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Colorectal endoscopic submucosal dissection in the West: A systematic review and meta-analysis

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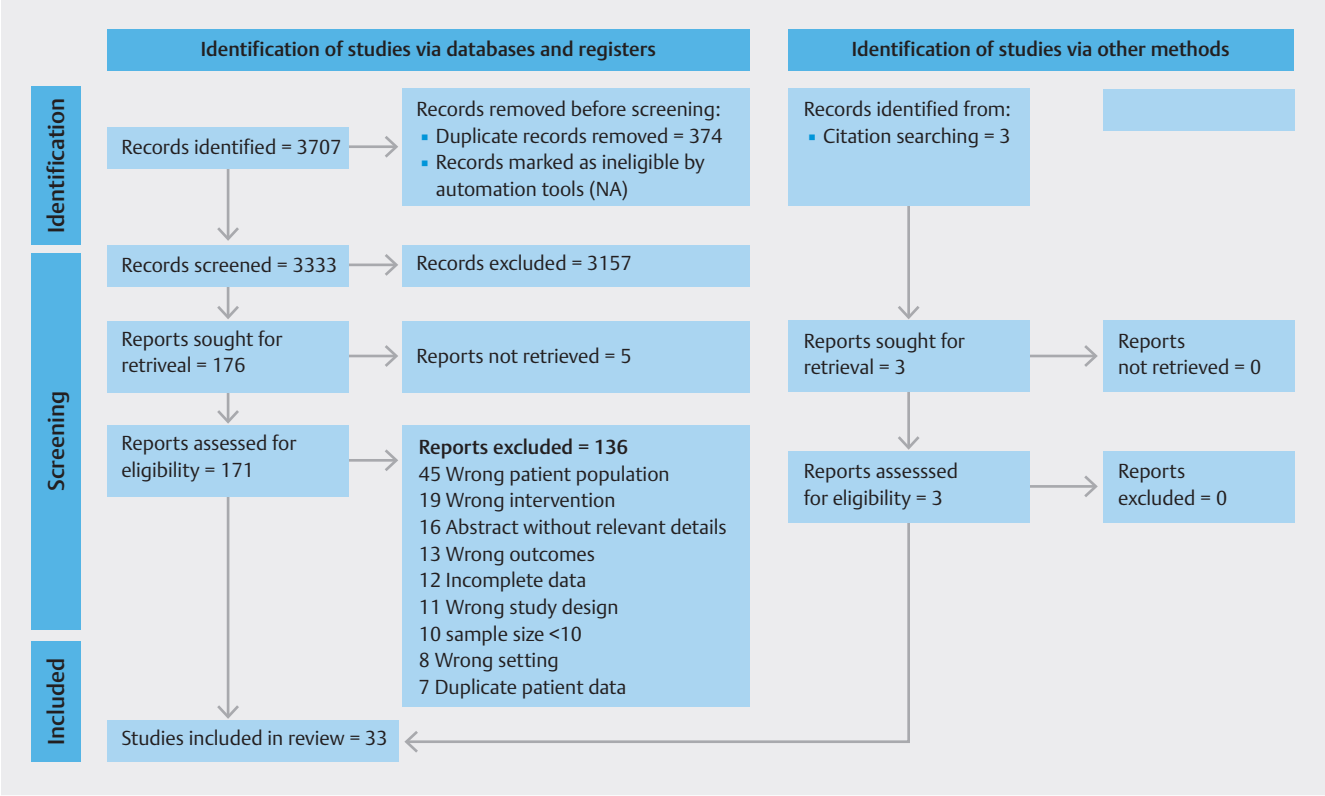
ABSTRACT

Background and study aims The advantages of endoscopic submucosal dissection (ESD) over endoscopic mucosal resection for large colorectal neoplasms are well established; however, the technical challenges and lack of adequate training in ESD limit its widespread adoption in Western countries.

Methods A literature search was performed in Medline, Embase, Web of Science, and the Cochrane Library for studies conducted in non-Asian countries evaluating the effectiveness of colorectal ESD. A random effects model was used to obtain pooled en bloc, R0 resection rates, and adverse events (AEs).

Results Thirty-three studies comprising 3,958 ESD procedures met the inclusion criteria. Of the polyps, 96.7% (2,817 of 2913) were ≥ 2 cm. Pooled en bloc resection (31 studies), R0 resection (29 studies), and curative resection rates were 84.6% (95% confidence interval [CI] [83.3%–85.9%]), 75.6% (95% CI [74.1%–77.0%]), and 81.9% (95% CI [78.6%–84.9%]), respectively. Surgery for invasive cancer was performed in 4.8% (23 studies). ESD-related perforation (25 studies) was observed in 5.5% and bleeding in 4.1% (delayed bleeding 3.4%). 1.8% of patients underwent surgery for procedure-related complications. A high degree of heterogeneity was observed for en bloc resection, R0 resection, and curative resection. Heterogeneity for AEs (perforation [I^2 13%], delayed bleeding [I^2 30%], and overall bleeding [I^2 49%]) was low to moderate.

Conclusions The effectiveness of colorectal ESD for large colorectal polyps and early colorectal cancers is improving in Western countries, and recent resection rates are comparable to that seen in Asia. Colorectal perforation is still observed in about 5% of ESD; however, < 2% of patients need emergency surgery for AEs.



▶ **Fig. 1** Study search strategy following the preferred reporting items for systematic reviews and meta-analysis (PRISMA) 2020 guidelines [10].

Introduction

Endoscopic submucosal dissection (ESD) is an advanced endoscopic resection technique developed in Japan to treat superficial upper gastrointestinal neoplasms [1]. Over the last decade, ESD has been popularized in Asia for the resection of large non-pedunculated colorectal polyps. Wide-field endoscopic mucosal resection (EMR) remains the most popular endoscopic technique for large colorectal polyps and low-risk submucosal invasive cancer in Europe and North America [2]. Both EMR and ESD offer a cost-effective treatment strategy with reduced hospital length of stay and morbidity compared to surgical treatment of these advanced colorectal mucosal neoplasms [3]. However, EMR has a much lower en bloc resection rate for larger lesions. A large multicenter study from Japan demonstrated an en bloc resection rate of < 50% for lesions > 2 cm [4].

High en bloc resection rate, low recurrence rate, and potential cure of intramucosal neoplasms make ESD an outstanding technique for large, sessile, and laterally spreading colorectal neoplasms [5]. Despite the well-established advantages of ESD over EMR for managing large and complex colorectal neoplasms, its acceptance outside of Asia lags. The excellent proficiency and outcomes in colorectal ESD in Japan and some other Asian countries are primarily accounted for by the high prevalence of gastric cancer, which provides an adequate learning opportunity for trainees to overcome the steep learning curve [6, 7]. On the contrary, several constraints, including reluctance to adopt a new technique, steep learning curve, limited availability of experts performing ESD, low incidence of gastric cancer, and a bias toward using EMR among endoscopists have impeded ESD training and its widespread application in non-Asian countries [8].

Despite the challenges, colorectal ESD is increasingly becoming popular in the United States and European countries. While previous studies have shown lower en bloc and R0 resection rates for colorectal ESD in non-Asian countries, more recent studies have demonstrated success in achieving acceptable performance levels [9]. The primary aim of the study was to evaluate R0, en bloc, and curative resection rates of colorectal neoplasms with ESD in the Western setting. We also aimed to assess the rate of ESD-related adverse events (AEs) and the need for surgery for colorectal perforation in patients undergoing ESD for colorectal neoplasms. Furthermore, we aimed to compare older studies (before 2017) with more recent studies (2017 and after), and high-volume with low-volume centers for the effectiveness of colorectal ESD and AEs associated with ESD.

Methods

Preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement 2020 was followed for reporting this review (▶ **Fig. 1**) [10]. The study was registered in the International Prospective Register of Systematic Reviews, PROSPERO (https://www.crd.york.ac.uk/PROSPERO/, registration number: CRD42021247492).

Literature search

A Johns Hopkins medical librarian (J.N.) conducted the literature search on May 11, 2021, in Medline (PubMed), Embase, Web of Science, and the Cochrane Library. Databases were searched again on August 23, 2022, for additional relevant publications since the original search. Controlled vocabulary (MeSH, Emtree) and keywords were used. The searches were limited to English language. Moreover, studies from relevant references not found in the above search were considered for inclusion.

Three main categories were included in the search, combined using the Boolean operators: 1) colorectal neoplasm; 2) endoscopic submucosal dissection; and 3) ESD. Details of the database search and search results are presented in Supplementary tables. All search results were exported to Covidence, and relevant studies were saved in a citation management tool (EndNote). The Bramer method was used to remove duplicates (Supplement tables).

Selection of manuscripts

Inclusion and exclusion criteria

Studies were considered for inclusion if ESD was used as the primary endoscopic treatment modality for colorectal neoplasms (neoplastic polyps and intramucosal carcinoma). Studies that reported en bloc and/or R0 resection rates were included in the quantitative analysis. Prospective and retrospective publications available as full text and abstracts with data on 10 or more patients were included. There was no time restriction for inclusion in the meta-analysis. Only studies published in English language were included.

Studies conducted in Asian countries (except when multicenter, including a non-Asian country) were excluded. Case series with data on fewer than 10 patients or ESD subgroups comprising less than 10 patients were excluded. Studies in which ESD was used as part of the hybrid procedure or ESD was used as salvage treatment were also excluded. In studies in which the same cohort of patients was published more than once by the same group of authors, the most recent publication with the highest number of patients was included for analysis. However, if the same authors recruited patients at different periods, each study was considered for inclusion. Studies on neuroendocrine tumors, animal models, or translational research studies, and review articles were also excluded from the analysis.

Study selection and data extraction

Two authors (RRS and NK) independently reviewed the full texts to determine study eligibility for data analysis. Any discrepancy in study selection and data extraction was resolved by common consensus. The following data were extracted from individual studies; study design and population studied, single-center or multicenter, the number of lesions treated, demographic characteristics (mean age, gender), ESD technique, tumor location, mean tumor size, mean procedure time, number of patients in follow-up, and mean follow-up duration. Data on Paris classification of colorectal neoplasms were collected when available. Lateral spreading tumors were defined as lesions > 10 mm that are relatively flat and tend to spread laterally or horizontally, as per Japanese classification. Histopathological information about the colorectal lesions was collected and categorized into low-grade dysplasia (LGD), high-grade dysplasia (HGD), intramucosal carcinoma (IM-CA), and submucosal carcinoma (SM-CA). Intramucosal carcinoma was defined as invasive carcinomas in which the invasion is confined to the lamina propria. Significant lesions, such as serrated polyps and neuroendocrine tumors (NET), were also noted.

Outcomes data abstracted were the number and proportion of tumors removed en bloc, the number of lesions with R0 resection, and the number of lesions in which an oncologically curative resection was achieved. Curative resection was defined as the lack of any positive margin, no subsequent need for surgery or other cancer treatments, and the absence of recurrence on follow-up. Data on the number of patients developing clinically significant post-procedure bleeding (varying definitions across studies: hemoglobin drop ≥ 2 g/dL, requiring hospitalization or prolongation of hospital stay, endoscopic hemostasis if delayed, or requiring transfusion), delayed bleeding (after initial 24 hours of ESD), and the number of ESD-related perforations was noted where available.

Subgroups

To compare the clinical outcomes between studies from the last 5 years and those before that, we categorized them into two groups: studies published before 2017 and those published in 2017 or after. Studies were also grouped into high-volume, and low-volume based on the volume of ESD performed. Annual performance of at ≥ 40 colorectal ESDs by an endoscopist was classified as high-volume and low-volume < 40 colorectal ESD were performed annually.

Outcomes

The primary clinical outcomes were R0, curative and en bloc resection rates following ESD for colorectal neoplasms, and ESD-related AEs (perforation rates, delayed and overall bleeding rates). Secondary outcomes were the rate of surgical intervention for ESD-related AEs and the number of surgical interventions performed following ESD for invasive cancer. Study subgroups, "before 2017" versus "2017 and after," and "high-volume" versus “low-volume” were compared for major clinical outcomes (R0, curative and en bloc resection rates, and AEs).

Statistical analysis

A simple random effects model was used to combine results from individual studies to summarize the distribution of each observation studied as recommended by DerSimonian et al [11]. A random effects model was chosen over a fixed effect model considering probable variability in sample means and the difference between the various population means. This model integrates any degree of heterogeneity in the analysis and estimates the degree of heterogeneity. A weighted estimate of the pooled data was used for all the quantitative variables. The weights were calculated as reciprocal of standard error [2] and these weights were then used to determine the final

▶ **Table 1** Characteristics of included studies.

First author	Year published	Study design	Country	N	Mean age	Mean tumor size (cm)	Mean procedure time (min)	Tumor morphology*	Histopathology (LGD, HGD, CA†)
Agapov	2014	Retrospective	Russia	44	64	3.5	120	Is 29, IIa 15	10,22,12
Azzolini	2011	Retrospective	Italy	11	56	5.9	132	Is 3, LST 8	4,7,0
Baldaque-Silva	2019	Prospective	Portugal, Sweden	43	NA	3.8	130	NA	NA
Brule	2022	Prospective	France	663	69	5.8	49	0-Is 85, IIb 566	216,376,55
Emmanuel	2018	Retrospective	UK	52	72	5.5	NA	NA	NA
Farhat	2011	Retrospective	France	85	65	NA	NA	NA	NA
Ge	2019	Retrospective	USA	77	64	4.8	105	Is 5, LST 72	0, 9, 10
Gupta	2022	Retrospective	USA	78	65	3.0	107	Is 15, IIa 56, IIc 6	15 CA
Hurlstone	2007	Retrospective	UK	42	68	NA	48	IIa 7, IIa + IIc 7, LST 28	28,12,2
Iacopini	2017	Retrospective	Italy	140	67	3.0	76	Is 15, LST 125	NA
Jacques	2019	Retrospective	France	192	67	5.4	103	Ip 13, LST 157	59, 73, 51
Kimura	2021	Retrospective	Brazil	71	66	6.8	176	Is 6, IIa 65	20,0, 51
Maselli	2019	Retrospective	Italy	136	68	4.0	85	Is 25, LST 97	29, 33, 60
Milano	2018	Retrospective	USA, Italy	23	66	2.6	120	Is 6, IIa 17	3 CA
Nugent	2021	Retrospective	USA	91	65	3.2	NA	NA	7 CA
Pagano	2019	Retrospective	Italy	57	69	2.9	NA	NA	21, 25, 11
Pérez-Cuadrado-Robles	2018	Retrospective	Belgium	171	67	4.0	116	Ip 4, LST 167	30, 125, 16
Probst	2012	Retrospective	Germany	76	64	4.5	176	Is 8, IIa 63, IIc 5	38, 24, 14
Rahmi	2014	Prospective	France	45	67	3.5	110	Is 14, LST 31	15, 21, 4
Ramos-Zabala	2020	Retrospective	Spain	80	65	3.1	155	Is 30, LST 50	47, 11, 22
Ronnow	2018	Retrospective	Sweden	301	72	4.0	98	Is 148, IIa 153	202, 94, 0
Rosa-Rizzotto	2016	Retrospective	Italy	48	63	NA	99	NA	NA
Santos-Antunes	2018	Retrospective	Portugal	114	64	3.9	119	NA	NA
Santos-Antunes	2021	Retrospective	Portugal	147	64	4.4	90	Is 7, Ip 5, LST 135	48, 67, 29, (3 serrated with dysplasia)
Sauer	2016	Retrospective	Germany	182	70	4.1	127	Is 33, LST 149	101, 48, 13
Soune	2010	Retrospective	France	26	NA	4.9	65	Is 9, IIa 15, IIb 1, IIc 1	9, 10, 7
Spadaccini	2022	Retrospective	Europe, USA, Australia	207	67	4.2	NA	Is 38, LST 161	207 CA
Spychalski	2015	Retrospective	Poland	33	67	3.8	95	Is 14, LST 19	18, 8, 3
Spychalski	2021	Retrospective	Poland	601	65	4.4	83	Is 125, IIa 287, Is + IIa 115, IIa + IIc 74	193, 272, 124
Taskin	2020	Retrospective	Turkey	279	64	4.2	NA	NA	90 CA
Thorlacius	2013	Retrospective	Sweden	29	74	NA	NA	Is 10, LST 19	19, 5, 5

▶ **Table 1** (Continuation)

First author	Year published	Study design	Country	N	Mean age	Mean tumor size (cm)	Mean procedure time (min)	Tumor morphology*	Histopathology (LGD, HGD, CA†)
Urban	2018	Retrospective	Czech Republic	27	68	2.3	176	LST 27	1, 10, 11
Wagner	2018	Retrospective	Austria	35	77	3.0	118	NA	21, 11, 3

*Paris classification and LST.
†Intramucosal adenocarcinoma and submucosal adenocarcinoma.
N, number of procedures; NA, data not available; LST, laterally spreading tumor.

mean value and confidence limits. Sampling variances were estimated from the study data when they were unknown. The heterogeneity of individual studies was assessed using Q statistics (significant if $P < 0.1$), and the magnitude of heterogeneity was estimated with I^2 statistic (< 25% low heterogeneity, 25% to 50% moderate heterogeneity, > 50% high heterogeneity).

Comprehensive Meta-Analysis 3.3.070 (Biostat, Englewood, New Jersey, United States) was used to obtain all the estimates for this meta-analysis. Other than the assessment of Q statistics for heterogeneity, statistical significance was set at $P < 0.05$. Subgroup analysis was performed for ESD performed on large (≥ 2 cm) colorectal polyps, high- (≥ 40 ESD annually) versus low-volume (< 40 ESD annually) centers, and studies before 2017 versus studies after 2017.

Results

Study and patient characteristics

A total of 5,921 studies (Supplementary table 1) met the initial search criteria and following removal of duplicates and exclusion of studies after abstract and full-text review, 33 studies (30 retrospective and three prospective) comprising 4,206 patients were included in the final quantitative analysis (▶ **Fig. 1**). Twenty-six studies were conducted in European countries, three were from the United States, one from Brazil, and three were multinational. The mean age of the patients was 66.30 years (SD = 1.07), the median tumor size was 4 cm (3.59–4.42), and the median procedure time was 113 minutes (96–130) (▶ **Table 1**).

Endoscopic morphology and histopathology of colorectal lesions

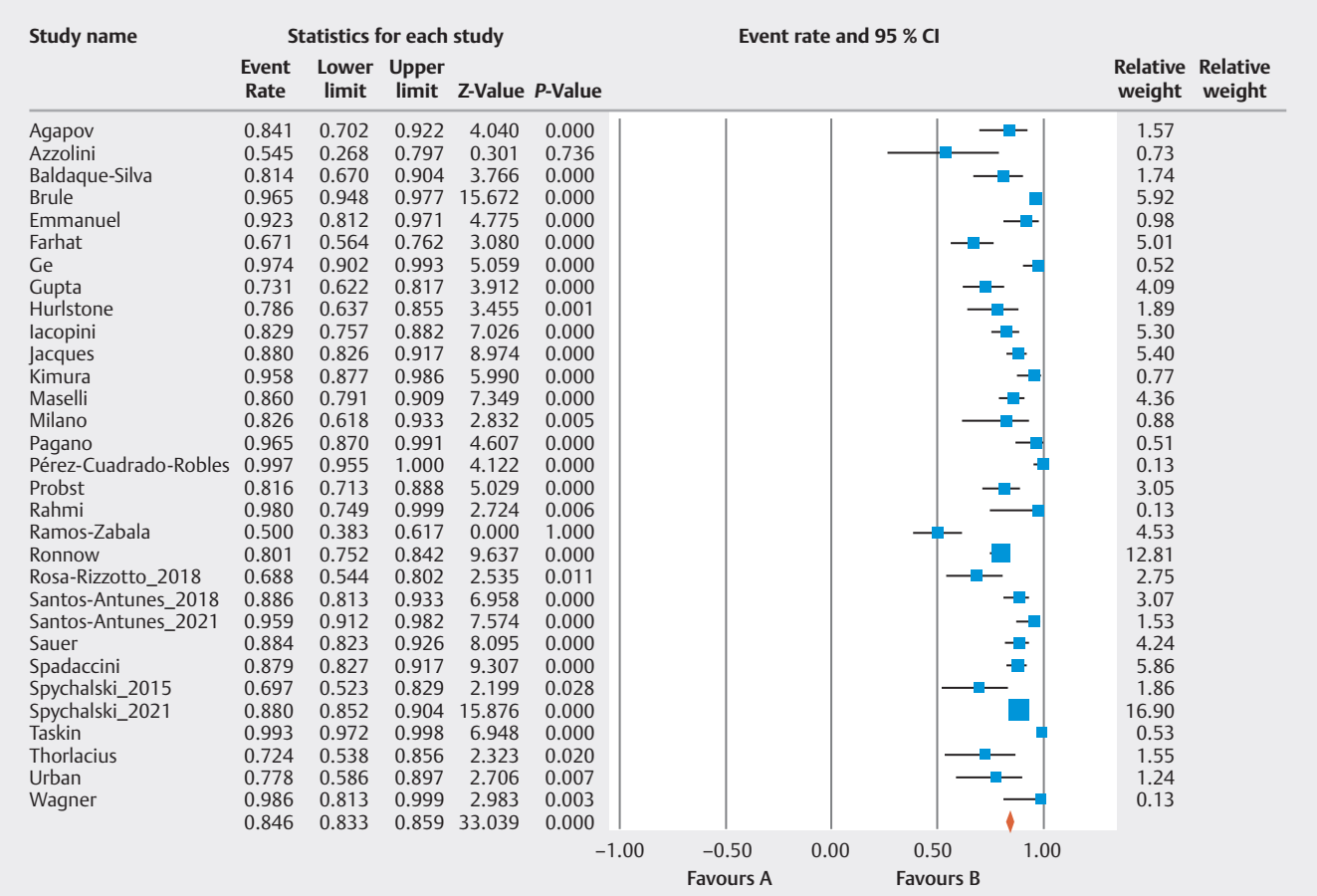
Based on the Paris classification, lesions were classified as Is (629), IIa (678), IIb (567), IIc (12), IIa + IIc (81), Is + IIa (115), and Ip (22). There were 1,245 lesions classified as LST. Histopathologic data were available for 3,810 lesions, and 1,956 (51.3%) were HGD (1,291) or adenocarcinoma (665). LGD was identified in 1,338 lesions (35.1%). Among 665 adenocarcinomas, 404 were SMCA (submucosal cancer), and 261 were IMCA (intramucosal cancer). Other neoplastic lesions were serrated polyps (43, 1.1%) and unspecified adenomas or NET (293, 7.7%). Twenty lesions (0.5%) were non-neoplastic, and 160 were unspecified.

Main outcomes

En bloc resection in the pooled sample of ESD procedures from 31 studies was 84.6% (95% confidence interval [CI] 83.3%–85.9%). R0 resection rate among 29 studies was 75.6% (95% CI 74.1%–77.0%), and 81.9% (95% CI 78.6%–84.9%) of ESD procedures achieved curative resection (22 studies). Forest plots showing individual study estimates and the pooled estimate for en bloc resection, R0 resection, and curative resection are presented in ▶ **Fig. 2**, ▶ **Fig. 3**, and ▶ **Fig. 4**, respectively. Procedure-related perforation rate was reported in 25 studies and was estimated to be 5.5% (95% CI 4.2%–7.0%) (Supplementary Fig. 1). Clinically significant bleeding was observed in 111 cases (4.1%, 95% CI 3.0%–5.5%) as reported in 26 studies. Forty-two patients (1.8%, 95% CI 1.3%–2.4%) from 30 studies required surgery for perforation or bleeding that failed conservative or endoscopic management. Surgery for invasive cancer was performed in 260 patients (4.8%, 95% CI 2.4%–9.4%) following ESD in 23 studies (▶ **Table 2**). Most studies did not stratify clinical outcomes based on morphologic classification or histopathologic characteristics.

High-volume versus low-volume centers

Thirteen studies were from high-volume centers and comprised 3,187 patients while 20 studies were from low-volume centers. The mean ages were 66.8 years and 66.7 years, respectively, in high-volume and low-volume centers. The en bloc resection rate was higher in high-volume centers (N = 2,775) (91.7%, 95% CI 87.8%–94.4% vs. 80.6%, 95% CI 73.9%–85.9%) compared to low-volume centers (N = 774). R0 resection rate was also higher in high-volume (N = 2,408) (78.9%, 95% CI 69.6%–86.0%) compared to low-volume centers (N = 659) (72.6%, 95% CI 66.2%–78.2%), but the difference was not significant statistically. The perforation rate was 5.1% in high-volume centers (111 of 2,024) and 7.8% in low-volume centers (N = 71 of 905); however, the difference was not significant. (**Supplementary files**). Eleven high-volume centers reported 27 surgeries for



▶ **Fig. 2** Forest plot showing the individual study estimates and the pooled estimate for en bloc resection.

complications (1.0%), which was less than that observed in 15 low-volume centers (15 surgeries, 1.9%).

Studies before and after 2017

We identified 11 studies published before 2017 comprising 621 patients and 22 studies published in 2017 or after comprising 3,585 patients. Studies published in 2017 and after reported higher pooled R0 resection rates (N = 2,701 of 3,415, 78.9%, 95% CI 69.6%–86.0% vs. N = 366 of 568, 72.6%, 95% CI 66.2%–78.2) and en bloc resection rates (N = 3,111 of 3,494, 89.9%, 95% CI 85.6%–93.0% vs. N = 438 of 568, 76.9%, 95% CI 69.2%–83.2%) compared with studies before 2017. The perforation rate was observed in 121 cases in studies published in 2017 and after (5.0%, 95% CI 3.7–6.7%) compared to 61 cases in studies before 2017 (7.9%, 95% CI 4.8%–12.9%); however, the difference was not significant (Supplement Fig. 4). Surgery for complications was 1.8% (N = 9) in studies published before 2017 versus 1.1% (N = 33) in studies published in 2017 and after.

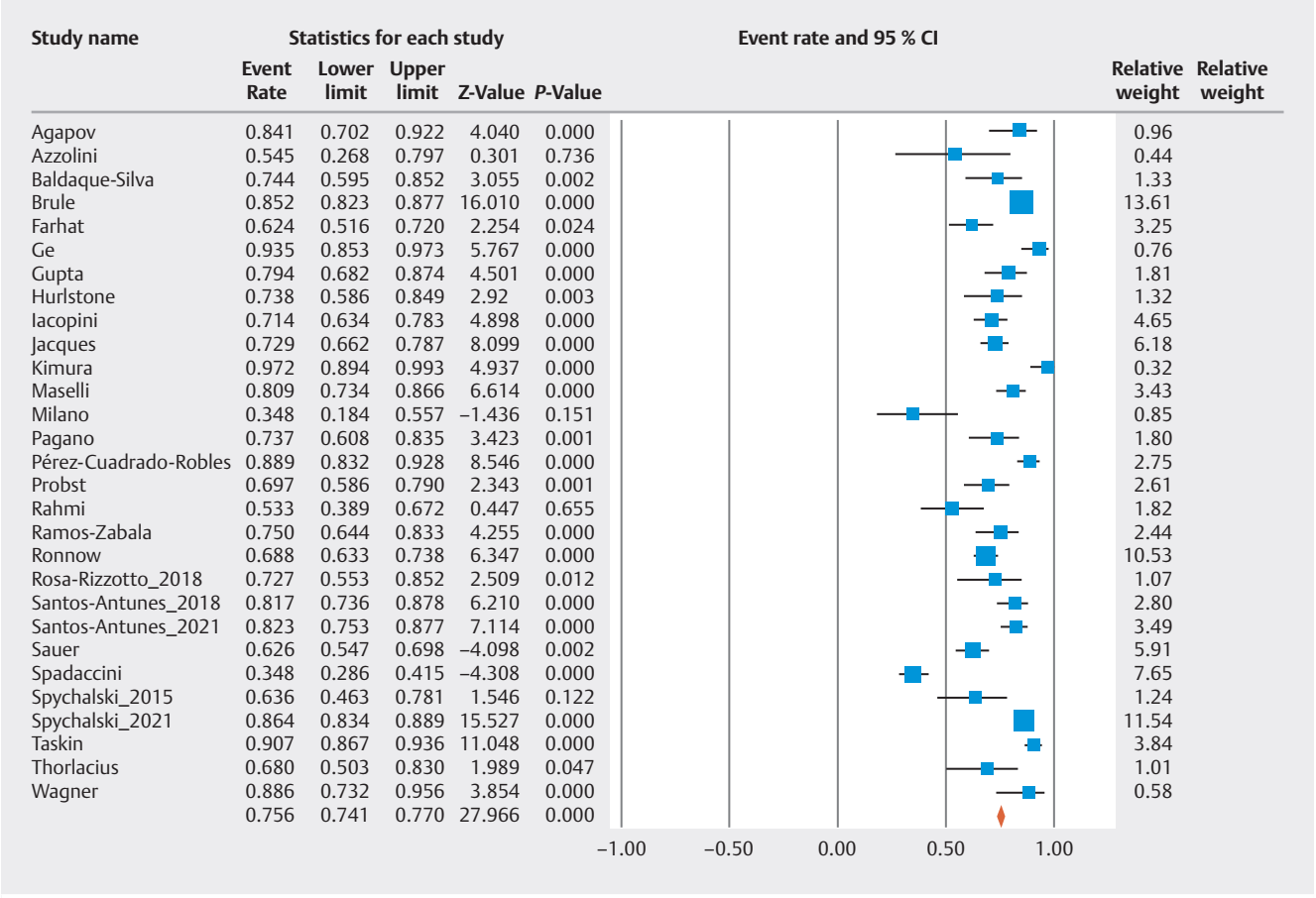
Test of heterogeneity

There was a high degree of heterogeneity among studies for R0 resection ($P < 0.01$, $I^2 = 92\%$), en bloc resection ($P < 0.01$, $I^2 = 88\%$), curative resection ($P < 0.01$, $I^2 = 73\%$), and surgery for invasive cancer ($p<.01$, $I^2 = 95\%$). There was low heterogeneity for perforation rate ($P = 0.27$, $I^2 = 13\%$) and moderate heterogeneity for delayed bleeding ($P = 0.07$, $I^2 = 30\%$) and overall bleeding ($P < 0.01$, $I^2 = 49\%$) (▶ **Table 2**).

Discussion

An increasing number of precancerous colorectal polyps and intramucosal colorectal cancers are being detected with improved colorectal cancer screening. Endoscopic resection of these precancerous lesions provides an excellent opportunity for cure without involving the morbidity associated with surgery [12]. While EMR is a well-accepted modality for endoscopic resection of colorectal neoplasms in the West, it is associated with a higher risk of recurrence that can range from 4% to 16%, with the risk being highest for large polyps resected piecemeal [13, 14]. ESD provides an opportunity for en bloc resection and curative resection of larger (> 2 cm) colorectal polyps and colorectal cancers confined to the mucosa that are at higher risk of submucosal invasion [8].

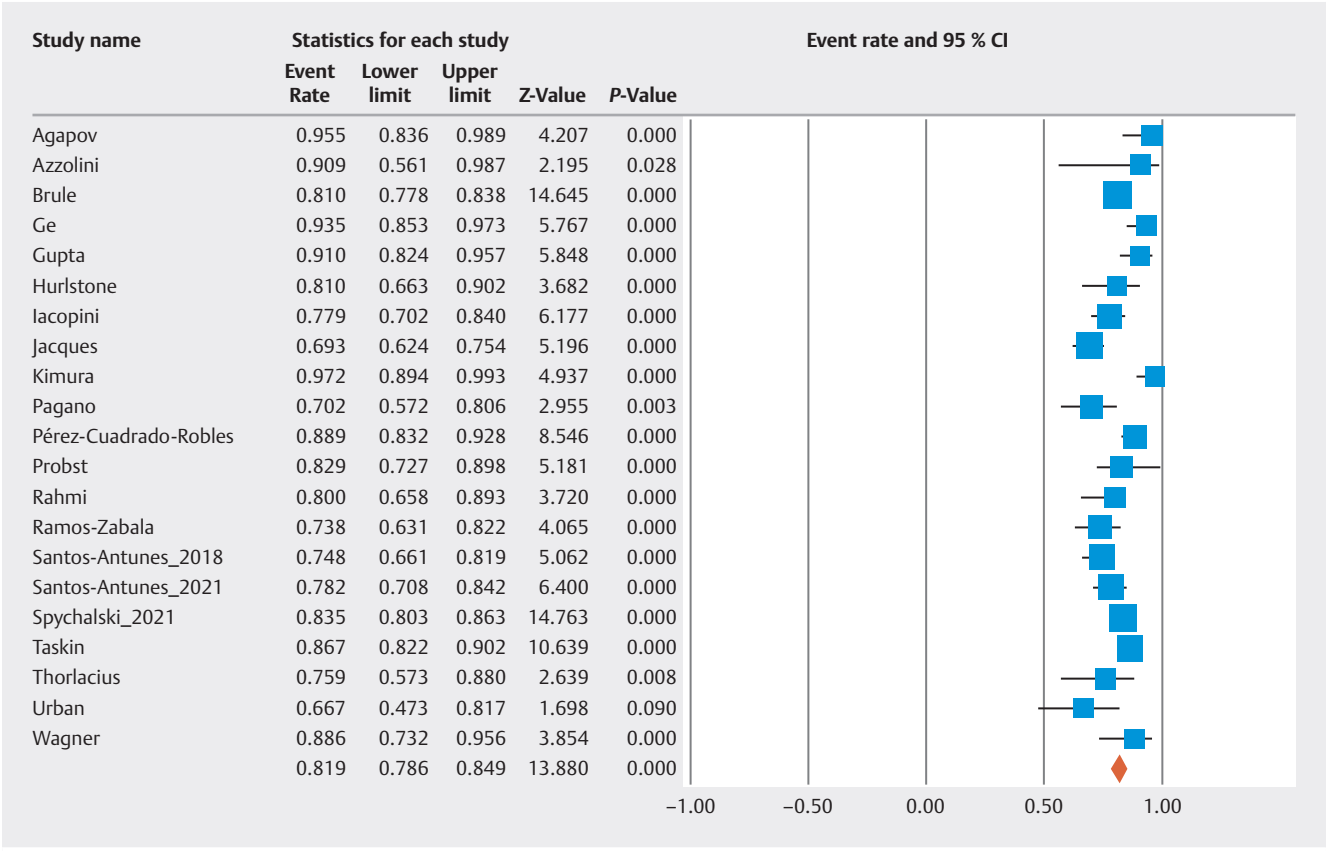
Our study comprising over 4,000 patients undergoing ESD for colorectal neoplasms is the largest and most comprehensive meta-analysis on this topic in the Western world. While most of the studies (29 studies) were from European countries, there



▶ **Fig. 3** Forest plot showing the individual study estimates and the pooled estimate for R0 resection.

was significant representation from North America (five studies comprising over 300 patients), South America (one study from Brazil), and Australia (one multinational study). We found that ESD attained an en bloc resection rate of 84.6% and an R0 resection rate of 75.6%. Studies in the last 5 years since 2017 show a trend toward improvement in both R0 (79% vs. 66%) and en bloc resection (90% vs. 77%) rates compared to those published before 2017. R0 resection rates of 76% from our study are comparable to 75% to 77% reported from Japanese studies [5, 15]. Moreover, the most recent studies and studies from high-volume centers in the West reported even better R0 resection rates of around 79%. The pooled curative resection rate (2443 of 2979) was higher than the R0 resection rate (3,067 of 4,010). This can be explained by the heterogeneity and the fact that curative resection was not reported in eight studies in which R0 resection was reported. The en bloc and curative resection rates are still inferior to those seen in Asian countries (> 90% and 87% to 89%, respectively). A large multicenter prospective study from Japan demonstrated an en bloc resection rate of 97%, curative resection rate of 90%, and only 0.5% of patients required surgery for AEs [16]. Ohata et al followed patients for 5 years after ESD for colorectal neoplasms and reported a 5-year disease-specific survival rate of 99.6% and local recurrence was seen in 0.5% at 3 years, and 1.6% at 5 years. These results demonstrate excellent long-term outcomes of colorectal ESD in Japan [17]. There is lack of long-term data of ESD for colonic neoplasms from countries outside Asia. Nonetheless, the recent trends for colorectal ESD in the West are encouraging and probably represent an improvement in expertise and training in colorectal ESD in the Western countries [4, 5, 18].

In our meta-analysis, the en bloc resection rate for ESD was significantly higher in studies involving centers that performed ≥ 40 ESDs annually compared to centers that performed < 40 ESDs annually (92% vs. 81%), while the R0 resection rate was slightly higher in centers performing more ESDs (79% vs. 73%). There was a trend toward a lower risk of colorectal perforation in studies from high-volume centers compared to low-volume centers (5% vs. 7%). Better effectiveness and safety of ESD in high-volume centers are expected and underscore the steep learning curve of colorectal ESD. ESD training in Japan is based on traditional apprenticeship and is learned from an experienced mentor over a few years. Unfortunately, this approach is not feasible in the United States and many other Western nations due to lack of enough mentors and time to acquire the skills. A common path to train endoscopists in performing ESD in the West, where exposure to gastric ESD is limited, involves attending ESD courses and seminars, observing experts at a high-volume center followed by practice in animal models, and finally performing ESD in selected human cases in which



▶ **Fig. 4** Forest plot showing the individual study estimates and the pooled estimate for curative resection.

▶ **Table 2** Clinical outcomes.

Clinical outcomes (no. of studies)	No. of outcomes (%)*	95% confidence interval	Q-value (*P* value)	I^2 statistics
R0 resection (29)	3,067 (75.6%)	74.1%–77.0%	361 (<.01)	92.25
En bloc resection (31)	3,549 (84.6%)	83.3%–85.9%	244.6 (<.01)	87.74
Curative resection (21)	2,443 (81.9%)	78.6%–84.9%	74.17 (<.01)	73.03
Surgery for invasive Cancer† (23)	260 (4.8%)	2.4%–9.4%	419.5 (<.01)	94.75
Adverse events				
Perforation (25)	182 (5.5%)	4.2%–7.0%	33.14 (.27)	12.50
Bleeding (26)	111 (4.1%)	3.0%–5.5%	45.08 (<.01)	48.98
Delayed bleeding (26)	66 (3.4%)	2.5%–4.7%	35.89 (.07)	30.34
Surgery for complication (30)	42 (1.8%)	1.3%–2.4%	53.11 (<.01)	54.81

*After ESD.
†Pooled estimate using random effects model.
ESD, endoscopic submucosal dissection.

the indications are clear and the risks are lower [19, 20]. Furthermore, the benchmark for en bloc, R0 and curative resections, and AEs are not well established for the Western countries.

Colorectal perforation was observed in just over 5% of ESD, and 4% of patients had clinically significant bleeding. Our observed perforation rate is comparable to earlier studies from Japan and other Asian countries (approximately 5%) [5, 18, 19, 20]. However, more recent studies from Asia report even lower perforation rates (< 3%) and rarely require surgery [21]. Fewer than 2% of patients required surgery for ESD-related AEs in our analysis; however, this was significantly higher compared to studies from Asia in which patients rarely (< 1%) undergo surgery for perforation [15, 18]. Surgery for colorectal perforation

was performed less commonly in high-volume centers (~1%) and for ESDs performed more recently (2017 and after). This trend in lower rate of surgery for perforations in recent studies is comparable to that seen in Asia and probably indicates a technological improvement in conservative management of AEs during ESD. Furthermore, proficiency in endoscopic closure techniques can avoid the need for surgery. Small perforations < 2 cm detected during ESD can be managed with clips while larger defects require endoscopic suturing. However, some of these require surgery [22]. ESD volume is an essential determinant of perforation, and this was replicated in our pooled analysis.

Limitations and strengths

Our study has some notable limitations. Most of the studies (30 of 33) in our meta-analysis were retrospective with potential selection bias. The moderate to high degree of heterogeneity between studies can be explained by the differences in study design, patient population, location and size of lesion, and pathology. However, lack of stratification based on type of lesion, size and site of lesion, and indications in most of the included studies limits our ability to investigate the likely sources of heterogeneity. In addition, variable endoscopist experience with the ESD technique and associated learning curve probably contributed to the heterogeneity. In many studies the findings were not stratified by the experience of operators with colorectal ESD or prior expertise with ESD in other luminal disorders. Furthermore, there was heterogeneity in selection of lesions by location (colonic or rectal), size, and morphology. Most of our included studies had lesion size > 2 cm. However, the morphology of lesions and histopathology of the colorectal neoplasms varied among the studies. In some studies, no information was provided about the indication for ESD and the morphology of the lesions.

Despite the limitations, our study has notable strengths. This is the only meta-analysis focusing on the effectiveness and safety of colorectal ESD in the West in recent years. Including 33 studies comprising over 4,000 patients from 17 countries ensures the generalizability of our findings in the practice area of focus (Western countries). We stratified the studies by year of publication and by the volume of colorectal ESD performed at each center to assess the effectiveness and safety of ESD in managing colorectal neoplasms. This allowed us to investigate the trends in the success of colorectal ESD in recent years compared to the past and the improvement in outcomes based on ESD volume.

Conclusions

ESD provides the best non-surgical curative management of noninvasive colorectal cancers. ESD has proven to be a promising technique for managing early colorectal neoplasms in many Asian countries for over a decade, establishing the acceptability and applicability of the technique. We observed a steady increase in the use of ESD and improvement in the effectiveness and safety of ESD in the management of colorectal neoplasms in Europe and the United States. These results are encouraging; however, incorporation of dedicated ESD training as part of advanced therapeutic endoscopy fellowship and applying ESD to manage other luminal neoplasms, such as gastric and esophageal cancers confined to the mucosa, is needed to enhance the experience and, hence, the success of colorectal ESD in the West.

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Conflict of Interest

Ritu R. Singh: No conflict of interest Julie Nanavati: No conflict of interest Harishankar Gopakumar: No conflict of interest Nikhil Kumta: Consultant for Apollo Endosurgery, Boston Scientific, and Olympus.

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