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Short-term outcomes of endoscopic submucosal dissection for the treatment of superficial gastric neoplasms in non-Asian countries: a systematic review and meta-analysis

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Abstract

Background Endoscopic submucosal dissection (ESD) is now considered the standard treatment for early gastric cancer (EGC). However, the widespread adoption of ESD in western countries has been slow. We performed a systematic review to evaluate short-term outcomes of ESD for EGC in non-Asian countries.

Methods We searched 3 electronic databases from inception until October 26, 2022. Primary outcomes were *en bloc*, R0 and curative resections rate by region. Secondary outcomes were overall complications, bleeding, and perforation rate by region. The proportion of each outcome, with the 95% confidence interval (CI), was pooled using a random-effects model with the Freeman-Tukey double arcsine transformation.

Results Twenty-seven studies from Europe (n=14), South America (n=11) and North America (n=2) were included, involving 1875 gastric lesions. Overall, *en bloc*, R0, and curative resection rates were achieved in 96% (95%CI 94-98%), 85% (95%CI 81-89%), and 77% (95%CI 73-81%) of cases, respectively. Considering only information from lesions with adenocarcinoma, the overall curative resection was 75% (95CI 70-80%). Bleeding and perforation were observed in 5% (95%CI 4-7%) and 2% (95%CI 1-4%) of cases, respectively.

Conclusion Our results suggest that short-term outcomes of ESD for the treatment of EGC are acceptable in non-Asian countries.

Keywords Endoscopic submucosal dissection, gastric cancer, meta-analysis

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Introduction

Endoscopic submucosal dissection (ESD) is an established technique for the treatment of patients with early gastric cancer (EGC) [1]. ESD allows *en bloc* resection of superficial neoplastic lesions to achieve curative treatment avoiding surgery. In Asian countries, ESD is the treatment of choice for EGC, with excellent long-term results [2-6].

In western countries, the diffusion of this technique is limited because of its high technical complexity and the lower incidence of superficial gastric neoplasms. Consequently, there are not many publications on this type of treatment and the results are heterogeneous [7]. However, in recent years, new studies have been published showing that the learning curve in western countries has improved, achieving curative rates similar to those obtained in Asian countries in some series [8-11].

To consider ESD as an effective treatment in the management of EGC in the West, the results that have been achieved in non-Asian countries must be recognized. Therefore, we performed

this review to evaluate the short-term outcomes of ESD for the treatment of superficial gastric neoplasms in non-Asian countries.

Materials and methods

This review was reported according to the 2020 PRISMA statement [12] and was registered on the PROSPERO database (CRD42021291604).

Search strategy

We searched in 3 electronic databases (PubMed, Embase, and Scopus) from inception to October 26, 2022. The complete search strategy is available in Supplementary Table 1. We included publications in English, Portuguese, Italian, and Spanish.

Eligibility criteria

We included randomized controlled trials, cohorts and case series studies, evaluating adult patients with superficial gastric neoplasms (adenomas and adenocarcinomas) treated with ESD in non-Asian countries within standard and expanded criteria. When more than one study from the same center was found, the larger series was selected. We excluded studies with less than 10 cases, abstracts and studies with other histological diagnoses.

Study selection

Articles were downloaded from electronic search to EndNote X8 software. After removal of duplicate records, selected studies were uploaded to Rayyan QCRI (https://rayyan.qcri.org/). Two authors (HBG and LMC) screened the studies according to the inclusion and exclusion criteria. Disagreements were resolved by a third researcher (CDA).

Data extraction

Two researchers (HBG and LMC) extracted data independently on a previously designed Microsoft Excel® spreadsheet. The following data were extracted: author name, study design, year and country of publication, sample size, lesion morphology, and previously described outcomes.

Outcomes

The primary outcomes were *en bloc*, R0, and curative resection rates of superficial gastric neoplasms by ESD. *En bloc* resection was defined as resection in one piece. R0 resection was defined as achievement of *en bloc* resection with free horizontal and vertical margins. Curative resection was defined as achievement of R0 with absence of lymphovascular invasion and submucosal infiltration <500 µm [1].

Secondary outcomes were the curative resection rate of superficial gastric neoplasms treated by ESD including only adenocarcinoma histology, overall complications, bleeding, and perforation rate.

Risk of bias assessment

To evaluate the risk of bias in cohort studies we employed the Newcastle-Ottawa scale (NOS) [13]. Studies were divided into 3 categories: low risk of bias (8-9 points); moderate risk of bias (5-7 points); and high risk of bias (0-4 points). For case series the Joanna Briggs Institute (JBI) Critical Appraisal Checklist was used [14]. Studies with scores of at least 5 are considered of acceptable quality.

Statistical analysis

Random-effects models were used for meta-analysis. The between-study variance (tau^2) was estimated using the Paule-Mandel estimator [15]. The proportions of each outcome, with their 95% confidence interval (CI), were pooled using the Freeman-Tukey double arcsine transformation. Heterogeneity was assessed using the chi-squared test (threshold P<0.10) and the I^2 statistic [16]. Heterogeneity was defined as: high if I^2>60%; moderate if I^2 was 30-60%; and low if I^2<30%. Subgroup analyses were performed according to the region (Americas vs. Europe) and by type of study design. The interaction test for subgroup differences was considered significant if the P-value for interaction (pfi) was <0.10 [17]. We conducted all meta-analyses using the *meta* package from R 4.1.3 (www.r-project.org).

Results

Study selection

We found 11,343 articles. After the removal of 4515 duplicates, 6828 studies underwent title/abstract and full-text screening. Finally, we included 27 studies for analysis (Fig. 1).

Study characteristics

The main characteristics of the 27 studies [8-11,18-40] are summarized in Table 1. Nineteen (n=1344) were cohorts and 8 (n=531) case series. Fourteen studies were conducted in

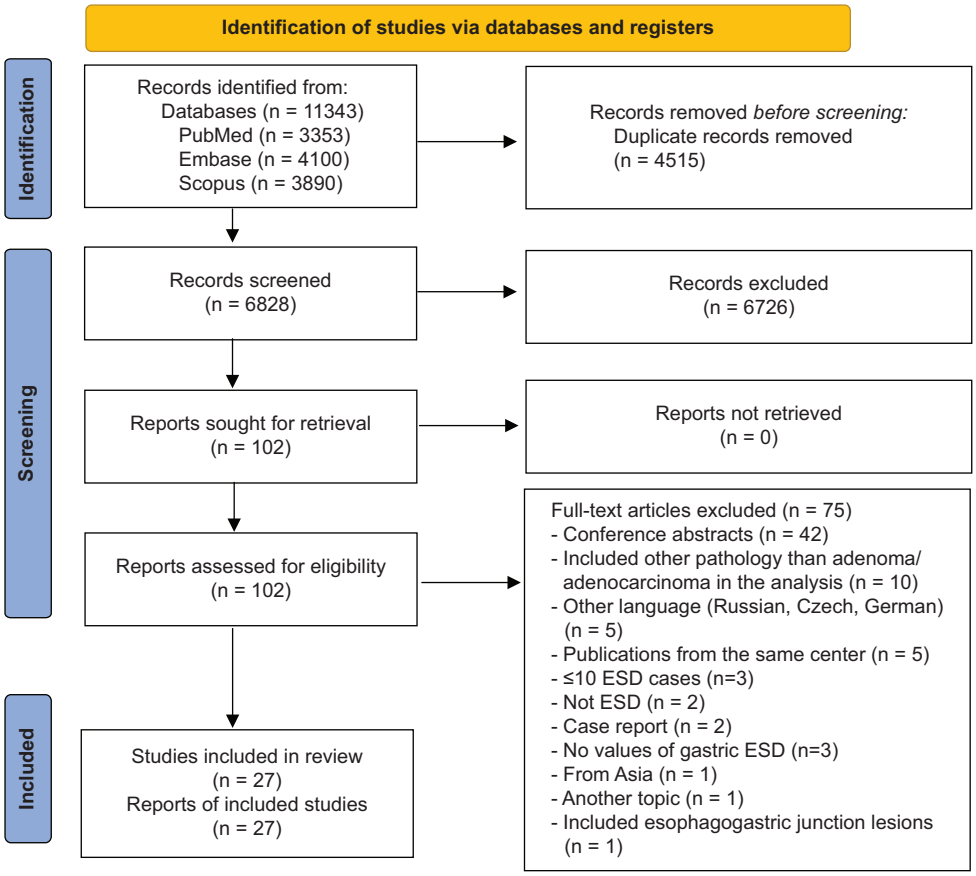

Figure 1 Flow diagram of study selection
ESD, endoscopic submucosal dissection

Europe and 13 in the Americas. Most of the resected lesions were located in the distal third of the stomach (51.6%). In addition, most of the resected lesions were located in the mucosa, without showing submucosal invasion (80.9%). No cases of death associated with the procedure were reported in the studies evaluated.

Risk of bias assessment

According to the NOS tool, 2 studies were scored with a low risk of bias and 16 with a moderate risk of bias (Supplementary Table 2). The quality assessment using the JBI critical appraisal tool is reported in Supplementary Table 3.

Effects of ESD on primary outcomes

Twenty-six studies reported data on the *en bloc* resection rate of superficial gastric neoplasms (n=1811) [8-11,18-26,28-40]. *En bloc* resection was achieved in 96% overall (95%CI 0.94-0.98; I^2=58%) (Fig. 2). Twenty-seven studies reported data on the R0 resection rate of superficial gastric neoplasms (n=1875) [8-11,18-40]. R0 resection was achieved in 85% overall (95%CI 0.81-0.89; I^2=75%) (Fig. 3). Twenty-four studies reported data on the curative resection rate of superficial gastric neoplasms (n=1787) [8-11,18,19,22-33,35-40]. Curative resection rate was achieved in 77% overall (95%CI 0.73-0.81; I^2=70%) (Fig. 4).

Fifteen studies reported data on the curative resection rate of superficial gastric neoplasms treated by ESD, including only adenocarcinoma histology (n=863) [8,9,11,18,24,26,28-30,32,35-39]. Curative resection including only adenocarcinoma histology was achieved in 75% overall (95%CI 0.70-0.80; I^2=67%) (Fig. 5).

According to the continent of origin, *en bloc* resection was 97% (95%CI 0.94-0.99; I^2=59%) in the Americas and 95% (95%CI 0.92-0.97; I^2=58%) in Europe (Fig. 2). The subgroup analyses by region did not reveal a subgroup effect (pfi=0.35). R0 resection rate was 90% (95%CI 0.85-0.94; I^2=68%) in the Americas and 80% (95%CI 0.75-0.86; I^2=70%) in Europe (Fig. 3). The test for subgroup differences by region suggested that there was a statistically significant subgroup effect (pfi<0.01). Curative resection rate was 82% (95%CI 0.77-0.86; I^2=56%) in the Americas and 73% (95%CI 0.66-0.79; I^2=74%) in Europe (Fig. 4). The test for subgroup differences by region suggested that there was a statistically significant subgroup effect (pfi=0.03). Curative resection rate including only adenocarcinoma histology was 78% (95%CI 0.70-0.84;

Table 1 Main characteristics of the included studies

Author [ref.], year	Design	Country	Sample size	Mean age (years)	Location			Morphology		Histology			Depth of invasion			Bleeding rate	Surgery for bleeding	Perforation rate	Surgery for perforation
					Upper third	Mid third	Lower third	Elevate	Flat/ depressed	Adenoma	Diff. adenoca.	Undiff. adenoca.	m	sm1	sm2				
Cardoso *et al* [18], 2008	Cohort	Brazil	15	71	46.7%	26.7%	26.7%	66.7%	33.3%	0	100%	0	93.3%	6.7%		0	0	20%	0
Catalano *et al* [19], 2009	Cohort	Italy	12	64	0	83.3%	16.7	50%	50%	NA	NA	NA	NA	NA	NA	8.3%	0	8.3%	8.3%
Chaves *et al* [36], 2010	Case series	Brazil	16	67	18.8%	31.2%	50%	25%	75%	0	81.2%	18.8%	81.3%	12.5%	6.2%	0	0	0	0
Baldaque *et al* [20], 2013	Case series	Portugal	16	NA	NA	NA	NA	NA	NA	87.5%	12.5%	0	87.5%	12.5%	0	0	0	0	0
Najmeh *et al* [21], 2015	Cohort	Canada	30	69	36.7%	6.7%	56.7%	NA	NA	30%	70%		83.3%	16.7%		6.7%	0	10%	3.3%
Galindo *et al* [22], 2015	Cohort	Chile	15	68	13.3%	33.3%	53.3%	20%	80%	20%	73.3%	6.7%	93.3%	6.7%		6.7%	0	20%	20%
Donoso *et al* [11], 2015	Cohort	Chile	16	72	25%	37.5%	37.5%	18.7%	81.3%	0	93.8%	6.2%	87.5%	6.2%	6.2%	0	0	6.2%	6.2%
Emura *et al* [23], 2015	Case series	Colombia	54	67	14.8%	25.8%	59.3%	24%	76%	27.8%	68.5%	0	85.2%	3.7%	11.1%	7.4%	3.7%	3.7%	0
Karpińska *et al* [24], 2016	Case series	Poland	58	69	25.9%	29.3%	44.8%	39.7%	62.1%	0	93.1%	6.9%	75.9%	8.6%	15.5%	10.3%	0	1.7%	0
Sooltangos *et al* [25], 2017	Cohort	United Kingdom	21	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	19%	0	0	0
Probst *et al* [26], 2017	Cohort	Germany	191	71	5.8%	31.9%	62.3%	35.1%	64.9%	0	100%		79.1%	6.8%	12.6%	6.3%	0	1%	0.5%
Petruzziello *et al* [27], 2017	Cohort	Italy	64	NA	NA	NA	NA	NA	NA	31.3%	65.6%	3.1%	NA	NA	NA	NA	NA	NA	NA
Mendonça *et al* [28], 2018	Cohort	Brazil	38	NA	NA	NA	NA	NA	NA	0	89.5%	10.5%	NA	NA	NA	NA	NA	NA	NA
Bausys *et al* [29], 2018	Cohort	Lithuania	42	72	26.2%	26.2%	47.6%	NA	NA	0	83.3%	4.8%	83.3%	16.7%		3	0	4.8%	4.8%
Chirinos *et al* [30], 2018	Case series	Peru	13	70	0	7.7%	92.3%	46.2%	53.8%	38.5%	61.5%	0	76.9%	7.7%	15.4%	0	0	7.7%	7.7%
Libânio *et al* [31], 2018	Cohort	Portugal	153	68	19.6%	30.7%	49%	NA	NA	47.1%	52.9%		85.6%	14.4%		8.5%	0	2.6%	0.7%

(*Contd...*)

Table 1 (*Continued*)

Author [ref.], year	Design	Country	Sample size	Mean age (years)	Location			Morphology		Histology			Depth of invasion			Bleeding rate	Surgery for bleeding	Perforation rate	Surgery for perforation
					Upper third	Mid third	Lower third	Elevate	Flat/ depressed	Adenoma	Diff. adenoca.	Undiff. adenoca.	m	sm1	sm2				
Mocker *et al* [32], 2018	Case series	Germany	26	NA	NA	NA	NA	69.2%	30.8%	0	80.8%	19.2%	NA	NA	NA	3.8%	0	3.8%	0
Pagano *et al* [33], 2019	Cohort	Italy	28	NA	NA	NA	NA	NA	NA	64.3%	35.7%	0	85.7%	7.1%	7.1%	10.7%	0	3.6%	3.6%
Costa *et al* [10], 2019*	Cohort	Portugal	113	NA	6.2%	38.9%	54.9%	NA	NA	75.2%	23.9%		88.5%	10.6%		10.6%	0	0.9%	0
Quero *et al* [34], 2020	Cohort	Italy	42	69	0	80%	25%	NA	NA	0	100%	0	38.1%	61.9		4.8%	0	0	0
Cañete-Ruiz *et al* [9], 2020	Cohort	Spain	35	67	11.4%	25.7%	62.9%	28.6%	71.4%	0	94.3%	5.7%	60%	40%	0	NA	NA	NA	NA
Ngamruengphong *et al* [35], 2020	Cohort	USA	311	NA	NA	NA	NA	NA	NA	55.3%	38.3%	6.4%	NA	NA	NA	NA	NA	NA	NA
Palacios *et al* [8], 2021	Case series	Peru	152	68	6.6%	32.9%	60.5%	46%	53.9%	21.7%	77%	1.3%	91.4%	1.3%	7.2%	5.9%	0	6.6%	1.3%
Arantes *et al* [37], 2021	Cohort	Brazil	77	NA	NA	NA	NA	NA	NA	45.5%	46.8%	7.8%	NA	NA	NA	2.6%	0	0	0
Mejía *et al* [38], 2021	Cohort	Chile	100	68	32	34%	34%	NA	NA	0	95%	5%	83%	9%	8%	4%	0	4%	4%
Fernandez *et al* [40], 2021*	Case series	Spain	196	NA	8.2%	42.3%	49.5%	56.6%	43.%	52.6%	37.2%	0	79.1%	10.7%	0	NA	NA	NA	NA
Costa *et al* [39], 2022	Cohort	Brazil	41	65	NA	NA	NA	43.9%	56.1%	24.4%	75.6%	0	NA	NA	NA	4.9%	0	2.4%	0

*Included cases that resulted negative for dysplasia or adenocarcinoma after resection

m, mucosal invasion; sm1, superficial submucosal invasion (<500 μm); sm2, deep submucosal invasion (≥500 μm); diff, differentiated; undiff, undifferentiated; adenoca, adenocarcinoma

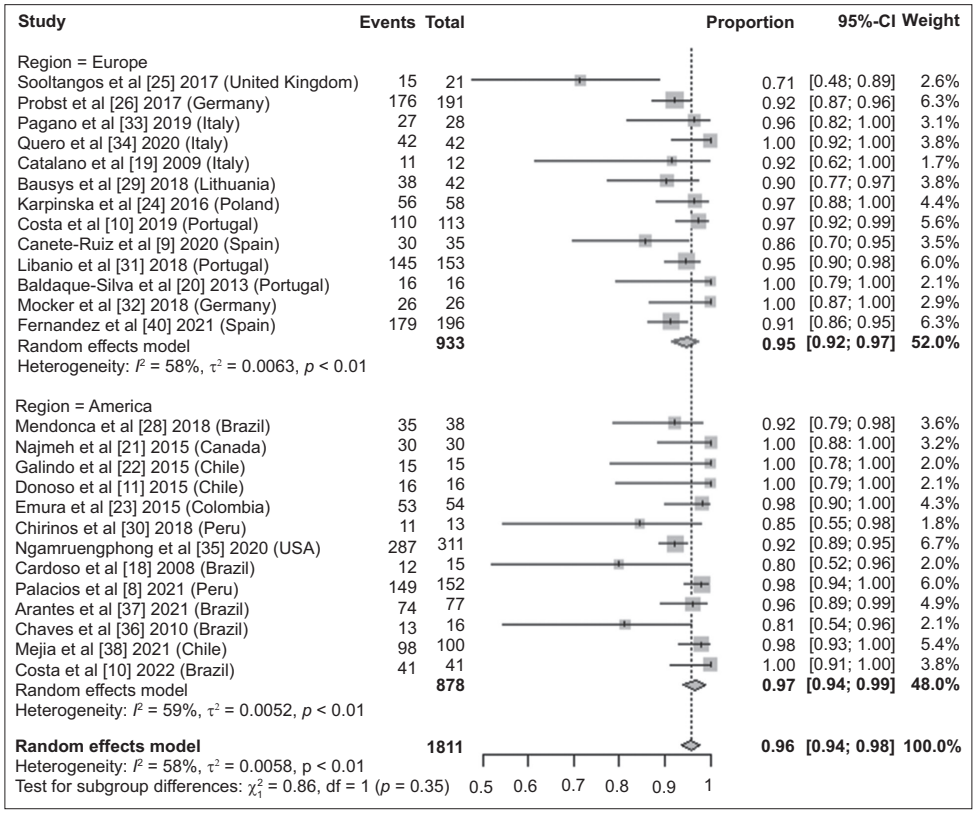

Figure 2 Forest plot showing the *en bloc* resection rate of superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval

I^2=71%) in the Americas and 69% (95%CI 0.63-0.74; I^2=0%) in Europe (Fig. 5). The test for subgroup differences by region suggested that there was a statistically significant subgroup effect (pfi=0.07).

Effects of ESD on secondary outcomes

Twenty-two studies reported data on overall complications, bleeding and perforation rate (n=1231) [8,10,11,18-26,29-34,36-39]. Overall complication rate was 8% (95%CI 0.06-0.11; I^2=50%), with no subgroup effect by region (P=0.64) (Supplementary Fig. 1). The overall bleeding and perforation rates were 5% and 2%, respectively (Supplementary Fig. 2, 3). The test for subgroup differences suggested that in these 2 analyses there was a statistically significant subgroup effect in the bleeding rate in favor of the Americas and in the perforation rate in favor of Europe (pfi<0.10). In the studies evaluated, surgery was required for the treatment of 2 and 14 cases of bleeding and perforation, respectively. No differences in the curative resection rates were found between studies with a cohort versus case series design (Supplementary Fig. 4, 5).

Discussion

In our review, we found that acceptable *en bloc*, R0 and curative resection rates are achieved in western countries. However, the results of R0 and curative resections are not yet comparable to those obtained in eastern countries [41,42]. If only lesions with adenocarcinoma were considered, the curative resection rate was similar between American and European countries.

In recent years, ESD has become the technique of choice for the treatment of superficial gastric neoplasms. ESD is superior to endoscopic mucosal resection, showing better *en bloc* and complete histologic resection and a lower local recurrence rate [43]. Moreover, ESD offers a less expensive procedure, a shorter recovery time and a better quality of life than surgery [41]. Even though ESD is associated with a higher rate of recurrence compared to surgery, adequate surveillance with upper endoscopy allows a similar survival rate [44].

Widespread adoption of ESD in western countries has been slow, with several factors being involved, such as the lack of training centers and the complexity of the technique. Furthermore, superficial gastric neoplasms are usually considered to be the ideal target for ESD training [45], but in many western countries, there is a lower incidence of gastric

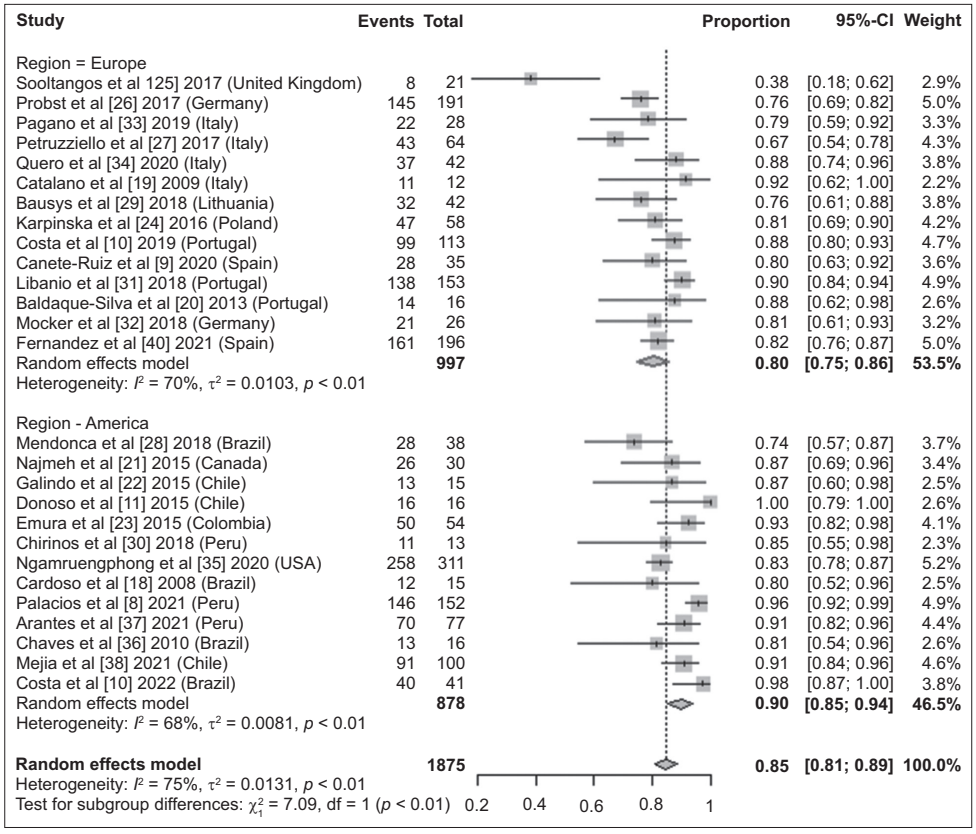

Figure 3 Forest plot showing the R0 resection rate of superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval

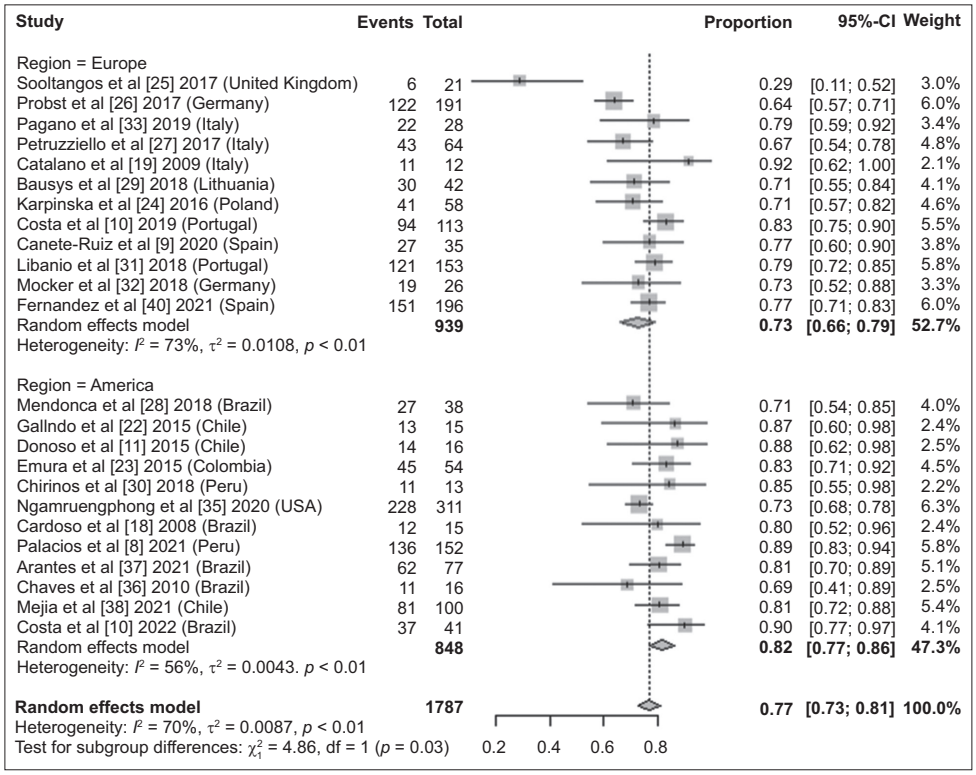

Figure 4 Forest plot showing the curative resection rate of superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval

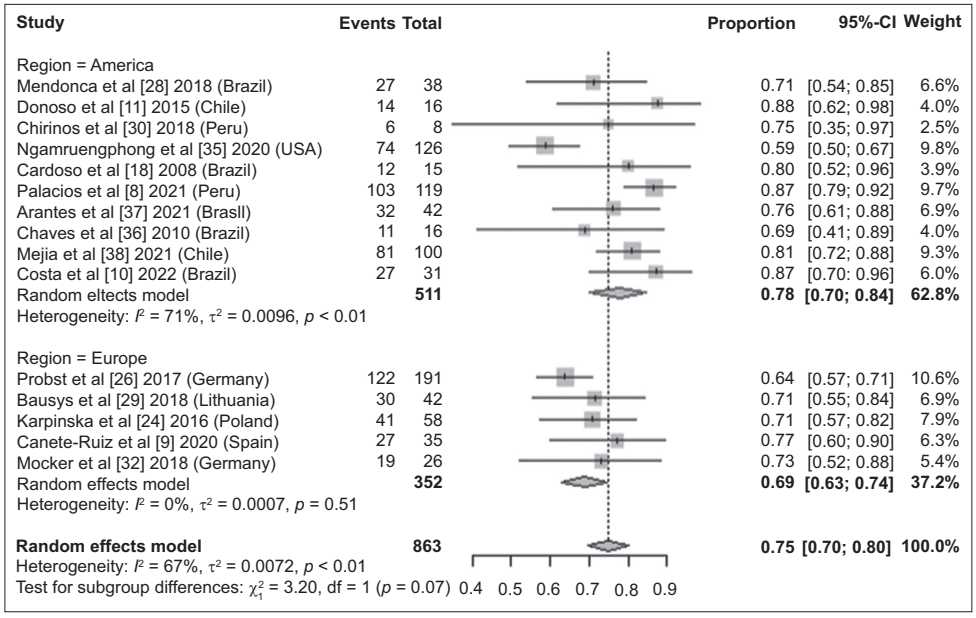

Figure 5 Forest plot showing the curative resection rate of superficial gastric neoplasms treated by endoscopic submucosal dissection including only adenocarcinoma histology
CI, confidence interval

cancer and a lower detection rate of EGC, these factors being a barrier to finishing the learning curve for this procedure [46].

A previous systematic review of ESD for superficial neoplasms of the digestive tract found that only 10% of 238 studies came from western countries [42]. This review showed that western countries had lower rates of curative resection and a higher frequency of perforations [42]. Nevertheless, when the analysis was performed to include only superficial gastric neoplasms, both eastern and western countries had similar outcomes [42]. This is probably because gastric lesions are considered less complex for dissection, which is why many endoscopists begin their training in this organ; curative resection rates could be similar between western and eastern countries in this review. However, several studies published later with a larger number of cases were not included.

A recent systematic review showed that in the West a 72% rate of curative resections was obtained if only lesions with adenocarcinoma were included [7]. In addition, an acceptable rate of associated complications was described (<10%) [7]. However, these outcomes are still below the values obtained in the East [41], and in this review they suggest that adherence to resection criteria and adequate staging are necessary before performing a procedure to improve the rates of curative resections.

Recently, new series of cases from western countries have been published, so it is important to update the ESD status outside of Asia. For this reason, we evaluate the short-term outcomes obtained to date in western countries from ESD for superficial gastric neoplasms. In our review, we found that the rate of *en bloc* resection was acceptable and similar to those obtained in a previous systematic review, in which an *en bloc* resection rate of 95% was described for eastern countries [42].

The rates of R0 and curative resections were 85% and 77%, respectively. Despite the advances in this procedure in the West, the values of R0 and curative resections are still below the values obtained in the East [41,42]. Bleeding and perforation rates were similar to those reported in other studies, with an overall complication rate of 8% [47,48]. No procedure-related mortality was reported in the studies. Despite greater experience in the West, there is still a gap between some outcomes of the West and the East. This effect is probably due to the different types of training received by endoscopists in the East. In the East, training is protocolized and usually takes several years, during which time endoscopists begin with theoretical training, then an observational phase, and finally by performing ESD under supervision. Nevertheless, the possibility of traveling to a high-volume ESD center in Japan or Korea, the continuous courses, and hands-on activities with either animal models or human cases, have gradually allowed this technique to spread outside of Asia, and in fact ESD is mentioned in several recent western guidelines as the treatment of choice for early gastric tumors [49-51]. Furthermore, given the need to establish protocolized training outside of Asia, a European core curriculum for ESD practice has been developed [52]. It is important to highlight within the learning curve the capacity to precisely diagnose an EGC that meets the criteria to be treated by ESD. The success of this type of treatment lies not only in an adequate technique, but also in the identification of the margins of the EGC and endoscopic characteristics that do not preclude endoscopic resection. It is likely that, in the first series from western

countries, a lack of training or proper equipment led to inadequate recognition of these features, which could have led to a lower rate of R0 resections. Another important point to highlight is the technique at the time of dissection. Despite the fact that the type of ESD strategy (conventional, tunneling, traction methods) was not clearly detailed in the publications reviewed, our experience indicates that gravity, position and additional factors, such as the presence of an ulcer or fibrosis, should be taken into account when deciding upon the ESD strategy.

To our knowledge, this is the most updated systematic review assessing ESD in the treatment of superficial gastric neoplasms in western countries. We found that, in western countries, *en bloc* resections had adequate results, and although the rates of R0 and curative resections are still below the values reported in Asian countries, dissection can be considered an adequate treatment for superficial gastric neoplasms. Therefore, surgery can be reserved for selected cases. We found moderate risks of bias in most of the cohorts in this review, mainly due to the lack of control selection and comparability of participants included. However, at present surgeries are not usually performed for the treatment of EGC, in order to include patients within a control group.

Our review has some limitations. Firstly, most of the studies were retrospective cohorts, resulting in a lack of high-quality information. Secondly, most of them did not distinguish between adenomas, differentiated and undifferentiated adenocarcinomas, when evaluating their outcomes, which is important since each of these histologies has different behavior. Thirdly, the differences in the endoscopists' expertise and materials used between studies could be a source of bias. Fourthly, we found high heterogeneity for most of our outcomes. This finding may be due to differences in the characteristics of the patients and the lesions included. To reduce this heterogeneity, some included studies should have been excluded. However, this was not done because the main objective of this review was to include the largest possible number of studies published in the West, which are scarce. We suggest that studies with a more rigorous methodology are still necessary to standardize the results between different centers. Finally, most of the studies found did not report long-term results, so we propose that more studies continue to be published, but taking into account follow-up information to determine the effect of ESD on the rate of disease recurrence and patient survival.

Our results suggest that short-term outcomes of ESD for the treatment of superficial gastric neoplasms by trained endoscopists are acceptable in non-Asian countries. High rates of curative resection can be safely achieved in western countries. Taking into account only lesions with adenocarcinoma, the curative resection rate was similar between American and European countries. This review indicates that ESD could be the first-line therapy for the treatment of all potentially endoscopically resectable superficial gastric neoplasia that meets the standard and expanded criteria in high-volume centers in the West.

Summary Box

What is already known:

- Endoscopic submucosal dissection is an established technique for the treatment of patients with superficial gastric neoplasms
- Most of the publications come from eastern countries, where this technique was initially developed
- To consider surgery as the treatment of choice in western countries, the results obtained to date in our hospitals must be known

What the new findings are:

- In western countries the rates of R0 and curative resections were 85% and 77%, respectively
- Although the rates of R0 and curative resections are still below the values reported in Asian countries, dissection can be considered an adequate treatment for superficial gastric neoplasms
- Bleeding and perforation rates were similar to those reported in other studies, with an overall complication rate of 8%
- Endoscopic submucosal dissection could be the first-line therapy for the treatment of all potentially endoscopically resectable superficial gastric neoplasia that meet the standard and expanded criteria in high-volume centers in the West

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Supplementary material

Supplementary Table 1 Electronic search strategy (October 26, 2022)

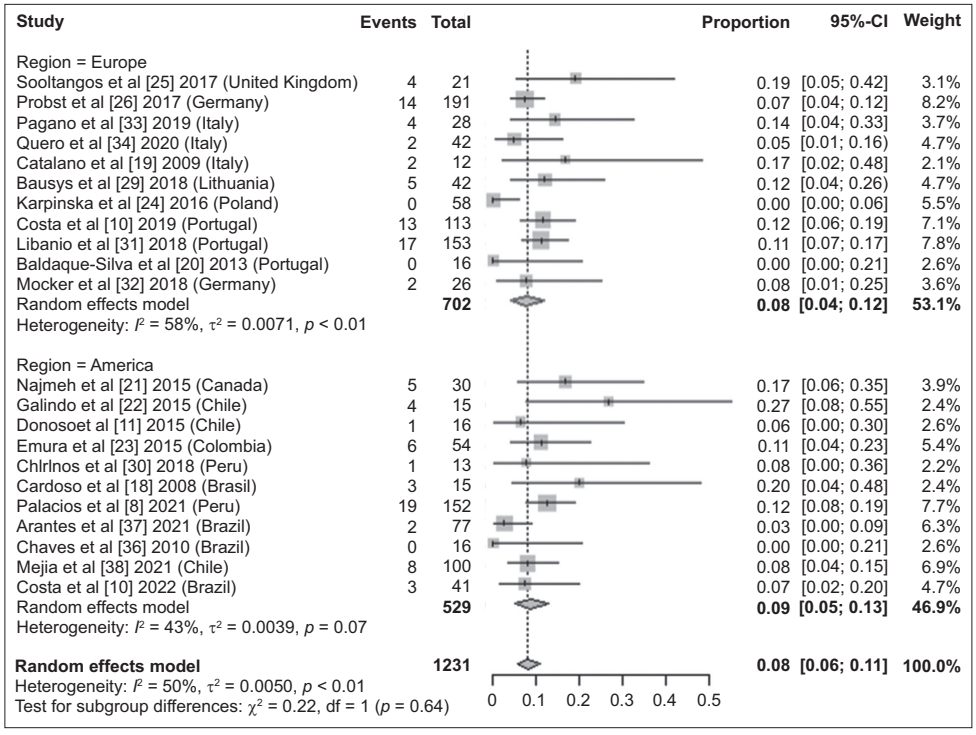
PubMed (3353 hits) ("stomach neoplasms"[mesh] OR "gastric cancer"[tiab] OR "stomach cancer"[tiab]) AND ("endoscopic mucosal resection"[mesh] OR "endoscopic submucosal resection"[tiab] OR "endoscopic mucosal resection"[tiab] OR "endoscopic resection"[tiab] OR "endoscopic dissection"[tiab] OR ESD[tiab] OR EMR[tiab])
EMBASE (4100 hits) ('gastric cancer'/exp OR 'gastric cancer' OR 'stomach cancer'/exp OR 'stomach cancer') AND ('endoscopic submucosal dissection'/exp OR 'endoscopic submucosal dissection' OR 'endoscopic submucosal resection'/exp OR 'endoscopic submucosal resection' OR 'endoscopic mucosal resection'/exp OR 'endoscopic mucosal resection' OR 'endoscopic resection'/exp OR 'endoscopic resection' OR 'endoscopic dissection' OR esd OR emr)
Scopus (3890 hits) TITLE-ABS-KEY (("gastric cancer" OR "stomach cancer") AND ("endoscopic submucosal dissection" OR "endoscopic submucosal resection" OR "endoscopic mucosal resection" OR "endoscopic resection" OR "endoscopic dissection" OR ESD OR EMR))

Supplementary Table 2 Newcastle-Ottawa scale for risk of bias assessment of cohort studies

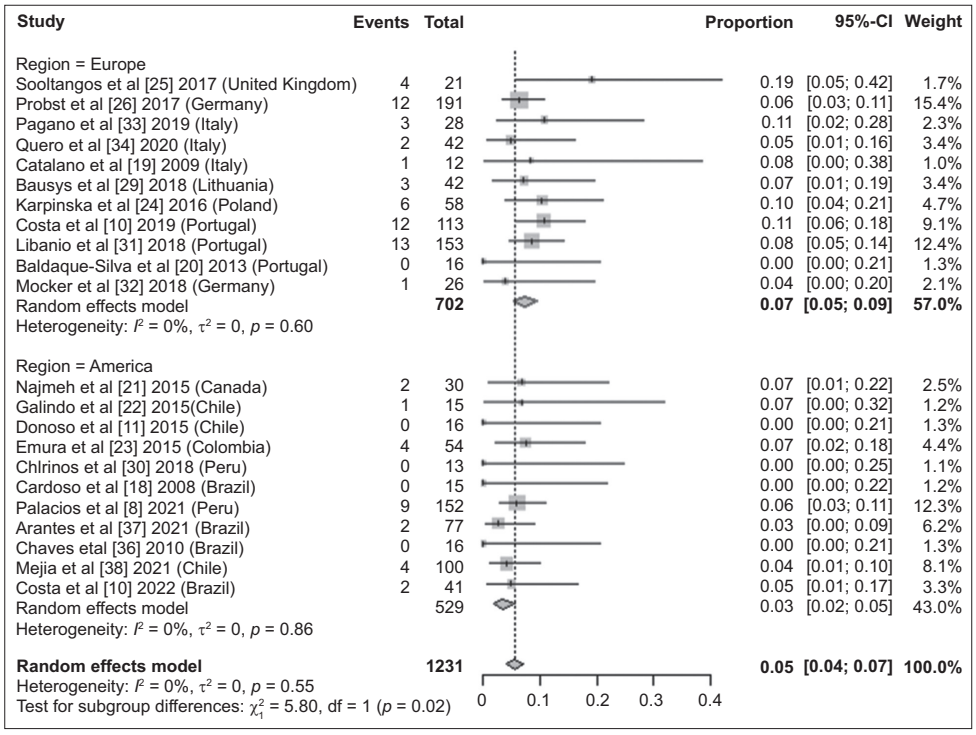
Study	Selection				COMPARABILITY	Outcome			Total (maximum=9)
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of the exposure	Outcome status at start of study		Assessment of the outcome	Length of follow-up	Adequacy of follow-up	
Cardoso *et al* [18], 2008	+	-	+	+	-	+	+	+	6
Catalano *et al* [19], 2009	+	-	+	+	-	+	+	+	6
Najmeh *et al* [21], 2015	+	+	+	+	-	+	+	+	7
Galindo *et al* [22], 2015	+	-	+	+	-	+	+	+	6
Donoso *et al* [11], 2015	+	-	+	+	-	+	+	+	6
Sooltangos *et al* [25], 2017	+	-	+	+	-	+	+	+	6
Probst *et al* [26], 2017	+	-	+	+	-	+	+	+	6
Petruzziello *et al* [27], 2017	+	-	+	+	-	+	+	+	6
Mendonça *et al* [28], 2018	+	-	+	+	-	+	+	+	6
Bausys *et al* [29], 2018	+	+	+	+	+	+	+	+	8
Pagano *et al* [33], 2019	+	-	+	+	-	+	+	+	6
Costa *et al* [10], 2019	+	-	+	+	-	+	+	+	6
Libânio *et al* [31], 2018	+	-	+	+	-	+	+	+	6
Quero *et al* [34], 2020	+	+	+	+	+	+	+	+	8
Cañete-Ruiz *et al* [9], 2020	+	-	+	+	-	+	+	+	6
Ngamruengphong *et al* [35], 2020	+	-	+	+	-	+	+	+	6
Arantes *et al* [37], 2021	+	-	+	+	-	+	+	+	6
Mejía *et al* [38],2021	+	-	+	+	-	+	+	+	6
Costa *et al* [39], 2022	+	-	+	+	-	+	+	+	6

Supplementary Table 3 Quality assessment with Joanna Briggs Institute (critical appraisal checklist for case series)

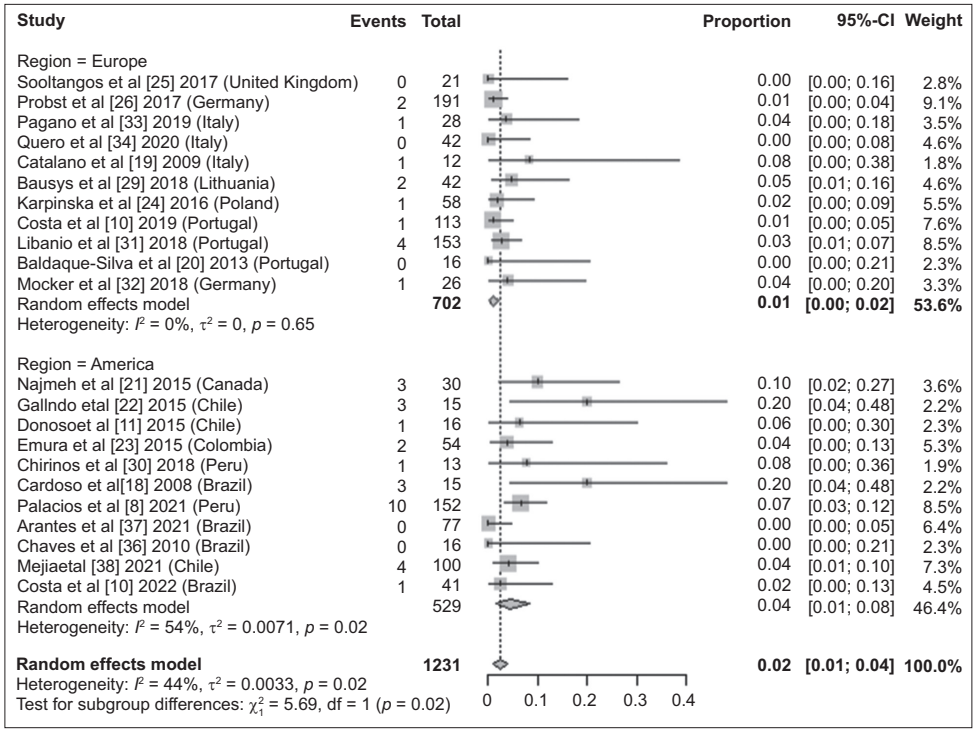
Checklist	Chaves *et al* [36], 2010	Baldaque *et al* [20], 2013	Emura *et al* [23], 2015	Karpińska *et al* [24], 2016	Chirinos *et al* [30], 2018	Mocker *et al* [32], 2018	Palacios *et al* [8], 2021	Fernandez *et al* [40], 2021
Were there clear criteria for inclusion in the case series?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the condition measured in a standard, reliable way for all participants included in the case series?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were valid methods used for identification of the condition for all participants included in the case series?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did the case series have consecutive inclusion of participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did the case series have complete inclusion of participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was there clear reporting of the demographics of the participants in the study?	No	No	Yes	Yes	Yes	No	Yes	Yes
Was there clear reporting of clinical information of the participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes or follow up results of cases clearly reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was there clear reporting of the presenting site (s)/clinic (s) demographic information	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Was statistical analysis appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes



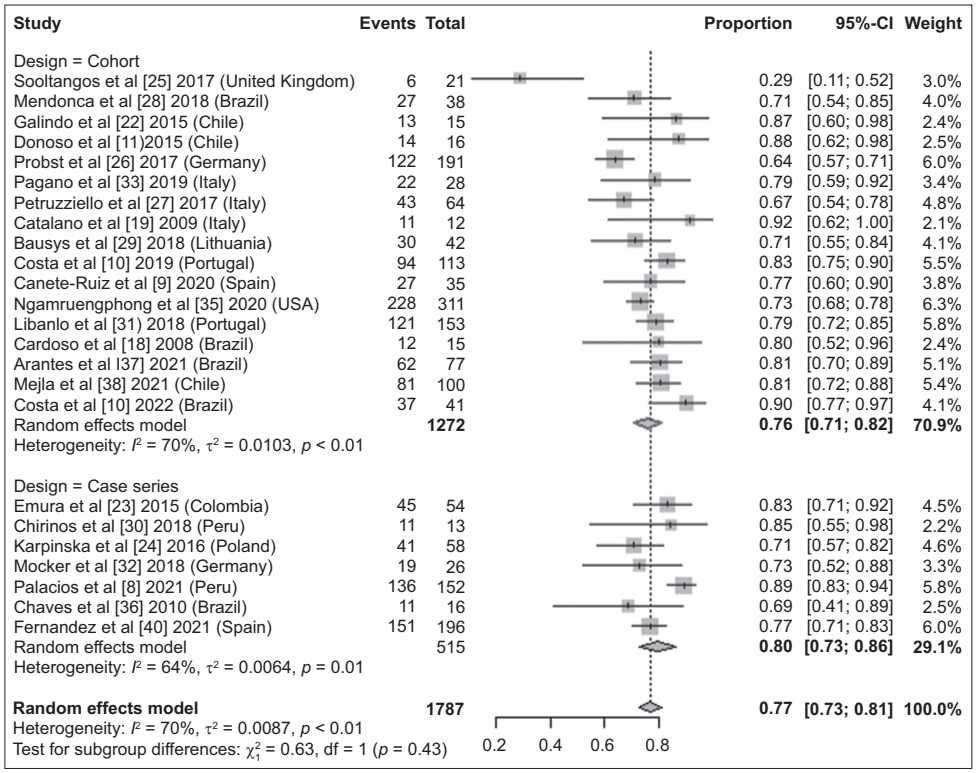
Supplementary Figure 1 Forest plot showing the overall complication rate in superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval



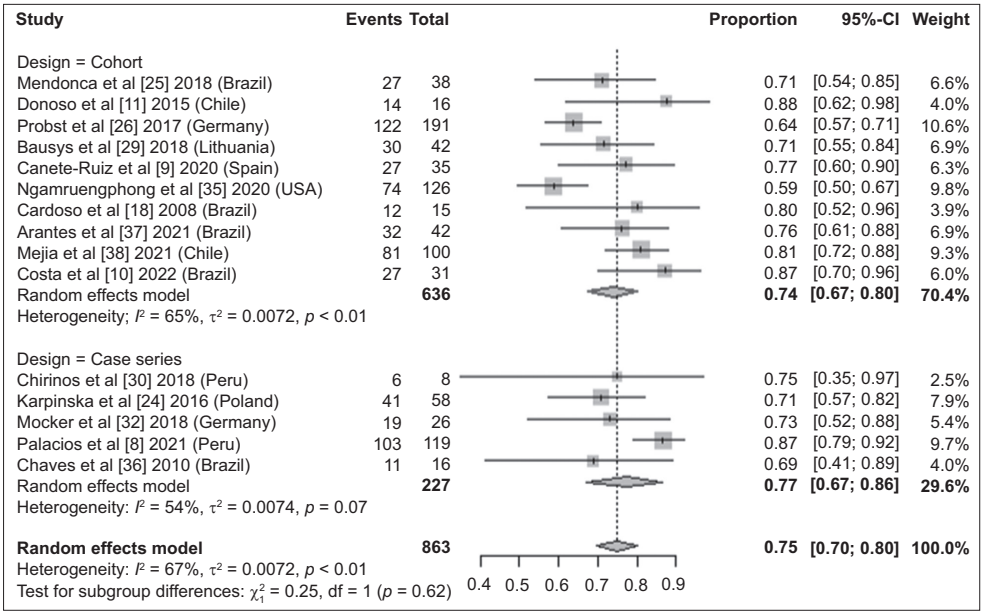
Supplementary Figure 2 Forest plot showing the bleeding rate in superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval



Supplementary Figure 3 Forest plot showing the perforation rate in superficial gastric neoplasms treated by endoscopic submucosal dissection
CI, confidence interval



Supplementary Figure 4 Forest plot showing the curative resection rate in superficial gastric neoplasms by study design
CI, confidence interval



Supplementary Figure 5 Forest plot showing the curative resection rate of superficial gastric neoplasms including only adenocarcinoma histology by study design
CI, confidence interval