilation (EBD), needle knife stricturotomy (NKSt), stent placement and digital dilation under endoscopic view. The mean number of sessions required was 2.5±0.9 per patient. The mean follow-up period following the first intervention was 3.4±3.0 years.

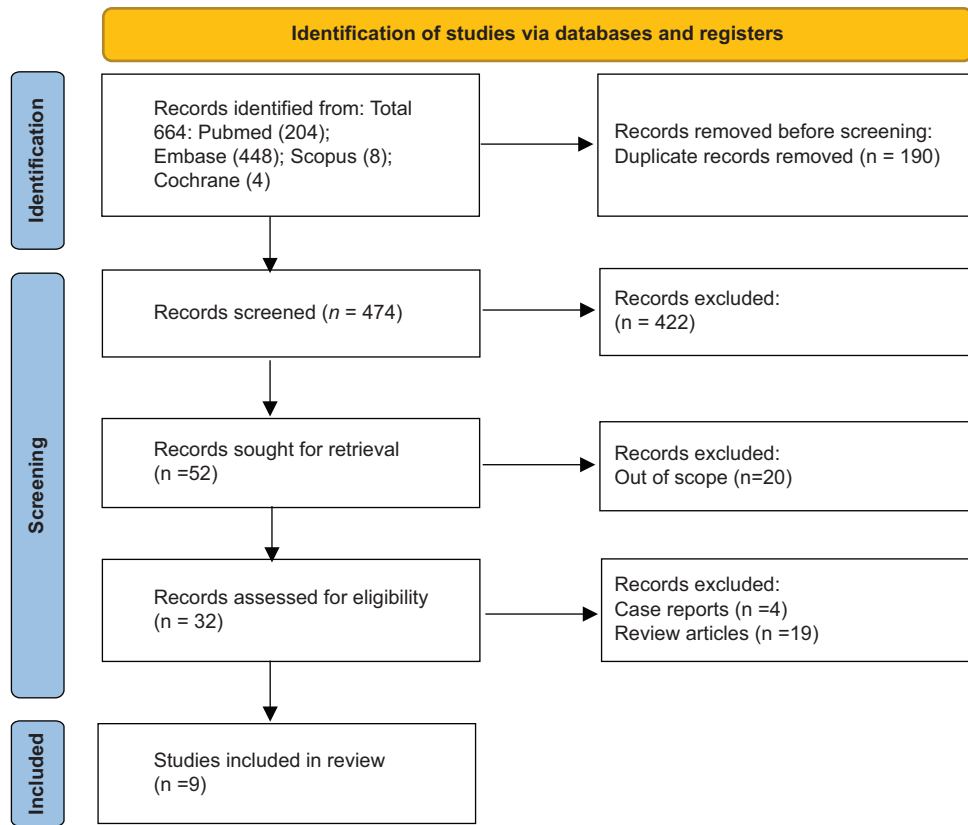


Figure 1 Study selection flow chart

Characteristics and quality of included studies

Table 1 shows the characteristics of the included studies. The quality assessment of the included studies was conducted independently and blindly by 2 authors (PP and MP). Discrepancies that arose were resolved by a third author (MAE) in an independent and blinded manner. Our systematic review employed 2 types of quality assessment: the interventional NIH (National Institute of Health) scale for pre-post studies without control groups, and controlled intervention study assessment [15]. According to the NIH scale for pre-post studies, 1 study was rated as high quality, receiving a score of 9, 4 studies were considered fair quality, scoring between 5 and 8, and 1 study was considered of poor quality, receiving a score of 3, as detailed in Supplementary Table 1. Studies of poor to moderate quality lacked sufficient data, often sourced from abstracts rather than full-text articles, limiting our ability to evaluate them thoroughly. In the interventional controlled trials, 3 studies achieved fair quality, with a score of 6-8 out of 14, based on various aspects outlined in the NIH quality assessment for controlled intervention trials, as noted in Supplementary Table 2. Given the specialization in handling intricate cases with proficient endoscopists and support staff, these studies did not involve randomization or blinding, as physicians had the autonomy to choose the procedure they felt most comfortable performing.

Pooled outcomes

Success

Technical success, defined as the ability to pass the endoscope through the stricture following the intervention, was achieved in 97.4% patients ($I^2=44%$) (Supplementary Fig. 1). Immediate clinical success, defined as improvement in symptoms following the first intervention, was achieved in 44.5% patients ($I^2=86%$) (Supplementary Fig. 2). Clinical success at the end of the follow-up period was reported in 8/9 studies and was seen in 81.7% patients ($I^2=81%$). However, 38 (6.8%) patients experienced pouch failure, defined as the need for surgical management such as pouch excision, diversion ileostomy or stricturoplasty during the follow-up period, due to refractory IPAA strictures ($I^2=67%$), while 50 (14.5%) patients ultimately required surgical interventions for management of refractory stricture or related complications ($I^2=55%$) (Figs. 2,3).

Adverse events

Nineteen (3.9%) patients experienced serious adverse events related to the endoscopic intervention ($I^2=0%$) (Fig. 4): 7 (2%) patients who underwent EBD developed perforation requiring surgical intervention ($I^2=0%$), while 12 (2.6%) patients, 9 and 3 in the EBD and NKSt groups, respectively, had major

Table 1 Characteristics of studies

Study [ref.] year	Study type, Country	Indication for IPAA	Patients (n)	Strictures (n)	Stricture location	Intervention	Follow-up period	Interventions/patient (mean)	Outcomes
Darlington [6] 2024	Retrospective, USA	UC (9)	9	9	Anastomotic stricture (9) - ileoanal or rectal	EBD	1 year	3.2±1.0	Technical success, success at the end of follow-up, adverse events
Emmanouil [7] 2019	Retrospective, Greece	UC (65)	65	71	Outlet (65), inlet (6)	Digital dilation under endoscopic view, NKSt	NA	NA	Success at the end of follow-up, pouch failure, adverse events
Fumery [8] 2018	Retrospective, France	UC (19); CD (1)	20	23	outlet (20), Inlet (2), Afferent limb (1)	EBD	2.0±0.4 years	3.8±1.3	Technical success, success at the end of follow-up, pouch failure, adverse events
James [9] 2018	Prospective, USA	UC (4)	4	4	Inlet (4)	EBD+stent	NA	NA	Immediate clinical success, adverse events
Lan [10] 2021	Retrospective, USA	UC (200)	200	NA	pouch inlet/afferent limb, outlet	NKSt (40), EBD (160)	2.9±0.8 years	1.07±0.3	Technical success, success at the end of follow-up, pouch failure, adverse events
Mohy-ud-din [11] 2020	Retrospective, USA	UC (3)	3	NA	NA	NKSt	4 months	NA	Technical success, success at the end of follow-up, pouch failure, adverse events
Quinn [12] 2019	Retrospective, USA	IBD (5)	5	5	inlet (3), outlet (2)	Stent (5)	NA	1.3±0.0	Technical success, success at the end of follow-up, adverse events
Shen [13] 2011	Retrospective, USA	UC (136); intermediate colitis (10); CD (2); toxic megacolon (2)	150	256	Outlet (9) - ileoanal or rectal	EBD	9.7±2.1 years	3.06±0.9	Technical success, success at the end of follow-up, pouch failure, adverse events
Wu [14] 2013	Retrospective, USA	UC (151)	151	240	Outlet (65), inlet (6)	EBD	4.1±2.6 years	NA	Success at the end of follow-up, pouch failure, adverse events

UC, ulcerative colitis; CD, Crohn's disease; IBD, inflammatory bowel disease; EBD, endoscopic balloon dilation; NKSt, needle knife stricturotomy

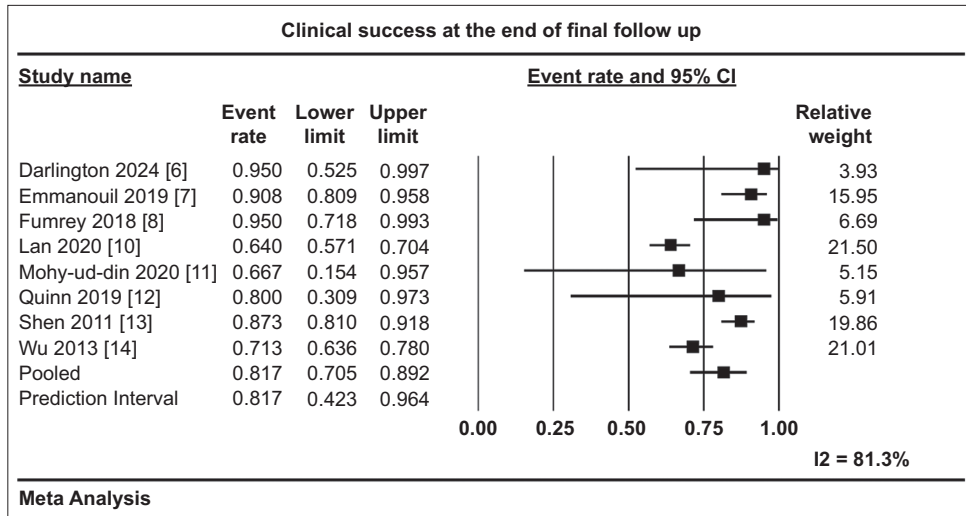


Figure 2 Forest plot: success at the end of follow up
CI, confidence interval

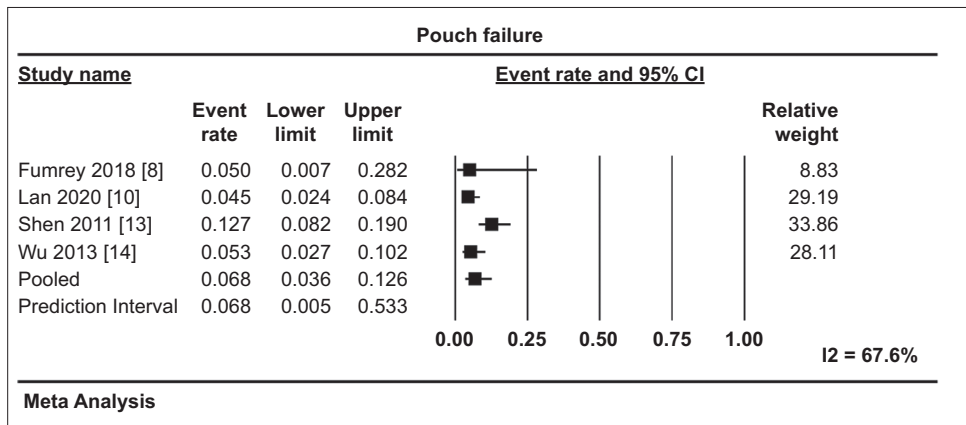


Figure 3 Forest plot: pooled event rate of pouch failure
CI, confidence interval

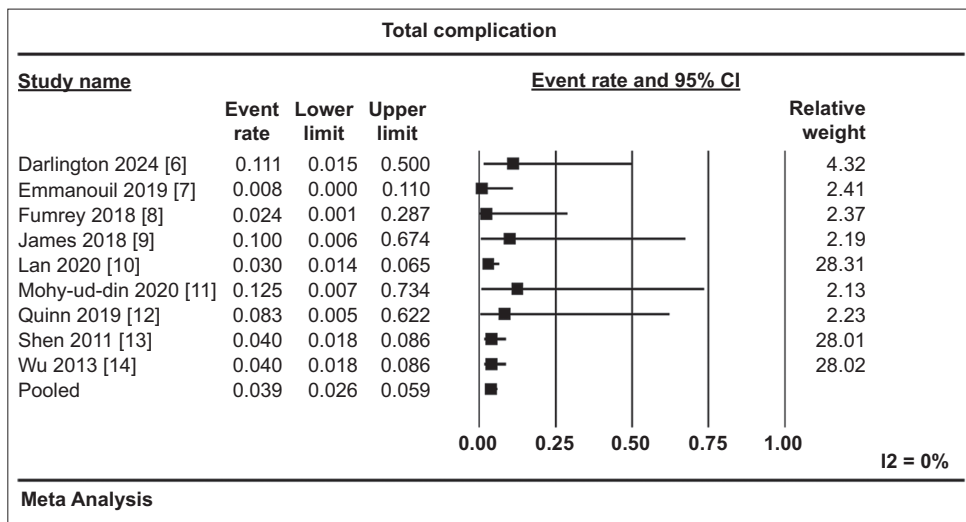


Figure 4 Forest plot: pooled severe adverse events
CI, confidence interval

postprocedural bleeding requiring blood transfusion following the intervention ($I^2=0\%$) (Supplementary Fig. 3,4).

Validation of meta-analysis

Sensitivity analysis

To assess whether any single study had a dominant effect on the meta-analysis, we excluded each study individually and analyzed the effect on the main summary estimate. No single study significantly affected the outcome or heterogeneity.

Heterogeneity

We assessed the dispersion of the calculated rates using the I^2 percentage values. Based on I^2 analysis for heterogeneity, considerable heterogeneity was noted for the pooled rate of immediate clinical success and success at the end of the follow-up period following endoscopic interventions. Low heterogeneity was noted for the pooled rate of intervention related to severe adverse events. The I^2 values for the pooled rates are summarized in Table 2.

Prediction interval

This meta-analysis was conducted using the random-effects model. Therefore, we calculated the prediction interval, which deals with the dispersion of the effects. The calculated prediction interval for clinical success at the end of follow up was 0.817 (95%CI 0.423-0.964) and for pouch failure it was 0.068 (95%CI 0.005-0.533) (Supplementary Fig. 5).

Discussion

Our study evaluated the efficacy and safety of endoscopic interventions for the management of IPAA strictures at

various pouch locations. Our analysis found a high technical success rate for endoscopic interventions (97%) in the management of IPAA strictures. However, the immediate clinical success rate was substantially lower (44.5%). This discrepancy arose because, in our analysis, most patients required more than 1 treatment session (2.5 ± 0.9 sessions per patient) to achieve symptomatic improvement [16,17]. In addition, serial dilations with a gradual increase in diameter, as opposed to single-session dilation, decreased the risk of perforation [18].

Strictures at different pouch locations may respond differently to various endoscopic and surgical interventions [5,16]. For proximal outlet (IPAA) strictures, non-endoscopic surgical dilation techniques have a success rate of 90-100% [5]. However, distal strictures (inlet, mid-pouch, afferent limb) often require more invasive surgical interventions, such as strictureplasty, bypass, or even reconstruction of the anastomosis, with success rates of 80-100% [5]. Distal strictures are accessible via minimally invasive endoscopic techniques and can potentially spare patients from having to undergo repeat surgery. Our analysis, including a comparable number of both proximal and distal strictures, showed an 81.7% success rate at follow up, with an acceptable complication rate.

A recent meta-analysis reported a 6% overall pouch failure rate, irrespective of the method used to treat the pouch-related complications [19]. This rate is similar to that seen in our analysis (6.8%), where pouch failure following failed endoscopic management of pouch strictures was analyzed. Strictures alone cannot be blamed for pouch failure, as most studies reported multiple risk factors, such as underlying disease activity prior to IPAA, surgical techniques, location of strictures, and post-IPAA non-mechanical complications [20,21].

In our analysis, the pooled event rate of iatrogenic perforation was 2%, comparable to rates following endoscopic dilation for other lower gastrointestinal strictures [18,22,23]. None of the patients treated with NKSt experienced perforation events. None of the patients in recent studies experienced iatrogenic perforation following endoscopic stricturotomy for strictures related to inflammatory bowel disease (IBD) [24,25]. Major bleeding events with EBD (1.8%) were more frequent,

Table 2 Pooled outcomes

Outcomes	Percentage (range)	I^2 (%)	Studies (n)
Technical success	97.4 (92-99)	46	9
Immediate clinical success	44.5 (12-82)	86	5
Success at the end of follow up	81.7 (70-89)	81	8
Pouch failure	6.8 (3.6-12)	67	4
Requirement for surgical intervention during or at the end of follow up	14.5 (7-27)	55	4
Any serious adverse events related to intervention	3.9 (2.6-5.9)	0	9
Perforation requiring surgical intervention	2 (1.1-3.6)	0	9
Postprocedural bleeding requiring blood transfusion	2.8 (1.7-4.7)	0	9

whereas with NKSt (6%) they were comparable to prior studies on EBD and NKSt for the management of IBD-related strictures [25,26].

To our knowledge, this is the first meta-analysis to specifically examine the safety and efficacy of endoscopic interventions for managing ileal pouch strictures following restorative proctocolectomy. Our study had several limitations. First, the predominance of retrospective studies within our analysis introduced a bias towards historical data. Second, 3 of the 9 studies included in the analysis originated from conference abstracts, which by their nature have not undergone a comprehensive inspection and peer-review process. Finally, the heterogeneity encountered in the analysis of clinical success, immediate and at end of follow up, was high. However, all the studies showed a high rate of clinical success, indicating that the heterogeneity may have been due to variations in the population sizes (3-200), the baseline severity of the disease and the length of the follow-up periods (1-9 years) across different studies, and not to other effects.

In conclusion, endoscopic treatment of ileal pouch strictures is effective and reasonably safe. Future studies comparing different endoscopic interventions for managing ileal pouch strictures at different locations are needed to develop effective treatments for each type of stricture.

Summary Box

What is already known:

- Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) improves the quality of life in patients with ulcerative colitis, by decreasing the symptom burden and avoiding the need for an end ileostomy
- Strictures following IPAA are common and can lead to pouch failure requiring surgical intervention
- Surgical management of IPAA strictures includes strictureplasty, bypass, or even reconstruction of the anastomosis

What the new findings are:

- Minimally invasive endoscopic interventions, such as endoscopic balloon dilation, needle knife stricturotomy and stent placement, are effective for the management of IPAA strictures
- Endoscopic interventions for IPAA strictures have a very high technical success rate and their clinical success rate is comparable to that of surgical management
- Endoscopic interventions are not only effective but also safe, with acceptably low rates of serious adverse events

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Supplementary material

Appendix A PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number	none
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale	4,5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	Appendix B
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	3, Appendix-B
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made	3,4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	6, Supplementary Tables 1,2
Summary measures	13	State the principle summary measures (e.g., risk ratio, difference in means)	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis	5
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies)	6, Supplementary Tables 1,2
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	5,8

(Contd...)

Appendix A (Continued)

Section/topic	#	Checklist item	Reported on page #
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	3, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	Supplementary Table 1,2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot	Table 1
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency	5, Table 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)	Supplementary Tables 1,2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16])	none
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers)	9,10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias)	9
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review	Title Page

Appendix B Search Strategy

Database	Results (n)
PubMed Search: (((((J pouch[Title/Abstract]) OR (IPAA[Title/Abstract])) OR (ileal pouch anal anastomosis[Title/Abstract])) OR (leal pouch anal anastomoses[Title/Abstract])) OR (ileal pouch anal anastomotic[Title/Abstract])) AND (((((stricture[Title/Abstract]) OR (strictures[Title/Abstract])) OR (anastomosis stricture[Title/Abstract])) OR (anastomoses stricture[Title/Abstract])) OR (anastomotic stricture[Title/Abstract]))	204
Embase ipaa: ab, ti OR 'ileal pouch-anal anastomosis':ab, ti OR 'j pouch':ab, ti OR 'ileal pouch-anal anastomoses':ab, ti AND 'stricture':ab, ti OR 'strictures':ab, ti OR 'anastomosis stricture':ab, ti OR 'anastomoses stricture':ab, ti OR 'anastomotic stricture':ab, ti	448
Scopus ((TITLE (ipaa) OR TITLE (ileal AND pouch-anal AND anastomosis) OR TITLE (j AND pouch) OR TITLE (ileal AND pouch-anal AND anastomoses))) AND ((TITLE (stricture) OR TITLE (strictures) OR TITLE (anastomosis AND stricture) OR TITLE (anastomoses AND stricture) OR TITLE (anastomotic AND stricture)))	8
Cochrane ((ipaa):ab OR (ileal pouch-anal anastomosis):ab OR (j pouch):ab OR (ileal pouch-anal anastomoses):ab) AND ((stricture):ab OR (strictures):ab OR (anastomosis stricture):ab OR (anastomoses stricture):ab OR (anastomotic stricture):ab)	4

Supplementary Table 1 Quality assessment of the included studies according to the National Institute of Health (NIH) quality assessment tool for before-after (pre-post) studies with no control group

Study [ref.] year	C 1	C 2	C 3	C 4	C 5	C 6	C 7	C 8	C 9	C 10	C 11	C 12
Emmanouil [7] 2019	Yes	CD	No	CD	No	Yes	CD	CD	Yes	CD	CD	No
Fumrey [8] 2018	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No
James [9] 2018	Yes	No	No	CD	No	Yes	Yes	CD	Yes	Yes	CD	No
Mohy-ud-din [11] 2020	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No
Quinn [12] 2019	Yes	Yes	No	Yes	No	Yes	CD	CD	Yes	CD	Yes	No
Shen [13] 2011	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No

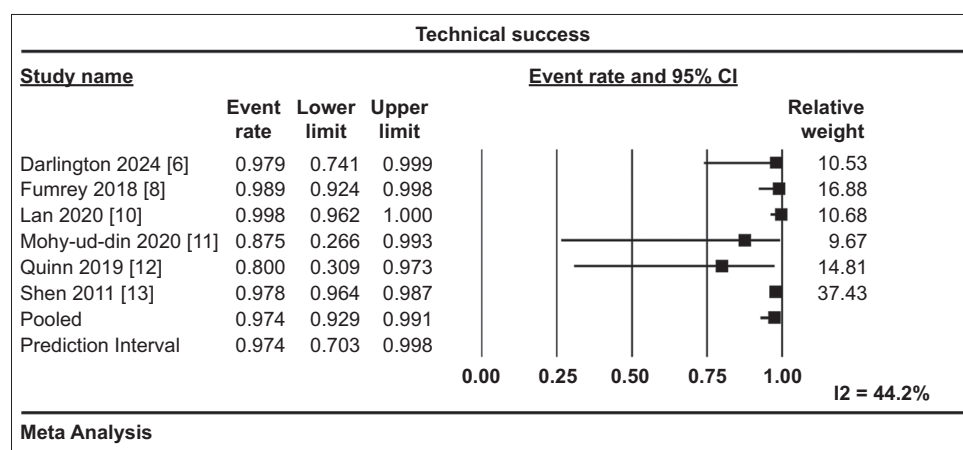
Criterion 1 – Was the research question or objective clearly articulated? Criterion 2 – Were the criteria for selecting the study population predefined and clearly outlined? Criterion 3 – Ensured the participation of eligible individuals; Criterion 4 – Selected subjects from the same population and timeframe, applying selection criteria consistently; Criterion 5 – Did the sample size provide sufficient confidence in the results? Criterion 6 – Evaluated if the intervention/test/service was distinctly described and uniformly administered across the study group; Criterion 7 – Examined if outcome measures were predetermined, clearly defined, valid, reliable, and consistently evaluated among all participants; Criterion 8 – Assessed whether outcome assessors were unaware of participants' exposures/interventions; Criterion 9 – Ensured loss to follow up was 20% or less; Criterion 10 – Determined if statistical methods analyzed changes in outcome measures pre and post-intervention, including the utilization of *P* values; Criterion 11 – Verified if outcome measures were taken multiple times before and after the intervention; Criterion 12 – Evaluate if statistical analysis accounted for individual-level data when interventions were conducted at a group level (e.g., entire hospital, community)

C, Criterion; CD, cannot be determined; NA, not applicable

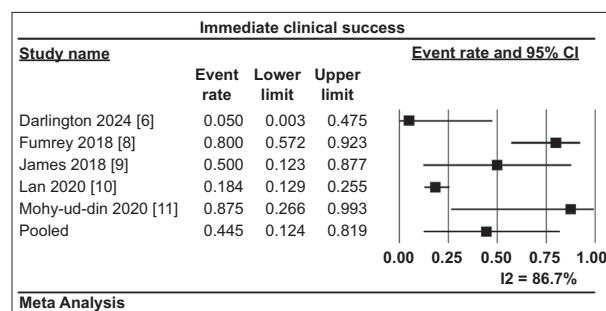
Supplementary Table 2 Quality assessment of the included studies according to the National Institute of Health (NIH) quality assessment of controlled intervention studies

Study [ref.] year	C 1	C 2	C 3	C 4	C 5	C 6	C 7	C 8	C 9	C 10	C 11	C 12	C 13	C 14
Darlington [6] 2024	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Lan [10] 2020	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Wu [14] 2013	No	No	No	No	No	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes

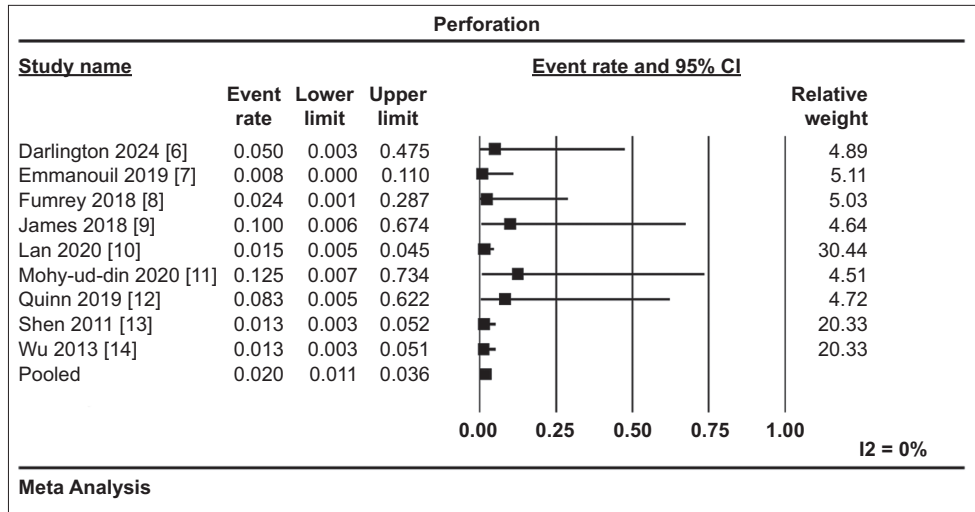
Criterion 1 – Did the study explicitly state its randomization method, such as being randomized, a randomized trial, a randomized clinical trial, or an RCT? Criterion 2 – Was the randomization process deemed adequate, involving the use of randomly generated assignments? Criterion 3 – Was treatment allocation concealed to prevent anticipations of assignments? Criterion 4 – Were both participants and providers unaware of which treatment group participants were assigned to? Criterion 5 – Were outcome assessors blinded to participants’ group assignments? Criterion 6 – Were the groups comparable at the outset regarding significant characteristics that might influence outcomes? Criterion 7 – Did the study demonstrate a dropout rate at the conclusion of 20% or less of the initially allocated treatment group? Criterion 8 – Was the discrepancy in dropout rates between treatment groups at the conclusion 15 percentage points or less? Criterion 9 – Was there robust adherence to intervention protocols in each treatment group? Criterion 10 – Were other interventions either avoided or kept consistent across all groups, such as background treatments? Criterion 11 – Were outcomes assessed using reliable and valid measures, consistently applied to all participants? Criterion 12 – Did the authors affirm that the sample size was adequate to detect differences in the primary outcome between groups with at least 80% power? Criterion 13 – Were outcomes reported or subgroup analyses predetermined before conducting analyses? Criterion 14 – Were all randomly assigned participants analyzed according to their original group allocation, utilizing an intention-to-treat analysis



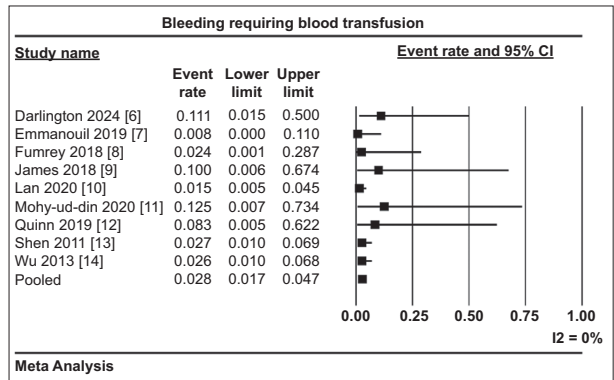
Supplementary Figure 1 Forest plot: technical success
 CI, confidence interval



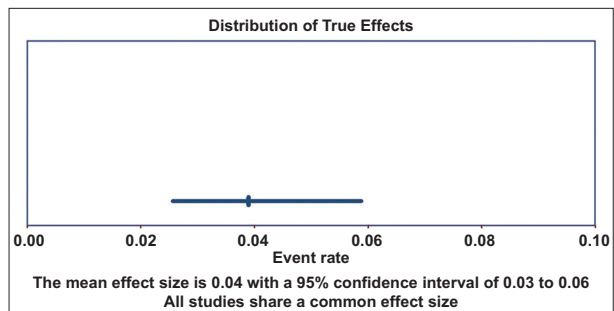
Supplementary Figure 2 Forest plot: immediate clinical success
 CI, confidence interval



Supplementary Figure 3 Forest plot: perforation following endoscopic intervention
CI, confidence interval



Supplementary Figure 4 Forest plot: bleeding requiring blood transfusion following endoscopic intervention
CI, confidence interval



Supplementary Figure 5 Prediction interval for serious adverse events following endoscopic intervention