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Efficacy, Safety and Long-Term Outcomes of Endoscopic Submucosal Dissection for Inflammatory Bowel Disease-Associated Colorectal Neoplasia: A Systematic Review and Meta-Analysis Comparing Asian and Western Outcomes

Maria Vitória Corte-Real Cabral Vicente Nunes

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Medicina Clínica

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Efficacy, Safety and Long-Term Outcomes of Endoscopic Submucosal Dissection for Inflammatory Bowel Disease-Associated Colorectal Neoplasia: A Systematic Review and Meta-Analysis Comparing Asian and Western Outcomes

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É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
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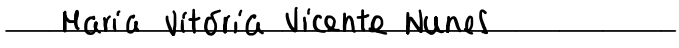

UC Dissertação - DECLARAÇÃO DE TRANSPARÊNCIA

RELATIVAMENTE À UTILIZAÇÃO DE FERRAMENTAS DE CHATBOT

GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, Maria Vitória Cort-Real Cabral Vicente Nunes, abaixo assinado, nº mecanográfico 201907034, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

Faculdade de Medicina da Universidade do Porto, 15 / 03 / 2025

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Maria Vitória Vicente Nunes

Dedicatória

Ao meu orientador, Dr. Rui Morais, agradeço o apoio, a disponibilidade e a simpatia ao longo deste percurso.

Ao meu coorientador, Professor Bernardo Sousa-Pinto, estou grata pelo rigor, disponibilidade e partilha de conhecimento, que muito enriqueceram este trabalho.

Um especial agradecimento ao Dr. Miguel Martins, por ter sido um colega de trabalho exemplar. Fomos o braço direito um do outro ao longo deste percurso e a sua disponibilidade e espírito de cooperação tornaram esta caminhada mais fácil e enriquecedora.

Aos meus amigos, pelo apoio incondicional, pelas palavras de incentivo e pelos momentos de descontração que tornaram esta jornada mais leve.

Ao meu pai, mãe, irmão e namorado pelo amor, paciência e suporte, sem os quais este caminho teria sido muito mais difícil.

A todos, o meu mais sincero obrigado. Este trabalho é tanto meu quanto vosso.

Efficacy, Safety and Long-Term Outcomes of Endoscopic Submucosal Dissection for Inflammatory Bowel Disease-Associated Colorectal Neoplasia: A Systematic Review and Meta-Analysis Comparing Asian and Western Outcomes

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Conflicts of Interest

No conflicts of interest to report

Statements

Study materials will be made available to other researchers upon request

Word count

5178

Abstract

Background and aims: Endoscopic submucosal dissection (ESD) is increasingly being adopted worldwide for the treatment of colorectal neoplastic lesions. However, its role in patients with inflammatory bowel disease (IBD) remains debatable, particularly due to increased risk of submucosal fibrosis from chronic inflammation, which can theoretically impact the clinical outcomes of this technique. This study aimed to assess the efficacy and safety of ESD for colorectal neoplastic lesions in IBD patients, comparing Asian and Western settings.

Methods: A systematic review was conducted by searching MEDLINE and Web of Science until January 2025. We included primary studies reporting ESD performance in IBD patients. We performed random-effects meta-analysis for several outcomes, including *en-bloc*, R0, and curative resection rates, frequency of adverse events (post-procedural bleeding and perforation), local recurrence and need for additional surgery after ESD. Certainty of evidence was assessed using GRADE.

Results: We included 20 studies (565 patients and 732 lesions). The meta-analytical frequencies of *en-bloc*, R0, and curative resection rates were 95.7% (95%CI=93.5-97.9%; I^2=60.1%), 84.6% (95%CI=79.4-90.1%; I^2=68.9%), and 83.9% (95%CI=76.3-92.4%; I^2=75.9%), respectively. Bleeding and perforation occurred in 7.0% (95%CI=4.4-11.2%; I^2=16.9%) and 7.9% (95%CI=5.3-11.9%; I^2=2.4%) of cases, respectively. Local recurrence frequency was 5.3% (95%CI=3.5-7.9%; I^2=0%). The meta-analytical need for additional surgery was 13.3% (95%CI=9.5-18.1%; I^2=42.5%). No differences were found between Asian and Western studies for any outcome. The certainty of evidence was considered "low" in 4 outcomes and "very low" in the remaining outcomes.

Conclusion: ESD appears effective and safe for treating colorectal neoplastic lesions in IBD patients. Similar results were observed between Asian and Western studies.

Keywords

Endoscopic submucosal dissection; inflammatory bowel disease, colorectal neoplasia

What You Need to Know

Background: ESD is increasingly being adopted for colorectal neoplastic lesions. However, its use in inflammatory bowel disease remains controversial due to chronic inflammation-induced submucosal fibrosis, potentially impairing procedure outcomes.

Findings: Our meta-analysis of 20 studies revealed high *en-bloc* (95.6%), R0 (64.6%) and curative resection (83.9%) rates. Moderate adverse events were reported, and 13% of cases required additional surgery.

Implications for patient care: ESD appears promising for treating colorectal neoplastic lesions in IBD, offering high resection success and acceptable safety; Similar procedure results were observed between Asian and Western regions.

1. Introduction

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is an idiopathic chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation that results from host-microbial interactions in genetically susceptible individuals[1, 2]. Left inadequately treated, the inflammatory nature of IBD can result in continuous bowel damage, with increased risk of developing colorectal cancer (CRC)[3]. Indeed, following the inflammation-dysplasia-carcinoma sequence, chronic inflammation of the colonic mucosa predisposes to the onset of dysplasia, a precursor of invasive cancer[4]. Therefore, there is a window of opportunity to reduce CRC development by identification and treatment of dysplastic lesions or CRC lesions in a stage amenable to local resection. In fact, the guidelines of the European Crohn's and Colitis Organisation (ECCO) and of the Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients (SCENIC) Consensus recommend tailored endoscopic surveillance in IBD patients[5,6], with the goal of allowing early detection and treatment of colorectal neoplastic lesions and, therefore, preventing IBD-related CRC.

Endoscopic submucosal dissection (ESD) is a minimally invasive procedure that has been demonstrated to be safe and effective to accurately treat large, superficial gastrointestinal neoplastic lesions. In particular, ESD allows *en-bloc* removal regardless of lesion size and of submucosal fibrosis, thus avoiding surgery in a large proportion of patients[7, 8, 9]. ESD is now a well-established technique of endoscopic resection in both the Asian and Western setting, particularly for esophageal, gastric and rectal lesions[7]. Nevertheless, a debate is still ongoing regarding the role of ESD on colonic lesions, particularly due to the higher risk of adverse events (AEs), longer duration of the procedure and lack of cost-effectiveness data, as compared to endoscopic mucosal resection (EMR)[10, 11]. In the particular case of patients with IBD, the colorectal submucosa often presents diffuse fibrosis due to chronic inflammation, making it difficult to obtain adequate mucosal lifting by submucosal injection and to recognize the safe submucosal depth for dissection[12]. Therefore, in these patients, the procedural risks may be higher and associated with reduced complete resection rate. Nevertheless, a growing body of evidence has been produced reporting on the use of ESD in neoplastic lesions from patients with IBD.

Taking into consideration the controversies regarding the adoption of ESD in IBD-associated colorectal neoplasia, we conducted a systematic review and meta-analysis with the aim of evaluating the frequency of ESD-related efficacy and safety outcomes in this population.

2. Materials and Methods

2.1 Search Strategy

This study was conducted following the Meta-Analyses and Systematic Reviews of Observational Studies[13] (MOOSE) guidelines. The study protocol was registered with PROSPERO under the registration number CRD420251011582. We searched MEDLINE (via Pubmed) and Web of Science from inception until January of 2025. The full search strategy was designed and conducted by four

investigators (MM, MVN, BSP, RM) and is available in Supplementary Material 1. In addition, reference lists of each included primary study and of relevant reviews were examined to identify studies missing on the initial search. We complemented our search with direct contact with experts in the field and with search for abstracts from conference papers presented in the main Gastroenterology meetings (United European Gastroenterology Week, Digestive Disease Week and American College of Gastroenterology Annual Meeting).

2.2 Study Selection

Studies were selected based on the following inclusion criteria: (1) Population: Adults (≥18 years) with a confirmed diagnosis of IBD and colorectal neoplasia, including dysplasia (low or high-grade) or carcinoma; (2) Intervention: ESD performed specifically for the treatment of colorectal neoplasia (dysplasia or carcinoma) in patients with IBD; (3) Reported Clinical Outcomes: Studies that reported on at least one of the following clinical outcomes related to ESD procedures: (a) Resection outcomes (*en-bloc* resection rate; resection margin status [R0 vs R1]); (b) Curative resection rates according to European Society of Gastrointestinal Endoscopy (ESGE) ESD guidelines (2022) criteria[7]; (c) Complication rates (major post-procedural bleeding; peri- or post-procedural perforation); (d) Local recurrence; (e) Development of metachronous Lesions; (f) Need for additional surgery after ESD (whether due to technical failure, AEs or recurrence); (4) Study Design: Cohort studies (prospective or retrospective) or case-control studies.

Two reviewers (MM and MVN) independently evaluated each study for eligibility first by title and abstract screening and then by full text reading based on the above-mentioned criteria. Any disagreements were solved by discussion. We made sure that we did not include overlap cohorts as separate studies.

2.3 Data Extraction

Data from each included primary study were extracted independently onto a standardized form by two reviewers (MM and MVN). Disagreements were solved by participation of a third (senior) author. Authors of primary studies were contacted whenever there was need for further information and/or for clarification on the data.

The following information was collected on study and population characteristics: (a) publication year, (b) country, type and center of study, (c) numbers of patients and lesions, (d) participants' distributions of age and gender, (e) type of IBD, duration, extent and severity of disease, (f) size, location and morphology of lesions, presence of submucosal fibrosis, disease activity of the surrounding mucosa, and characteristics of the lesion border. In addition, we collected data on the following outcomes: (a) *en-bloc* resection rate, (b) complete resection rate (R0 resection), (c) curative resection rate, (d) procedural time, (e) follow-up duration, (f) frequency of AEs, (g) frequency of metachronous lesions and synchronous neoplasia, (h) need for additional surgery after ESD and (i) histopathological results.

Location of lesions was divided into the right colon (including cecum, ascending colon and transverse colon), the left colon (including descending colon and sigmoid colon) and the rectum. Following the principles of the Paris

classification[14], pedunculated and sessile lesions were classified as polypoid, while superficial elevated, flat and depressed lesions were categorized as non-polypoid. In addition, laterally spreading tumors were classified as non-polypoid lesions. Endoscopic submucosal fibrosis was classified using a three-point scale: F0, F1, and F2, according to the original classification of Matsumoto A. et al.[15]. In brief, F0-F1 includes no or mild fibrosis and F2 represents substantial or severe fibrosis.

En-bloc resection was defined as the retrieval of the target lesion in a single specimen. R0 resection was considered whenever pathological evaluation showed free horizontal and vertical margins. Curative resection was defined as a R0 resection in the absence of deep submucosal invasion (≥1000 μm), lymphovascular involvement or a poorly differentiated adenocarcinoma component[7]. Post-procedural bleeding (PPB) was defined as clinically significant bleeding (hematochezia, melena, or hemoglobin decrease >2 g/dL) resulting in an emergency department visit, admission, or intervention (endoscopy, angioembolization, surgery). Delayed perforation was defined by the presence of post polypectomy coagulation syndrome symptoms with imaging or surgical evidence of full-thickness injury of the colonic wall. All AEs were classified according to the Adverse Events in Gastrointestinal Endoscopy (AGREE) Classification[16]. Local recurrence was defined as the presence of neoplastic lesion at the resection site during a follow-up colonoscopy. Synchronous and metachronous lesions were defined as new colorectal lesions in a location other than the primary lesion site, detected less and more than six months after index ESD, respectively.

2.5 Quality Assessment and Certainty of Evidence Assessment

The quality of each included study was assessed using the NIH Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies[17]. This quality score consists of 14 questions, the details of which are provided in Supplementary Table 1. Considering that 4 of the questions were deemed not applicable, we determined 10 points as the maximum quality score. Two authors (MM and MVN) did the quality scoring independently and a final score for each study was determined by discussion. We assessed the certainty of evidence for each outcome using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework[18].

2.6 Statistical Analysis

All analyses in this study were performed using the R software version 4.3, with the use of the meta package. We conducted a random-effects meta-analysis to calculate the pooled estimates for each outcome. Pooled proportions with corresponding 95% confidence intervals were calculated for categorical outcomes (we pooled log-transformed proportions, back-transforming meta-analytical results into the natural scale) and a pooled mean was calculated for the mean procedure time, a continuous outcome. The *Cochran's Q test* and *the* I^2 statistic were used to assess heterogeneity. A $p<0.10$ for the *Cochran's Q test* or an I^2 >50% were considered to represent substantial heterogeneity.

To explore sources of heterogeneity, we performed a leave-one-out sensitivity analysis. In addition, in order to explore across-regional differences in

outcomes, we performed a predetermined subgroup analysis comparing Asian and Western countries (European and North American countries). We also performed univariable meta-regression considering the year of publication, the region of origin (Asian vs. Western), the type of study (multicenter or single-center), the quality of the study and the number of lesions for characterization as independent covariates.

3. Results

3.1 Study Selection

We identified 363 studies by searching electronic bibliographic databases. Additionally, two articles were identified from reference lists of relevant reviews and one record was retrieved from direct contact with authors. After duplicates were removed, 263 studies were screened for title and abstract analysis. Of those, 39 records were selected for full-text evaluation. Of the 39 studies, 20 fulfilled the inclusion criteria and were featured in the final analysis [19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38]. A flow diagram of the systematic review study selection process is presented in Figure 1.

3.2 Characteristics of the Included Studies and Lesions

The characteristics of the included studies are shown in Table 1. The included studies were published between 2017 and 2025. Among them, three studies had a prospective design [26, 23, 28]; nine studies were multicenter [22, 32, 19, 25, 37, 23, 28, 21, 29]. Eight studies were conducted exclusively in Western countries[19, 20, 21, 26, 27, 28, 29, 32] while ten were performed in Asian countries[22, 24, 25, 30, 31, 33, 34, 35, 36, 38]. Overall, 13 studies were assessed as of good quality (≥8 out of 10 fulfilled quality criteria) [22, 23, 24, 26, 29, 30, 31, 32, 33, 34, 36, 37, 38] and seven studies were considered of fair quality (6-8 out of 10) [19, 20, 21, 25, 27, 28, 35]. No study was considered to be of poor quality. The quality assessment results are available in Supplementary Figure 1.

The assessed primary studies included a total of 565 patients, in whom a total of 732 IBD-associated colorectal neoplastic lesions were removed. More than half of patients were male (n=335; 60.9%), with the mean participants' age being of 59.5 years. Most patients had UC (n=511; 90.4%). The mean disease duration was 18.5 (SD=10.9) years and about 66.5% (n=165) of UC patients had extensive colitis. Lesions were more commonly located in the left-side of the colon (n=269; 42.9%) than in the rectum (n=210; 33.5%). The mean lesion size was 31.2 (SD=18.2) mm, with a non-polypoid morphology being evident in 87.4% (n=521) of the lesions. Severe submucosal fibrosis (F2) was present in 52.7% (n=214) of lesions. Only nine studies reported on the border of lesions, which was described as well-defined in 97.7% (351/359) of cases. The lesion characteristics are presented in Supplementary Table 2. Study outcomes for each study are summarized in Table 2.

3.3 Meta-analysis Results

The pooled frequency of *en-bloc* resection was 95.7% (95%CI=93.5-97.9%; I^2=60.1%) (Figure 2). The pooled frequencies were 84.6% (95%CI=79.4-

90.1%; I²=68.9%) for R0 resection and 83.9% (95%CI=76.3-92.4%; I²=75.9%) for curative resection (Figure 2). Performing meta-analysis restricted to studies that reported on both R0 and curative resection analysis (10 studies), we obtained pooled frequencies of 87.5% (95%CI=81.3-94.1%; I²=69.5%) for R0 resection and 83.9% (95%CI=76.3-92.4%; I²=75.9%) for curative resection. The mean procedural time was 80.5 minutes (95%CI=67.6-93.4; I²=88.7%) (Supplementary Figure 2).

The pooled frequencies of PPB and intraoperative perforation were 7.0% (95%CI=4.4- 11.2%; I²=16.9%) (Figure 3(a)) and 7.9% (95%CI=5.3-11.9%; I²=2.4%) (Figure 3(b)), respectively.

The local recurrence was 5.3% (95%CI=3.5-7.9%; I²=0%) (Figure 3(c)). The metachronous and synchronous neoplasia recurrence frequencies were 11.3% (95%CI=6.4-20.6; I²=81.6%) (Supplementary Figure 3) and 26.4% (95%CI=12.5-56.0; I²=0.0%), respectively. The pooled rate of additional surgery following ESD was 13.3% (95%CI=9.5-18.1%; I²=42.5%) (Figure 3(d)). The reasons for needing additional surgery after ESD included technical failure, AEs or recurrence. The meta-analytic results are summarized in Table 3.

3.4 Leave-one-out sensitivity analysis

For the need for additional surgery outcome, omitting Matsumoto K et al[31] resulted in a substantial decrease in heterogeneity from 40% to 0%. A similar effect was observed for the outcome PPB, where omitting Kasuga K et al[24] reduced heterogeneity from 16.9% to 0%. The impact was less pronounced for the outcome of metachronous lesions, with heterogeneity decreasing from 81% to 66% upon removal of Matsumoto K et al[31]. For the remaining outcomes, leave-one-out sensitivity analyses did not result in substantial changes of heterogeneity.

3.5 Subgroup analysis based on the region

Across all outcomes analyzed, there were no significant subgroup differences between Asian and Western regions (Table 2).

3.6 Meta-regression

Meta regression results are available in Supplementary Table 4. Overall, intraoperative perforation rates appear to be significantly increasing over the years (OR=1.162 per year (95%CI=1.019-1.324); p=0.025). Additionally, studies evaluating a larger number of lesions showed a significantly lower relative frequency of metachronous lesions (OR=0.981 per lesion (95%CI=0.966-0.998); p=0.025). No other significant results were observed in meta regression analysis.

3.7. Certainty of evidence assessment

Overall, evidence certainty was considered "low" in 4 of 10 outcomes and "very low" in the remaining outcomes. The full Certainty of Evidence Assessment is available in Supplementary Table 3.

4. Discussion

In this systematic review and meta-analysis of 20 studies, ESD appears to be a safe and efficacious procedure for the treatment of IBD associated-colorectal neoplasia. Interestingly, no differences were found between Asian and Western studies for any evaluated outcome.

The optimal treatment approach for large non-pedunculated colorectal lesions remains a subject of debate among different centers. EMR was the first to be described in the 1990s[39]. While effective for the treatment of most lesions, its ability to achieve *en-bloc* resection is limited, particularly for lesions larger than 15-20 mm, which often require piecemeal removal[7]. ESD emerged some years later, offering the advantage of enabling *en-bloc* resection regardless of lesion size, thereby reducing the risk of local recurrence. However, ESD is associated with longer procedure times, increased risk of complications (such as perforation and PPB), and higher costs. According to the 2022 ESGE Guideline[7], EMR remains the primary technique of choice, except for lesions located in the rectum or in cases with visual suspicion of superficial submucosal invasion, where alternative approaches like ESD should be considered. Along these lines, a French randomized controlled trial from 2023[40] comparing ESD and EMR in large (>25mm) non pedunculated colonic adenomas found that ESD was associated with a lower risk for early recurrence (at 6 months) but at the cost of a greater risk of AEs. In fact, this study demonstrated that if the entire cohort had undergone ESD, the number needed to treat to prevent one surgery for cancer would have been 60.

The controversy surrounding the use of ESD versus EMR for colorectal lesions increases in the specific setting of IBD-associated colorectal neoplasia. In these patients, treatment with ESD is associated with several additional challenges, including extensive submucosal fibrosis, thinner muscular layer and semilunar folds[40], which make the procedure more complex and increases the risk of AEs[34]. Additionally, there is an added difficulty in accurately defining the lesion margins. Indeed, the technical difficulties of ESD in IBD-associated colorectal neoplasia are reflected in our study by a local recurrence rate of 5.3%. This is particularly relevant considering that the same outcome in non-IBD patients could be as low as 2.0%[40, 41]. These results validate how difficult and challenging it is to delineate the lesion in patients with IBD. Furthermore, the need for additional surgery following ESD was 13.3%, further illustrating the technical challenges of the procedure in IBD-related colorectal neoplasia. It is important to notice that EMR in IBD patients is also associated with technical difficulties. Indeed, the *en-bloc* resection rate in these patients appears to be as low as 8.7%, with an 8.7% need for additional surgery and an average procedure time of 72.5 minutes[42], which is close to the value reported in our meta-analysis for ESD (80.5 min). Additionally, in IBD patients undergoing EMR, the local recurrence rate is even higher than in sporadic colorectal neoplasia (30.4% vs. 20.9%)[42]. This is likely attributable to the lower EMR *en-bloc* resection rate in IBD patients, although the pathophysiological nature of the underlying disease process may further promote recurrent neoplasia to a greater extent than in non-IBD cases[42]. Therefore, considering the current body of evidence, ESD may play an important role in these cases, particularly in lesions in which a complete *en-bloc* resection or a clear definition of the resection borders is not possible.

Our study demonstrated outcomes consistent with previous studies on the matter. Compared with previous systematic reviews, it included a larger number of studies, with more than twice the number of evaluated lesions, a broader geographical representation and more robust methods to explore sources of heterogeneity and assess the quality of the body of evidence, making it the most comprehensive analysis of ESD efficacy and safety in IBD-associated colorectal neoplasia to date. Malik et al.[43] analyzed 291 IBD-associated lesions and performed subgroup and meta-regression analysis, but their limited Western representation may have affected the robustness of their regional comparison. In contrast, our study includes greater representation of Western studies, allowing for a more reliable comparison between Asian centers and those in Europe and North America. Zeng et al[44] examined 192 UC-associated lesions and did not conduct subgroup or meta-regression analysis, limiting their ability to explore heterogeneity. Our study, in contrast, includes both UC and CD patients and we performed sensitivity, subgroup and meta-regression analyses, offering a more robust insight into outcome variability. Manta et al[28] conducted a systematic review following a case series, however, the absence of metanalysis limited quantitative synthesis.

Our sensitivity analysis found that the study by Matsumoto et al[31] decisively contributed for the heterogeneity of the need for additional surgery and metachronous lesions and that the study by Kasuga et al[24] significantly contributed to the PPB summary estimate heterogeneity. Both these studies[24,24] comprised cohorts of less than 10 patients. Indeed, the reduced sample size of these two studies increases the susceptibility to “more extreme results” due to random variation, potentially leading to a higher heterogeneity.

Our subgroup analysis provided furthers insights by comparing Asian and Western outcomes. We found no differences in ESD outcomes between these regions, suggesting that, although ESD originated in Asia, similar outcomes may be achieved in the Western setting. Nevertheless, it should be noted that a selection and publication bias may be present, since most of the Western studies are from specialized expert centers. In fact, although a direct comparison cannot be established, the Western outcomes in the current study were superior to those reported on the latest meta-analysis on colorectal ESD on the Western setting (including mostly patients without IBD), with higher rates of *en-bloc* (93.1% vs. 84.6%), R0 (85.7%. vs. 75.6%) and curative resection (86.5%. 81.9%), albeit with higher rate of perforation (7.6% vs. 5.5%) and need for surgery (13.3% vs. 1.8%)[45]. Therefore, these results should be interpreted with caution, before a widespread adoption of this technique in this specific population can be recommended.

Regarding meta-regression results, intraoperative perforation rates appear to be significantly increasing over the years. We hypothesize that this may be attributed to the treatment of increasingly complex lesions and to a rise in the number of reported AEs. Additionally, our results found that studies evaluating a larger number of lesions detected a significantly lower relative frequency of metachronous lesions, likely due to the previously discussed fact that most studies were from ultra-specialized centers. Although sensitivity and meta-regression analyses provided valuable insights, these assessments do not always capture whether variability between studies truly impacts clinical approach.

This study has some limitations that should be acknowledged. Firstly, there is the possibility of publication biases, potentially resulting in the non-inclusion of relevant primary studies. To minimize the impact of such biases, we conducted an extensive literature search in bibliographic databases, which was complemented with other strategies. For instance, abstracts from conference papers were included, as these often contain preliminary or unpublished data. In addition, reference lists of each included article and relevant review articles were examined and direct contact with authors was also established.

Another limitation is the substantial unexplained heterogeneity which was observed for most outcomes. This may possibly be attributable to multiple factors, which we were not fully able to evaluate (in particular, due to lack of information at a patient level), including variability in patient characteristics, such as disease severity, comorbidities, and prior treatments. In addition, differences in the center's expertise, inconsistency in outcome definitions and variability in sample sizes, patient selection criteria, and follow-up protocols across studies may also be a contributing factor to the observed heterogeneity. In an effort to explore and understand potential sources of heterogeneity, we performed sensitivity, subgroup and meta-regression analyses. Of note, more recent methods exist to quantify heterogeneity, considering the relative importance of the different outcomes based on predefined decision thresholds (i.e., providing some clinical context to the quantification of heterogeneity[46]). However, such thresholds have not been established for colorectal ESD, so that we were unable to apply these methods.

Furthermore, given the observational nature of the included studies, some challenges arise. Firstly, information regarding the criteria of lesion selection, the degree of submucosal fibrosis, the surrounding mucosa and the clarity of lesion borders could not be retrieved from all studies. Secondly, not all studies reported on all studied outcomes. Lastly, we must acknowledge the predominance of UC cases over CD (90% vs 10%) in our study. This imbalance was somewhat expected given the discontinuous nature of CD, which makes it challenging to distinguish IBD-related colorectal neoplasia and contributes to fewer studies in this subgroup. Nevertheless, the limited representation of CD patients may affect the generalizability of our findings to the broader IBD population. Therefore, further studies including a larger proportion of patients with CD are needed to better elucidate the applicability of ESD in this subgroup.

Our study also has several strengths. The literature search was rigorously performed to include all studies that used ESD for IBD-associated colorectal neoplasia, with no low-quality studies included in our analysis. This is also the most recent meta-analysis evaluating outcomes of ESD technique for colorectal dysplasia in IBD, with the highest number of patients and lesions. In addition, our study provides the largest representation of Western studies so far. In fact, our analysis includes about 321 IBD-associated lesions that underwent ESD in Asian centers and 369 in Western ones, allowing a balanced comparison of the technique's outcomes across different regions.

In conclusion, this systematic review meta-analysis provides strong evidence supporting the efficacy and safety of ESD in patients with IBD-related colorectal neoplasia. Our study demonstrates high rates of successful resection with low AEs rates and local recurrence. Nevertheless, the need for additional surgery is non-negligible. Despite promising results from the current study, with similar observed outcomes between Asian and Western settings, adequate

patient selection and training in ESD is of paramount importance, before this technique can be widely recommended.

Figures and Tables

Supplementary Material

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Figure 1. Flow diagram of the included studies

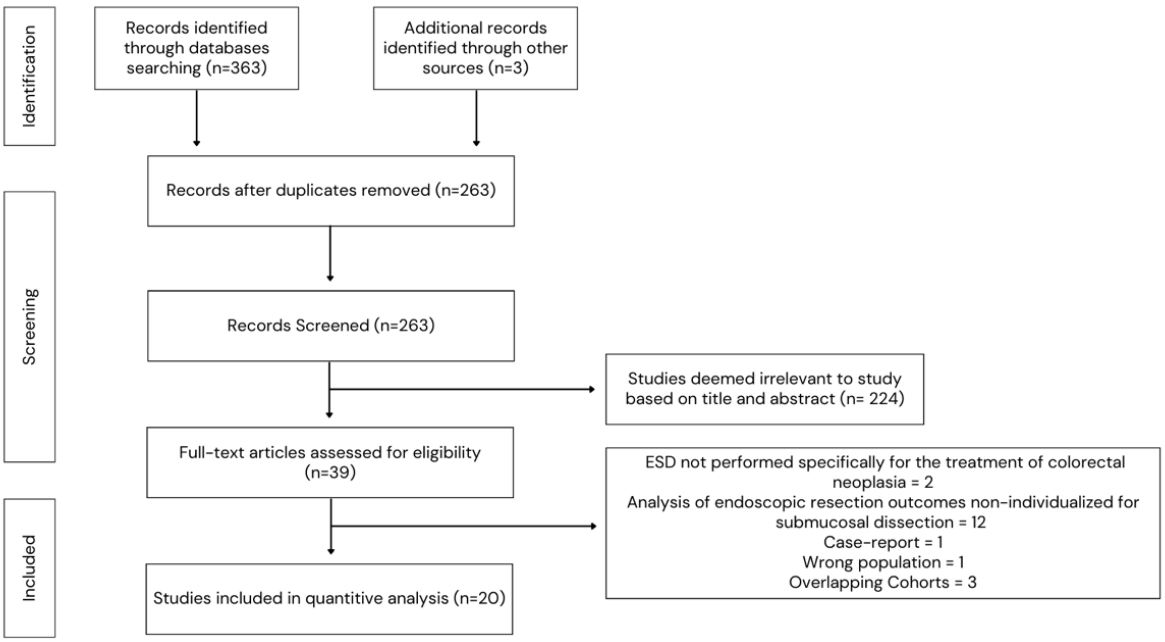


Table 1. Study and population characteristics

Study	*Type and Center of Study*	*Quality Score*	*Patients (n)*	*Male (n) [%]*	*Mean Age (y) [SD]*	*Mean Disease Duration (y) [SD]*	*Type of IBD (n, UC/CD)*	*Extent of colitis (n, E/L/P)*	*CD involvement (n, Sb/C/P)*
Alkandari A et al.[19] (2019), UK, Italy and Poland	Retrospective, Cohort, Multicenter	7/10	NA	NA	NA	NA	NA	NA	NA
Dalal RS et al.[20] (2020), US	Retrospective, Cohort, Single-center	5/10	12	7 [58.3]	63.2 [3.3]	NA	11/1	NA	NA
Geyl S et al.[21] (2025), France	Retrospective, Cohort, Multicenter	7/10	82	50 [61.0]	62.0 [13.0]	22.0 [12.0]	63/19	32/24/7	NA
Hirai M et al.[22] (2023), Japan	Retrospective, Cohort, Multicenter	8/10	NA	NA	NA	NA	NA	NA	NA
Iacopini F et al.[23] (2015), Italy and Japan	Prospective, Cohort, Multicenter	8/10	9	4 [44.4]	57.0 [10.2]	14.2 [3.8]	9/0	6/3/0	NA
Kasuga K et al.[24] (2021), Japan	Retrospective, Cohort, Single-center	8/10	9	4 [44.4]	62.5 [14.5]	20.7 [6.6]	9/0	7/0/2	NA
Kinoshita S et al.[25] (2018), Japan	Retrospective, Cohort, Multicenter	7/10	25	18 [72.0]	61.0 [11.0]	19.0 [9.0]	25/0	19/3/2	NA
Kochhar G et al.[26] (2018), US	Prospective, Cohort, Single-center	8/10	7	5 [71.4]	54.0 [17.0]	NA	5/2	NA	NA
Lightner AL et al.[27] (2021), US	Retrospective, Cohort, Single-center	7/10	25	19 [76.0]	61.3 [13.4]	22.7 [22.8]	16/9	6/9/0	9/9/1
Manta et al.[28] (2021), Italy	Prospective, Cohort, Multicenter	6/10	53	31 [58.5]	58.5 [11.0]	15.2 [3.7]	53/0	30/NA/NA	NA
Maselli R et al.[29] (2025), Italy	Retrospective, Cohort, Multicenter	8/10	91	53 [58.2]	60.8 [12.5]	15.3 [8.7]	76/15	NA	NA
Matsui A et al.[30] (2021), Japan	Retrospective, Case-control, Single-center	8/10	12	6 [50.0]	59.0 [15]	20.0 [11.0]	12/0	10/2/0	NA
Matsumoto K et al.[31] (2019), Japan	Retrospective, Case-control, Single-center	8/10	7	5 [71.0]	53.0 [8.2]	15.5 [6.3]	7/0	4/2/1	NA
Ngamruengphong S et al.[32] (2022), US	Retrospective, Cohort, Multicenter	8/10	41	25 [61.0]	60.0 [11.0]	25.2 [12.2]	33/8	NA	NA
Nishio M et al.[33] (2020), Japan	Retrospective, Case-control, Single-center	8/10	39	22 [56.0]	55.2 [3.7]	16.0 [5.0]	39/0	30/0/9	NA
Nishio M et al.[34] (2024), Japan	Retrospective, Cohort, Single-center	9/10	55	34 [62.0]	53.5 [15.0]	17.8 [9.2]	55/0	38/17/0	NA
Park S et al.[35] (2023), South Korea	Retrospective, Cohort, Single-center	7/10	36	24 [66.7]	NA	NA	36/0	NA	NA
Sakurai T et al.[36] (2020), Japan	Retrospective, Cohort, Single-center	8/10	15	NA	NA	NA	15/0	NA	NA
Suzuki N, et al.[37] (2017), UK and Japan	Retrospective, Cohort, Multicenter	8/10	32	18 [56.0]	66.2 [9.2]	20.5 [10.0]	32/0	NA	NA
Yang DH et al.[38] (2019), South Korea	Retrospective, Case-control, Single-center	8/10	15	10 [66.7]	57.2 [13.6]	12.7 [5.5]	15/0	13/2/0	NA

UC, ulcerative colitis; CD, Crohn's disease; E, extensive colitis; L, left-sided colitis; P, proctitis; Sb, small bowel involvement, C, colonic involvement; P, perianal disease; NA, not available

Table 2. Study Outcomes

Study	Mean procedure time (min) [SD]	Enbloc resection (n) [%]	R0 resection (n) [%]	Curative resection (n) [%]	PPB (n) [%]	PPB (n, AGREE I or II/ AGREE III/ AGREE IV/ AGREE V)	Intraoperative Perforation (n) [%]	Delayed Perforation (n) [%]	Perforation (n, AGREE I or II/ AGREE III/ AGREE IV/ AGREE V)	Mean Follow-up time (months) [SD]	Local Recurrence (n) [%]	Metachronous Lesions (n) [%]	Synchronous neoplasia (n) [%]	Need for additional surgery (n) [%]	Histopathology
Alkandari A et al.[19] (2019)	NA	27 [65.9]	NA	NA	NA	NA	NA	NA	NA	57.7 [18.2]	NA	NA	NA	NA	NA
Dalal RS et al.[20] (2020)	NA	12 [100.0]	8 [66.7]	NA	0 [0.0]	0/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	NA	1 [11.1]	NA	NA	1 [8.3]	SSA 0, Adenoma/LGD/HGD 9, Adenocarcinoma 2, IND 1
Geyl S et al.[21] (2025)	86.2 [52.8]	80 [88.9]	72 [80.0]	70 [78.0]	7 [7.7]	NA	13 [14.4]	0	0/13/0/0	23.9 [5.7]	6 [6.6]	10 [11.0]	NA	14 [17.1]	SSA 0, Adenoma/LGD/HGD 41, Adenocarcinoma 0, IND 2
Hirai M et al.[22] (2023)	NA	93 [96.8]	NA	NA	NA	NA	NA	6 [6.2]	NA	34.9 [NA]	NA	2 [2.1]	NA	NA	SSA 12, Adenoma/LGD/HGD 34, Adenocarcinoma 48, IND 0
Iacopini F et al.[23] (2015)	75.2 [25.7]	8 [80.0]	8 [80.0]	7 [70.0]	1 [10.0]	0/1/0/0	0 [0.0]	0 [0.0]	0/0/0/0	31.5 [19.5]	0 [0.0]	NA	NA	1 [10.0]	SSA 1, Adenoma/LGD/HGD 7, Adenocarcinoma 2, IND 0
Kasuga K et al. (2021)[24]	112.5 [41.6]	10 [90.9]	9 [81.8]	9 [81.8]	3 [27.2]	NA	0 [0.0]	0 [0.0]	0/0/0/0	45.7 [39.7]	0 [0.0]	2 [22.0]	NA	1 [11.1]	SSA 2, Adenoma/LGD/HGD 8, Adenocarcinoma 1, IND 0
Kinoshita S et al.[25] (2018)	72.0 [54.0]	25 [100.0]	19 [76.0]	14 [56.0]	0 [0.0]	0/0/0/0	1 [4.0]	0 [0.0]	NA	32.5 [18.0]	0 [0.0]	1 [4.0]	NA	5 [20.0]	SSA 0, Adenoma/LGD/HGD 11, Adenocarcinoma 14, IND 0
Kochhar G et al.[26] (2018)	NA	6 [85.7]	NA	NA	0 [0.0]	0/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	24.0 [NA]	0 [0.0]	NA	NA	1 [14.2]	SSA 2, Adenoma/LGD/HGD 5, Adenocarcinoma 0, IND 0
Lightner AL et al.[27](2021)	43.7 [33.0]	22 [88.0]	23 [92.0]	NA	NA	NA	1 [4.0]	NA	0/1/0/0	24.5 [11.5]	0 [0.0]	NA	NA	3 [12.0]	SSA 0, Adenoma/LGD/HGD 17, Adenocarcinoma 3, IND 5
Manta et al.[28] (2021)	NA	53 [100.0]	51 [96.2]	51 [96.2]	7 [13.2]	0/7/0/0	3 [5.6]	NA	0/3/0/0	35 [13.5]	0 [0.0]	2 [3.8]	NA	2 [3.8]	SSA 4, Adenoma/LGD/HGD 37, Adenocarcinoma 4, IND 0
Maselli R et al.[29] (2025)	86.0 [14.0]	92 [95.9]	82 [85.4]	80 [83.3]	4 [4.2]	0/4/0/0	7 [7.3]	1 [1.0]	1/7/0/0	23.4 [16.1]	3 [3.1]	3 [3.1]	NA	11 [11.5]	SSA 14, Adenoma/LGD/HGD 68, Adenocarcinoma 14, IND 7
Matsui A et al. [30] (2021)	155.0 [133.0]	17 [100.0]	12 [70.6]	12 [70.6]	0 [0.0]	0/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	24.7 [23.6]	0 [0.0]	1 [8.3]	3 [25]	1 [8.3]	SSA 0, Adenoma/LGD/HGD 10, Adenocarcinoma 7, IND 0
Matsumoto K et al.[31] (2019)	52.5 [14.5]	10 [83.3]	8 [66.7]	8 [66.7]	0 [0.0]	0/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	175.2 [56.9]	0 [0.0]	5 [71.0]	2 [29]	4 [57.1]	SSA 0, Adenoma/LGD/HGD 12, Adenocarcinoma 0, IND 0
Ngamruengphong S et al.[32] (2022)	94.0 [43.6]	43 [95.5]	34 [75.5]	NA	4 [9.8]	2/2/0/0	1 [2.4]	0 [0.0]	0/1/0/0	21.5 [6.0]	1 [2.6]	11 [31.4]	NA	3 [8.6]	SSA 4, Adenoma/LGD/HGD 37, Adenocarcinoma 4, IND 0
Nishio M et al.[33] (2020)	67.0 [47.0]	38 [97.4]	38 [97.4]	38 [97.0]	0 [0.0]	0/0/0/0	4 [10.0]	0 [0.0]	4/0/0/0	41.2 [11.7]	0 [0.0]	2 [5.4]	NA	4 [12.1]	SSA 9, Adenoma/LGD/HGD 30, Adenocarcinoma 0 IND 0
Nishio M et al.[34] (2024)	74.5 [44.5]	54 [98.1]	53 [96.3]	52 [94.5]	0 [0.0]	0/0/0/0	9 [16.0]	1 [2.0]	9/1/0/0	17.3 [8.4]	0 [0.0]	NA	NA	4 [7.3]	SSA 8, Adenoma/LGD/HGD 46, Adenocarcinoma 1, IND 0
Park S et al.[35] (2023)	NA	22 [88.9]	28 [77.8]	NA	NA	NA	NA	0 [0.0]	0/0/0/0	46.0 [30.0]	3 [9.6]	7 [22.6]	NA	5 [13.8]	NA
Sakurai T et al.[36] (2020)	NA	NA	NA	NA	0 [0.0]	0/0/0/0	NA	NA	NA	NA	0 [0.0]	1 [7.7]	NA	NA	SSA 4, Adenoma/LGD/HGD 11, Adenocarcinoma --, IND 2
Suzuki N, et al.[37] (2017)	117.5 [71.0]	29 [90.6]	23 [71.8]	NA	1 [3.0]	1/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	37.0 [17.5]	1 [3.0]	3 [11.5]	NA	4 [12.5]	SSA 0, Adenoma/LGD/HGD 26, Adenocarcinoma 4, IND 2
Yang DH et al.[38] (2019)	62.0 [NA]	14 [93.3]	12 [80.0]	NA	0 [0.0]	0/0/0/0	0 [0.0]	0 [0.0]	0/0/0/0	25.9 [17.6]	2 [14.3]	2 [14.3]	NA	1 [7.1]	SSA 1, Adenoma/LGD/HGD 11, Adenocarcinoma 2, IND 1

PPB, post-procedural bleeding; SSA, sessile serrated adenoma/lesion; LGD, low-grade dysplasia: HGD, high-grade dysplasia; IND, indefinite/negative for dysplasia; NA, not available

Figure 2. Forest Plots for *en-bloc*, R0 and curative resections

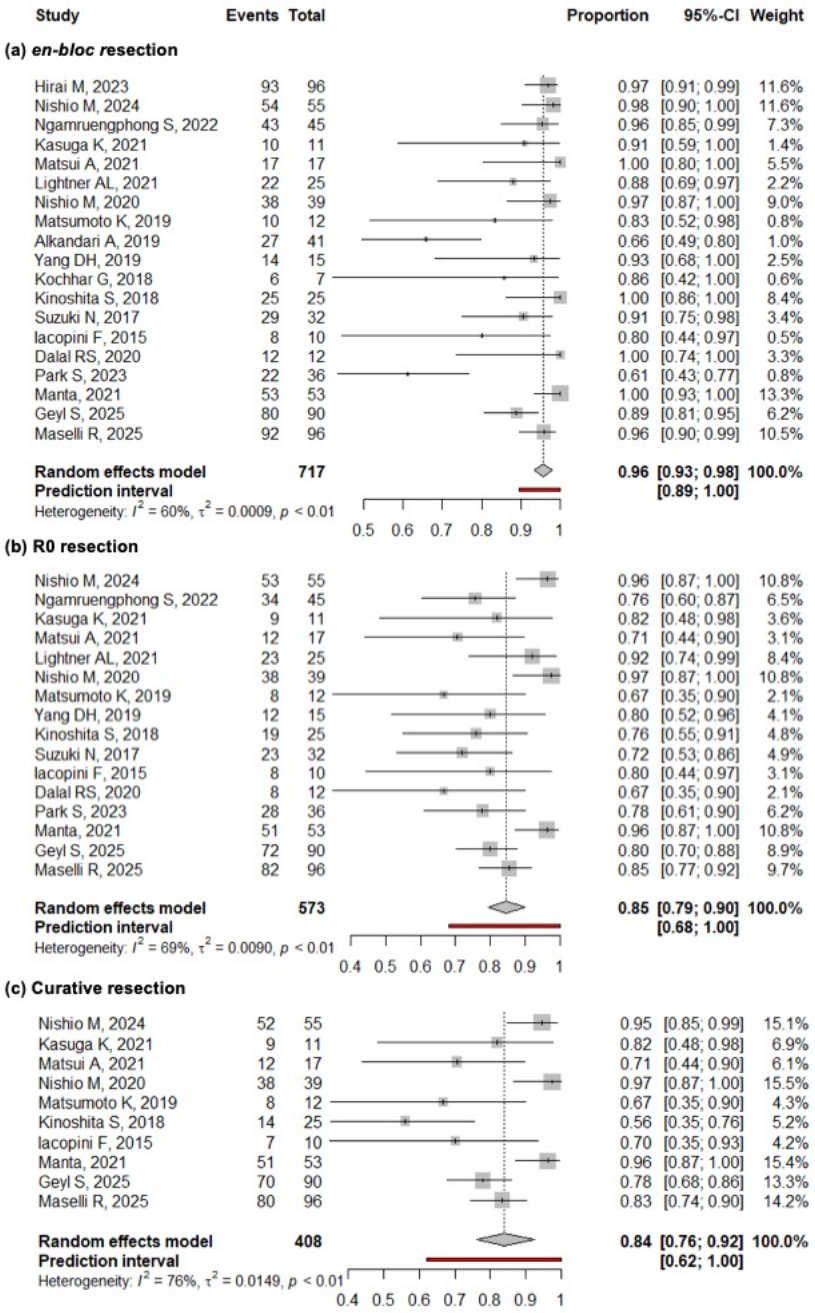


Figure 3. Forest Plots for post-procedural bleeding, intraoperative perforation, local recurrence and need for additional surgery

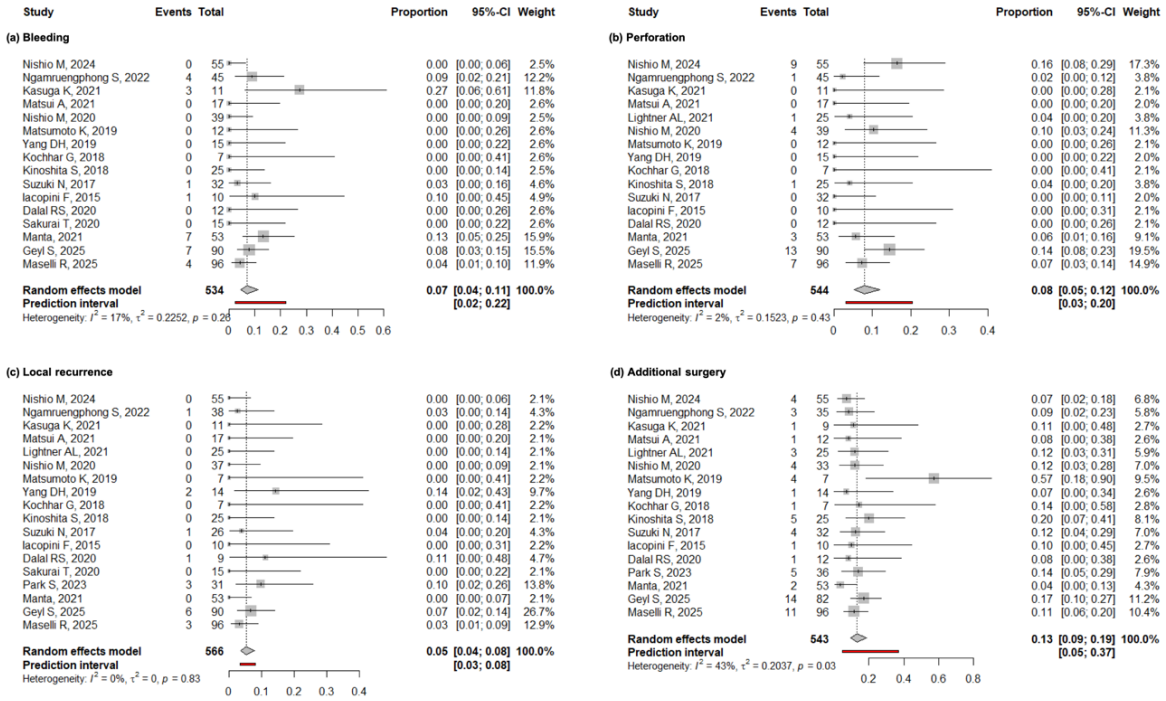


Table 3. Summary of pooled rates and Subgroup Analysis

Outcome	***Overall pooled frequency*** *(95% confidence interval); [I²; heterogeneity]; [no. of studies]*	***Asian pooled frequency*** *(95% confidence interval); [I²; heterogeneity]; [no. of studies]*	***Western pooled frequency*** *(95% confidence interval); [I²; heterogeneity]; [no. of studies]*	***p-value***
Enbloc resection	95.7 (93.5-97.9); [60.1]; [19]	97.4 (95.5-99.4); [50.7]; [9]	93.1 (87.9-98,6); [72.8]; [8]	0.1394
R0 resection	84.6 (79.4-90.1); [68.9]; [16]	84.6 (76.2-93.9); [64.2]; [8]	85.7 (78.8-93,3); [73.8]; [6]	0.8440
Curative resection	83.9 (76.3-92.4); [75.9]; [10]	80.9 (68.1-96.0); [71.5]; [6]	86.5 (75.9-97.6); [87.2]; [3]	0.5671
Mean procedure time	80.5 (67.6-93.4); [88.7]; [12]	77.9 (58.6-97.3); [79.8]; [6]	77,7 (55.7-99.6); [92.7]; [4]	0.9841
Pos-procedural bleeding	7.0 (4.4-11.2); [16.9]; [16]	---	---	---
Intraoperative Perforation	7.9 (5.3-11.9); [2.4]; [16]	9.3 (4.9-17.5); [0.0]; [7]	7.6 (4.4-13.2); [19.4]; [7]	0.6444
Local Recurrence	5.3 (3.5-7.9); [0.0]; [18]	6.0 (3.0-11.9); [0.0]; [9]	4.8 (2.8-8.2); [0.0]; [7]	0.6119
Metachronous lesions	11.3 (6.4-20.6); [81.6]; [14]	12.3 (5.6-26.9); [81.7]; [9]	9.2 (3.1-2.7); [85.5]; [4]	0.6742
Synchronous neoplasia	26.4 (12.5-56.0); [0.0]; [2]	---	---	---
Need for additional surgery	13.3 (9.5-18.1); [42,5]; [17]	15.4 (8.6-27.7); [63.0]; [8]	12.1 (8.5-17.1); [0.0]; [7]	0.4799

Supplementary Material

Supplementary Material 1. Literature search strategy (QUERY)

For MEDLINE (PubMed)

(("Inflammatory Bowel Diseases"[MeSH] OR "Inflammatory Bowel Disease"[Title/Abstract] OR "IBD"[Title/Abstract]
OR "Ulcerative Colitis"[MeSH] OR "Ulcerative Colitis"[Title/Abstract] OR "Proctocolitis"[Title/Abstract] OR "Proctosigmoiditis"[Title/Abstract] OR "Left-sided Colitis"[Title/Abstract]
OR "Crohn's Disease"[MeSH] OR "Crohn's Disease"[Title/Abstract] OR "Crohn Disease"[Title/Abstract] OR "Regional Enteritis"[Title/Abstract] OR "Terminal Ileitis"[Title/Abstract] OR "Ileocolitis"[Title/Abstract] OR "Indeterminate Colitis"[Title/Abstract])
AND
("Endoscopic Submucosal Dissection"[MeSH] OR "Endoscopic Submucosal Dissection"[Title/Abstract] OR "ESD"[Title/Abstract]
OR "Endoscopic Resection"[Title/Abstract] OR "Endoscopic Treatment"[Title/Abstract] OR "Endoscopic Mucosal Resection"[MeSH] OR "EMR"[Title/Abstract]
OR "Therapeutic Endoscopy"[MeSH] OR "Endoscopic Surgery"[MeSH] OR "Endoscopic Surgery"[Title/Abstract])
AND
(("Colorectal Lesions"[MeSH] OR "Colorectal Neoplasms"[MeSH] OR "Colorectal Lesion"[Title/Abstract] OR "Colorectal Lesions"[Title/Abstract]
OR "Colorectal Neoplasm"[Title/Abstract] OR "Colorectal Neoplasms"[Title/Abstract] OR "Colorectal Tumor"[Title/Abstract] OR "Colorectal Tumour"[Title/Abstract]
OR "Colorectal Cancer"[Title/Abstract] OR "Colorectal Cancers"[Title/Abstract]
OR "Colon Lesion"[Title/Abstract] OR "Colon Lesions"[Title/Abstract] OR "Colon Neoplasm"[MeSH] OR "Colon Neoplasms"[MeSH]
OR "Colon Tumor"[Title/Abstract] OR "Colon Tumour"[Title/Abstract] OR "Colon Cancer"[Title/Abstract] OR "Colon Cancers"[Title/Abstract]
OR "Rectal Lesion"[Title/Abstract] OR "Rectal Lesions"[Title/Abstract] OR "Rectal Neoplasm"[MeSH] OR "Rectal Neoplasms"[MeSH]
OR "Rectal Tumor"[Title/Abstract] OR "Rectal Tumour"[Title/Abstract] OR "Rectal Cancer"[Title/Abstract] OR "Rectal Cancers"[Title/Abstract])
OR ("Dysplasia"[MeSH] OR "Dysplasia"[Title/Abstract] OR "Colorectal Dysplasia"[Title/Abstract])))

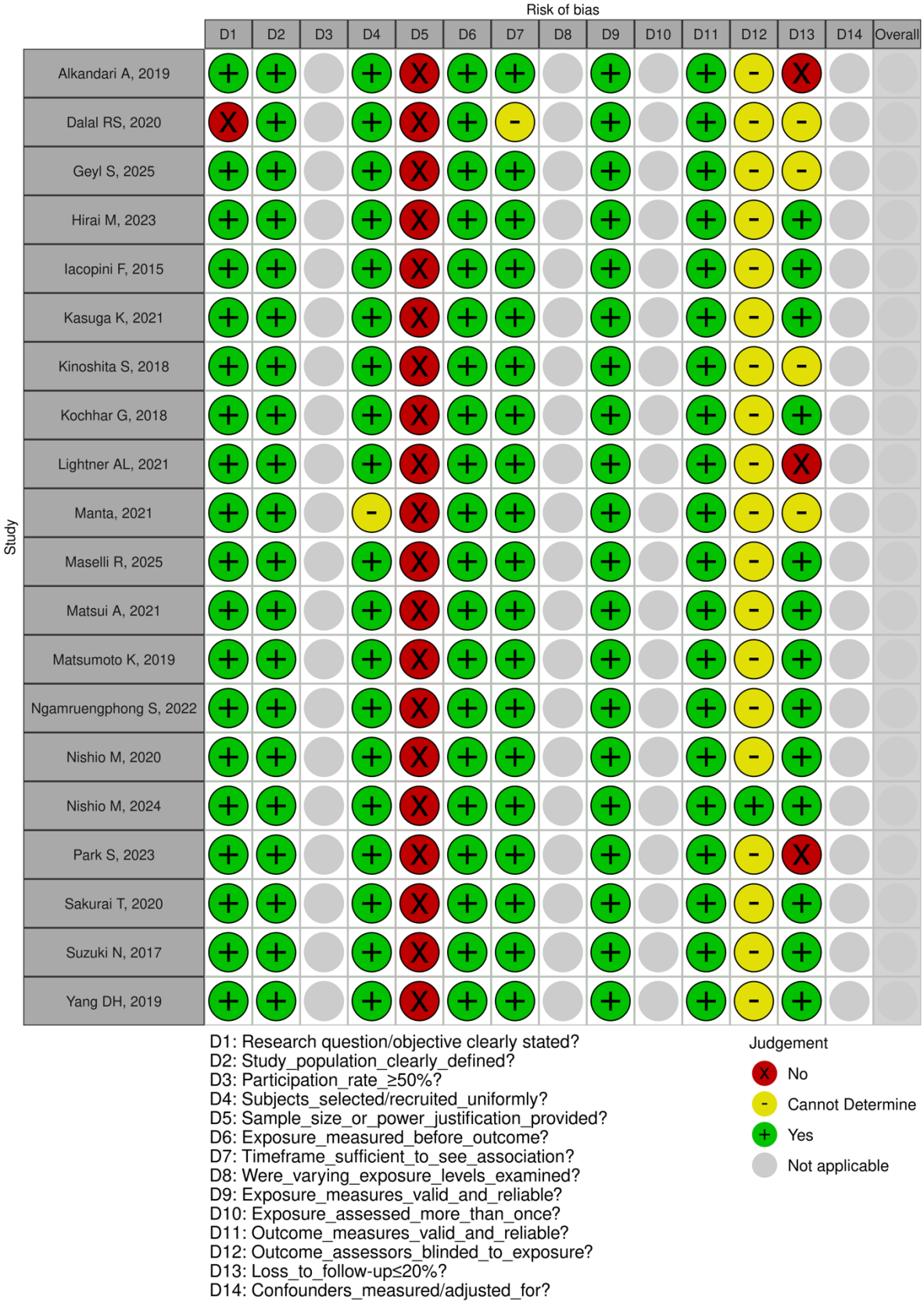
For Web of Science

TS= ("Inflammatory Bowel Disease" OR "IBD"
OR "Ulcerative Colitis" OR "Proctocolitis" OR "Proctosigmoiditis" OR "Left-sided Colitis"
OR "Crohn's Disease" OR "Crohn Disease" OR "Regional Enteritis" OR "Terminal Ileitis" OR "Ileocolitis" OR "Indeterminate Colitis")
AND
TS= ("Endoscopic Submucosal Dissection" OR "ESD"
OR "Endoscopic Resection" OR "Endoscopic Treatment" OR "Endoscopic Mucosal Resection" OR "EMR"
OR "Therapeutic Endoscopy" OR "Endoscopic Surgery")
AND
TS= ("Colorectal Lesion" OR "Colorectal Lesions" OR "Colorectal Neoplasm" OR "Colorectal Neoplasms"
OR "Colorectal Tumor" OR "Colorectal Tumour" OR "Colorectal Cancer" OR "Colorectal Cancers"
OR "Colon Lesion" OR "Colon Lesions" OR "Colon Neoplasm" OR "Colon Neoplasms"
OR "Colon Tumor" OR "Colon Tumour" OR "Colon Cancer" OR "Colon Cancers"
OR "Rectal Lesion" OR "Rectal Lesions" OR "Rectal Neoplasm" OR "Rectal Neoplasms"
OR "Rectal Tumor" OR "Rectal Tumour" OR "Rectal Cancer" OR "Rectal Cancers"
OR "Dysplasia" OR "Colorectal Dysplasia")

Supplementary Table 1. Quality Score Assessment

Study	Research question/objective clearly stated?	Study population clearly defined?	Participation rate ≥50%?	Subjects selected/recruited uniformly?	Sample size or power justification provided?	Exposure measured before outcome?	Timeframe sufficient to see association?	Were varying exposure levels examined?	Exposure measures valid and reliable?	Exposure assessed more than once?	Outcome measures valid and reliable?	Outcome assessors blinded to exposure?	Loss to follow-up ≤20%?	Confounders measured/adjusted for?	Overall
Alkandari A, 2019	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	No	Not applicable	Not applicable
Dalal RS, 2020	No	Yes	Not applicable	Yes	No	Yes	Cannot Determine	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Cannot Determine	Not applicable	Not applicable
Geyl S, 2025	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Cannot Determine	Not applicable	Not applicable
Hirai M, 2023	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Iacopini F, 2015	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Kasuga K, 2021	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Kinoshita S, 2018	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Cannot Determine	Not applicable	Not applicable
Kochhar G, 2018	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Lightner AL, 2021	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	No	Not applicable	Not applicable
Manta, 2021	Yes	Yes	Not applicable	Cannot Determine	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Cannot Determine	Not applicable	Not applicable
Maselli R, 2025	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Matsui A, 2021	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Matsumoto K, 2019	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Ngamruengphong S, 2022	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Nishio M, 2020	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Nishio M, 2024	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Yes	Yes	Not applicable	Not applicable
Park S, 2023	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	No	Not applicable	Not applicable
Sakurai T, 2020	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Suzuki N, 2017	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable
Yang DH, 2019	Yes	Yes	Not applicable	Yes	No	Yes	Yes	Not applicable	Yes	Not applicable	Yes	Cannot Determine	Yes	Not applicable	Not applicable

Supplementary Figure 1. Quality Score Assessment Results



Supplementary Table 2. Lesion characteristics

Study	*Lesions (n)*	*Mean Size (mm) [SD]*	*Location (n, R/L/Rt)*	*Morphology (n, P/NP)*	*Border (n, clear/unclear)*	*Surrounding mucosa (n, Remission/Active)*	*Submucosal fibrosis (n, F0-1/F2)*
Alkandari A et al. (2019)	41	NA	14/14/13	7/34	NA	NA	6/72
Dalal RS et al. (2020)	12	34.7 [17.6]	3/9/0	1/11	NA	11/1	NA
Geyl S et al. (2025)	90	42.3 [24.8]	18/31/39	12/78	NA	65/23	36/46
Hirai M et al. (2023)	96	NA	25/71/0	14/82	88/8	NA	NA
Iacopini F et al. (2015)	10	30.2 [4.1]	2/5/3	1/9	10/0	10/0	3/7
Kasuga K et al. (2021)	11	32.5 [8.8]	3/3/5	3/8	11/0	NA	7/4
Kinoshita S et al. (2018)	25	22.0 [13.0]	8/6/11	5/20	25/0	25/0	0/25
Kochhar G et al. (2018)	7	41.0 [NA]	5/2/0	NA	NA	NA	NA
Lightner AL et al. (2021)	25	30.3 [11.8]	14/5/6	NA	NA	7/18	NA
Manta et al. (2021)	53	34.5 [7.5]	NA	NA	NA	53/0	45/8
Maselli R et al. (2025)	96	34.8 [16.2]	19/34/43	10/86	96/0	54/37	NA
Matsui A et al. (2021)	17	12.0 [27.0]	2/5/10	1/16	NA	NA	NA
Matsumoto K et al. (2019)	12	14.5 [3.5]	0/5/7	2/10	12/0	10/2	NA
Ngamruengphong S et al. (2022)	45	31.7 [14.5]	7/15/23	2/43	NA	NA	27/18
Nishio M et al. (2020)	39	19.0 [11.0]	12/20/7	4/35	39/0	39/0	NA
Nishio M et al. (2024)	55	24.2 [13.2]	13/31/11	6/49	55/0	NA	28/27
Park S et al. (2023)	36	NA	NA	NA	NA	NA	NA
Sakurai T et al. (2020)	15	NA	NA	NA	NA	NA	NA
Suzuki N, et al. (2017)	32	NA	1/9/22	6/26	NA	29/3	27/5
Yang DH et al. (2019)	15	36.0 [12.2]	1/4/10	1/14	15/0	15/0	13/2

R, righ colon; L, left colon; Rt, rectum; P, polypoid; NP, nonpolypoid; F0-F1, none or mild fibrosis, F2, substantial fibrosis; NA, not available

Supplementary Table 3. Certainty of Evidence Assessment

Certainty assessment							N events / N patients (effect size)	Certainty	Importance
N studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Enbloc resection									
19	non-randomised studies	not serious	serious[a]	not serious	not serious	none	655/717 (95.7%)	⊕◯◯◯ Very low	CRITICAL
R0 resection									
16	non-randomised studies	not serious	serious[b]	not serious	not serious	none	480/573 (84.6%)	⊕◯◯◯ Very low	CRITICAL
Curative resection									
10	non-randomised studies	not serious	very serious[c]	not serious	not serious	none	342/408 (83.9%)	⊕◯◯◯ Very low	CRITICAL
Mean procedure time									
12	non-randomised studies	not serious	very serious[d]	not serious	not serious	none	-/427	⊕◯◯◯ Very low	IMPORTANT
Post Procedural-Bleeding									
16	non-randomised studies	not serious	not serious	not serious	not serious	none	27/534 (7.0%)	⊕⊕◯◯ Low	CRITICAL
Intraoperative Perforation									
16	non-randomised studies	not serious	not serious	not serious	not serious	none	39/544 (7.9%)	⊕⊕◯◯ Low	CRITICAL
Local Recurrence									
18	non-randomised studies	not serious	not serious	not serious	not serious	none	17/566 (5.3%)	⊕⊕◯◯ Low	CRITICAL
Metachronous lesions									
14	non-randomised studies	not serious	very serious[e]	not serious	serious[f]	none	52/536 (11.3%)	⊕◯◯◯ Very low	CRITICAL
Synchronous neoplasia									
2	non-randomised studies	not serious	not serious	not serious	serious[g]	none	5/19 (26.4%)	⊕◯◯◯ Very low	IMPORTANT
Need for additional surgery									
17	non-randomised studies	not serious	not serious	not serious	not serious	none	65/543 (13.3%)	⊕⊕◯◯ Low	CRITICAL

CI: confidence interval

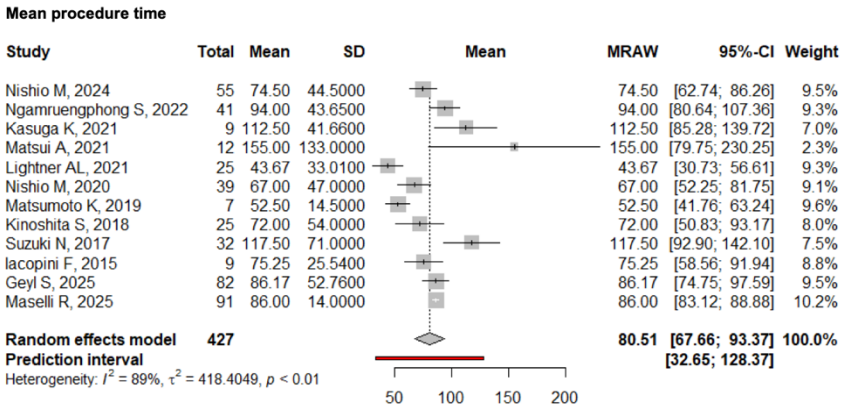
Explanations

a. High unexplained heterogeneity (I^2= 60.1%); b. High unexplained heterogeneity (I^2= 68.9%); c. Very high unexplained heterogeneity (I^2= 75.9%); d. Very high unexplained heterogeneity (I^2= 88.7%); e. Very high unexplained heterogeneity (I^2= 81.6%); f. High imprecision, as demonstrated by the wide confidence interval [95%CI=(6.4; 20.6%)]; g. High imprecision, as demonstrated by the wide confidence interval [95%CI=(12.5; 56.0%)]

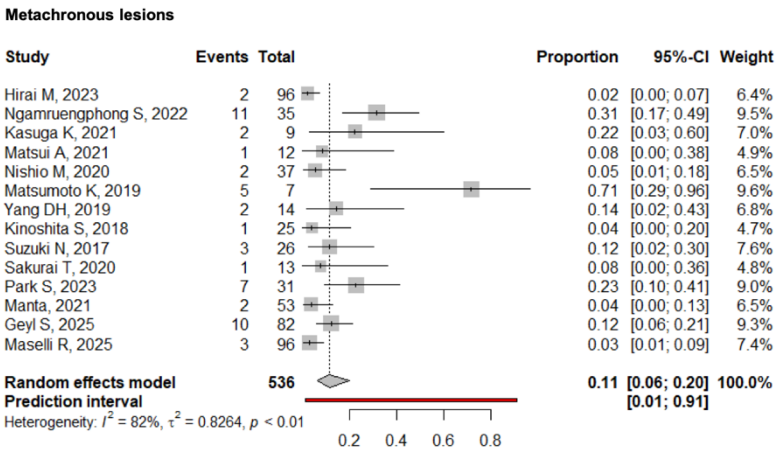
Supplementary Table 4. Meta regression Results

Outcome	*Year of Publication OR (95%CI) [p-value]*	*Region of Origin (Asian vs. Western) OR (95%CI) [p-value]*	*Type of Study (Multicenter or Single-center) OR (95%CI) [p-value]*	*Quality of the Study OR (95%CI) [p-value]*	*Number of Lesions for Characterization OR (95%CI) [p-value]*
En-bloc resection	1.001 (0.999-1.012) [0.892]	0.979 (0.932-1.029) [0.408]	1.000 (0.948-1.056) [0.987]	0.998 (0.971-1.026) [0.867]	1.000 (0.999-1.001) [0.898]
R0 resection	1.011 (0.986-1.037) [0.400]	1.001 (0.874- 1.146) [0.993]	1.051 (0.927-1.192) [0.437]	1.012 (0.940-1.090) [0.751]	1.001 (0.999-1.004) [0.281]
Curative resection	1.019 (0.98-1.059) [0.356]	1.042 (0.832- 1.306) [0.719]	1.078 (0.883-1.316) [0.461]	1.010 (0.895-1.139) [0.875]	1.001 (0.998-1.005) [0.428]
Mean procedure time	0.018 (-0.021-0.058) [0.356]	0.041 (-0.184- 0.267) [0.719]	0.075 (-0.124-0.274) [0.461]	0.010 (-0.111-0.130) [0.875]	0.001 (-0.002-0.005) [0.428]
Post Procedural-Bleeding	1.000 (0.841-1.189) [0.997]	1.456 (0.458- 4.631) [0.524]	0.839 (0.296-2.376) [0.741]	0.781 (0.458-1.331) [0.363]	0.996 (0.982-1.011) [0.610]
Intraoperative Perforation	1.162 (1.019-1.324) [0.025]	0.83 (0.356- 1.939) [0.667]	1.195 (0.510–2.799) [0.682]	1.207 (0.780-1.868) [0.399]	1.011 (0.998-1.025) [0.100]
Local Recurrence	0.990 (0.860-1.140) [0.889]	0.757 (0.327- 1.754) [0.517]	1.555 (0.697-3.469) [0.281]	0.752 (0.450-1.259) [0.279]	0.996 (0.984-1.008) [0.525]
Metachronous lesions	0.913 (0.718-1.162) [0.460]	0.751 (0.198- 2.852) [0.674]	2.410 (0.816-7.117) [0.111]	1.406 (0.535-3.692) [0.489]	0.981 (0.966-0.998) [0.025]
Synchronous neoplasia	---	---	---	---	---
Need for additional surgery	0.957 (0.849- 1.078) [0.467]	0.676 (0.326- 1.404) [0.294]	1.197 (0.603-2.378) [0.600]	0.963 (0.767- 1.209) [0.741]	1 (0.998-1.003) [0.643]

Supplementary Figure 2. Mean Procedure Time Forest Plot



Supplementary Figure 3. Metachronous Lesions Forest Plot



MOOSE Checklist for Meta-analyses of Observational Studies

Item No	Recommendation	Reported on Page No	Comments
Reporting of background should include			
1	Problem definition	10	Paragraph 2
2	Hypothesis statement	10	Paragraph 3
3	Description of study outcome(s)	11	Paragraph 8
4	Type of exposure or intervention used	10	Paragraphs 2 and 3
5	Type of study designs used	11	Paragraph 5
6	Study population	10	Paragraph 2
Reporting of search strategy should include			
7	Qualifications of searchers (eg, librarians and investigators)	10-11	Paragraph 4
8	Search strategy, including time period included in the synthesis and key words	10, Supplementary Material 1	Paragraph 4
9	Effort to include all available studies, including contact with authors	11	Paragraph 4
10	Databases and registries searched	10-11	Paragraph 4
11	Search software used, name and version, including special features used (eg, explosion)	Supplementary Material 1	-
12	Use of hand searching (eg, reference lists of obtained articles)	11	Paragraph 4
13	List of citations located and those excluded, including justification	Fig 1	-
14	Method of addressing articles published in languages other than English	Not Applicable	-
15	Method of handling abstracts and unpublished studies	11	Paragraph 4
16	Description of any contact with authors	11	Paragraph 4
Reporting of methods should include			
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	11	Paragraph 5
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	11	Paragraph 8
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	11-12	Paragraphs 7-10
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	Not Applicable	-
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	12, Supplementary Table 1, Supplementary Figure 1	Paragraph 11
22	Assessment of heterogeneity	12-13	Paragraphs 12 and 13
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	12	Paragraph 12
24	Provision of appropriate tables and graphics	Tables 1-3, Figs 2-3	-
Reporting of results should include			

25	Graphic summarizing individual study estimates and overall estimate	Fig 2, Fig 3, Supplementary Figure 2, Supplementary Figure 3	-
26	Table giving descriptive information for each study included	Table 3, Supplementary Table 2	-
27	Results of sensitivity testing (eg, subgroup analysis)	14, Table 3, Supplementary Table 4	Paragraphs 20-22
28	Indication of statistical uncertainty of findings	13-14, Table 3	Paragraphs 17-19
Reporting of discussion should include			
29	Quantitative assessment of bias (eg, publication bias)	Only qualitative analysis was performed	Paragraph 31
30	Justification for exclusion (eg, exclusion of non-English language citations)	Not Applicable	-
31	Assessment of quality of included studies	17	Paragraph 34
Reporting of conclusions should include			
32	Consideration of alternative explanations for observed results	16-17	Paragraphs 29, 30 and 32
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	16-17	Paragraphs 21 and 33
34	Guidelines for future research	17-18	Paragraphs 33 and 35
35	Disclosure of funding source	Not Applicable	-

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

Guide for Authors - Clinical Gastroenterology and Hepatology (CGH) Journal

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Systematic Reviews and Meta-analyses are solicited and unsolicited manuscripts that feature an organized and detailed review of the scientific literature about a particular topic. This section is peer-reviewed and acceptance for publication is not guaranteed. The length must not exceed 6,000 words (references are included in this word count) and a maximum combination of six tables and/or figures can be included. For meta-analyses of randomized, controlled trials, authors must provide a PRISMA checklist at manuscript submission following the PRISMA reporting guidelines found here: http://prisma-statement.org/. For meta-analyses of observational studies, authors must follow the MOOSE reporting guidelines found here: http://www.editorialmanager.com/jognn/account/MOOSE.pdf. Your manuscript will be returned to you if it does not meet these criteria.

- **Manuscript:** only **Microsoft Word** documents will be accepted.
- **Title page:** title; authors' names; authors' institutions; corresponding author contact information; conflict of interest statement **(for all authors)**; statement if data, analytic methods, and study materials will or will not be made available to other researchers. If study materials will be made available, specify where they will be made available.
- **Word count: 6,000** words (inclusive of main text, references, and table/figure legends).
- **Abstract: 260** words, structured as follows: background and aims; methods; results; conclusion; 4-5 keywords.
- **Tables/Figures: 6 tables (no panels) and/or figures (up to 6 panels) total**.
- Please submit figures as **separate attachments** in **JPEG, TIFF, EPS,** or **PDF** formats (**300 PPI** resolution).
- **Randomized Controlled Trials:** Provide **PRISMA checklist** as a supplemental attachment.
- **References:** please **list names of authors who share first authorship in bold** text. In addition, **include the phrase "Author names in bold designate shared co-first authorship" at the end of the references section**. In the references, please list names of authors who share first authorship in bold text. In addition, include the phrase "Author names in bold designate shared co-first authorship" at the end of the references section. *CGH* requires authors to cite underlying or relevant datasets in their manuscript by citing them in the text and including a data reference in the Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.
- **What You Need to Know:** This note will appear as a box on the second page of the published version of each article, containing summarizations about your study under the following 3 headings: **BACKGROUND, FINDINGS, IMPLICATIONS FOR PATIENT CARE**. Please provide **25-30 words** under each of these 3 headings that very briefly summarize your study in relation to each category.

Submission Checklist

All manuscripts should be typed in 12-point font size and double-spaced and should contain the following sections in the order given below. All manuscripts submitted to *CGH* are made available for online review. Authors should submit their manuscripts, with figures and tables, electronically via our website, http://www.editorialmanager.com/cgh. Complete instructions for online submission are located on the website.

Cover Letter

CGH strongly encourages authors to suggest three to four referees (include their e-mail address, phone, and fax numbers) and the Associate Editor they believe best qualified to review their paper. Authors may also list a non-preferred Associate Editor and non-preferred referees, but the ultimate selection of an Associate Editor and referees is at the sole discretion of the Editor and Associate Editor, respectively. A list of our current Associate Editors can be found at http://www.cghjournal.org/content/board-of-editors.

State reasons for deviations, if any, from standard format and clarify any potential conflicts related to the exclusive nature of the publication.

Cover letters must include the following 4 ICMJE required statements: 1) the paper is not under consideration elsewhere; 2) none of the paper's contents have been published previously; 3) all authors have read and approved the manuscript; 4) the full disclosure of any potential conflicts of interest or that no such relationship exists.

Title Page

Title—Use no abbreviations. Limit: 120 characters including spaces. Must state the main finding of the study. *Short Title*—Limit: 45 characters with spaces. *Authors*—Include first names of all authors and name and full location of department and institution where work was performed. *Grant Support*—List grant support and other assistance. Abbreviations—List abbreviations alphabetically. (Note: In general, the use of abbreviations is discouraged.) *Correspondence*—Provide name, complete address, e-mail address, and telephone number of corresponding author. *Disclosures*—All authors must disclose any potential conflicts (financial, professional, or personal) that are relevant to the manuscript. If the author(s) has nothing to disclose, this must be stated. *Preprint server*—If your manuscript is posted to a preprint server, you must indicate as such on the title page and include the DOI of the preprint. *Writing Assistance*—The names and funding source for individuals who provided writing assistance must be listed. *Author Contributions*—This information no longer needs to be included on the Title Page. Instead, the Corresponding Author will select from a list of roles for each co-author from CRediT Taxonomy. Detailed instructions can be found at https://www.editorialmanager.com/cgh when submitting a manuscript. *Data Transparency Statement*—statement of whether data, analytic methods, and study materials will or will not be made available to other researchers. If study materials will be made available, specify where they will be made available.

Corresponding Author Duties:

When submitting a manuscript, the Corresponding Author needs to contribute the following:

- Have an active account on editorialmanager.com/cgh with a current email address.
- Submit the manuscript with all of the steps.
- List a current email address for all co-authors, so they can confirm their roles and co-authorship for the paper.
- Respond promptly to all editorial correspondence.

Abstract

Abbreviations must be spelled out at least once. Do not use footnotes or references. Structured abstracts should be 260 words or less and include the following sections:

Background and Aims

Provide one-to-two sentences of background information to indicate why the study is interesting and important. Provide one sentence to state the main question addressed by the article.

Methods

Methods should include information on the following aspects of study design, when applicable.

- Design—describe the basic study design, e.g., randomized controlled trial, cross sectional study, cohort study, case series, survey, etc.
- Setting—specify whether the study was conducted in a primary or tertiary care setting, in an ambulatory care clinic or hospital, in the general community, etc.
- Participants—indicate the number of study subjects, how they were selected, what key features were included. What data were collected?
- Intervention—report the method of administration and duration of the intervention. Describe control groups and what methods were used to analyze the data.
- Describe main outcome measures.

For studies that are quality improvement (QI) related, authors must include a statement about IRB review. Authors must include one of the two statements: 1) This study received IRB approval and include protocol number; or 2) This study was exempt from IRB review after institutional IRB review.

Results

Describe the main findings of the study, including confidence intervals or P values. Report the absolute values and risk differences so that readers can determine the absolute, as well as the relative, impact of the results. Please be consistent in reporting either number or percentage values.

Conclusions

State conclusions that are directly supported by the evidence and the implications of the findings. For clinical trials, state the clinical trial registration web site and number (eg, ClinicalTrials.gov, Number NCT002209456).

Keywords

Include three-to-four keywords associated with your manuscript, separated by semicolons (eg, active vitamin D; parathyroid hormone-related peptide; hypercalcemia; bone resorption).

The keywords should be terms not already included in the title or abstract. Should your manuscript be accepted, the keywords will appear with the published manuscript, making it easier to find in literature search engines such as PubMed.

Please also consider including some of the keywords on DEI topics, noted below. They will not count toward the overall keyword limit.

- URM/URIM (underrepresented minorities and race and ethnic categories such as: Black/African-American; Hispanic/Latinx; Native American/Indigenous/American Indian)
- AAPI (Asian-American/Pacific Islander)
- MENA (Middle Eastern/North African)
- White/Caucasian
- Race/Racial
- Bias
- Disparities/Disparity/ Disparate/Parity
- Socioeconomic
- Equity
- Diverse/Diversity
- Unequal

- Equality
- Equal
- Income
- Gender
- Inclusion
- Status

We recommend following the SAGER guidelines for sex and gender reporting. Regarding the abstract, if only one sex is included in the study, or if the results of the study are to be applied to only one sex or gender, the title and the abstract should specify the sex of animals or any cells, tissues and other material derived from these and the sex and gender of human participants.

What You Need to Know

All revised original research submissions (including Alimentary Tract articles; Pancreas, Biliary Tract, and Liver articles; and Systematic Reviews and Meta-analyses) must include text for a "What You Need to Know" box to appear on the second page of the published article. Transfers from *Gastroenterology* must follow *CGH* guidelines. The text should include and relate to the following three headings:

- Background
- Findings
- Implications for patient care

Please provide 1-2 sentences (25-30 words) under each of these three headings that succinctly summarize your study in relation to each category. Avoid copying text from the abstract. This text should not include nonstandard abbreviations. Please upload this content in a single Word document file, separate from other manuscript materials.

Body of Paper

Introduction

We recommend following the SAGER guidelines for sex and gender reporting. Regarding the introduction, authors should report, where relevant, whether sex and/or gender differences may be expected.

Methods

We recommend following the SAGER guidelines for sex and gender reporting. Regarding the Methods, authors should report how sex and gender were taken into account in the design of the study, whether they ensured adequate representation of males and females, and justify the reasons for any exclusion of males or females.

Describe ethical guidelines followed; cite approval of institutional human research review committee or animal welfare committee; describe in detail hazardous procedures or chemicals involved, including precautions observed.

Outline statistical methods used.

Identify drugs and chemicals used by generic name (if trademarks are mentioned, manufacturer name and city are given).

All gene and protein names must be written according to NCBI or HUGO nomenclature. Official NCBI gene full names and symbols are preferred, although "Other Aliases" will be

accepted. The Editors acknowledge that exceptions to these guidelines exist, and these will be considered on a case-by-case basis.

Results

We recommend following the SAGER guidelines for sex and gender reporting. Regarding the Results, where appropriate, data should be routinely presented disaggregated by sex and gender. Sex- and gender-based analyses should be reported regardless of positive or negative outcome. In clinical trials, data on withdrawals and dropouts should also be reported disaggregated by sex.

Discussion

We recommend following the SAGER guidelines for sex and gender reporting. Regarding the Discussion, the potential implications of sex and gender on the study results and analyses should be discussed. If a sex and gender analysis was not conducted, the rationale should be given. Authors should further discuss the implications of the lack of such analysis on the interpretation of the results.

References

Cite references in order of appearance in text using superscripted Arabic numerals. Cite personal communications and unpublished data directly in text without being numbered. All abbreviations should follow the *Index Medicus* abbreviations.

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article. Follow *CGH* requirements for style:

Article (list 3 authors followed by et al):

13. Meltzer SJ, Ahnen DJ, Battifour H, et al. Protooncogene abnormalities in colon cancers and adenomatous polyps. Gastroenterology 1987;92:1174-1180.

Book:

18. Day RA. How to write and publish a scientific paper. Philadelphia: Institute for Scientific Information, 1979.

Article in Book:

22. Costa M, Furness JB, Llewellyn-Smith IF. Histochemistry of the enteric nervous system. In: Johnson LR, ed. Physiology of the gastrointestinal tract. Volume 1. 2nd ed. New York: Raven, 1987:1-40.

Dataset:

5. Oguro M, Imahiro S, Saito S, et al. Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1; 2015. http://dx.doi.org/10.17632/xwj98nb39r.1.

Tables

Tables should be prepared without the use of tabs; most table editor programs can be uploaded successfully. If your table contains decimal fractions, please round your numbers to two

places after the decimal point. Tables must be created in Word document and must not be embedded as image file. Please spell out all abbreviations used in the table in an accompanying footnote.

Figures

For additional information regarding journal guidelines for figure submissions, please see our Figure Submission FAQs. For information and examples of appropriate figure edits, please visit our author resource on Image Integrity.

- **Images**: Images can be clinical, pathologic (gross or microscopic), endoscopic, or radiographic. They should be of high quality (300 PPI or greater, clear, and in good focus) and illustrate the diagnosis well.
- **Photographs**: Remove all names and all other patient identifiers from photos and radiographic studies.
- **Line Art and Graphs**: Graphs, charts and other line art may be reformatted and/or redrawn by our Graphics staff for consistency with the overall style of the AGA Institute journals. Please be sure that any graphs or line art you submit are at a resolution of at least 300 ppi so that they are readable to reviewers.
- **Figure Legends**: Please do not embed or flatten the text into the image files. Figure legends should be included in the manuscript body, immediately before the references, or typed and submitted in .doc (Word document) or .rtf (rich text format). This text will be reformatted in the style of the AGA Institute journals.
- **Gel Electrophoresis Labels**: Protein molecular weight or DNA marker sizes must be indicated on all figure panels showing gel electrophoresis.
- **Preferred Figure File Formats**: The preferred formats for figure files are tiff (.tif) and jpeg (.jpg). For questions regarding the conversion of other file formats to .jpg or .tif, please view our Figure Submission FAQs.
- **Accepted Figure File Formats**: Other acceptable file formats include: .bmp, .gif, .pbm, .pcx, .png, .pct, .msp, .tif, .eps, .xbm, .psd, .ai, .indd, .pdf, and .tga files. When sending image files, please do not embed them in Word. You may submit mixed file formats (image1.jpg, image2.tif, image3.eps, etc).
- **Image File Formats not Supported at this Time**: Microsoft Word, Microsoft PowerPoint, Microsoft Excel Spreadsheets, ChemDraw, CorelDraw, Canvas, FreeHand, SigmaPlot, QuarkXpress, and Equation Editor. You may export image files from these programs as PDF, JPEG, or other acceptable file formats. For questions regarding the conversion of these file formats to our preferred formats, please view our Figure Submission FAQs.
- **File Naming Convention**: Figures should be named consecutively such as "figure 1.tif," "figure 2.jpg," etc, with the file extension appended (.tif, .jpg, .eps, etc). Each figure should be saved as a separate electronic file.
- **Color Files**: Figures should be submitted in the CMYK color space. Authors are encouraged to present color figures in a manner that will allow the data to be interpreted by colorblind readers. *CGH* suggests that authors present dual-labeled images in green and magenta rather than in green and red.
- **Font**: If your figures include text, an 8 to 10 point Arial font should be used. Acceptable fonts are "sans serif" fonts such as Helvetica, Arial, and Myriad. Examples of unacceptable fonts ("serif" fonts) are Times New Roman, Palatino, and Garamond. Lettering should begin with an upper case letter, followed by lower case lettering.
- **Multiple Panel Figures**: Please submit each panel (image) separately. However, you may submit a multiple panel version to suggest the order in which you would like the panels arranged. You may also include a written, suggested layout. Each individual panel should be of the highest possible quality (300 PPI or higher) at actual print size.
- **Cost**: Authors of full-length original research articles are required to pay for the printing of color figures ($650 for the first color figure and $100 each for additional figures). Authors may choose to publish their color images online-only and the print versions in black and white free of charge. Authors should upload only one set of figure files to their submission. Authors will be queried after acceptance by our publisher, Elsevier, about payment for printed color figures. Should authors not wish to pay for color figures, Elsevier will change the color figures to black and white.

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