



Endoscopic resection of esophageal and gastric submucosal tumors from the muscularis propria layer: submucosal tunneling endoscopic resection versus endoscopic submucosal excavation: A systematic review and meta-analysis

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Abstract

Background Submucosal tunneling endoscopic resection (STER) and endoscopic submucosal excavation (ESE) are less-invasive therapeutic alternatives to surgical resection for the removal of esophageal or gastric submucosal tumors (SMTs). This study aimed to comparing STER versus ESE for the resection of esophageal and gastric SMTs from the muscularis propria.

Methods This systematic review and meta-analysis was reported in accordance with PRISMA guidelines through December 2020. Pooled outcome measures included complete resection, *en bloc* resection, bleeding, perforation, adverse events, recurrence, procedure duration, and length of hospital stay. Risk ratio (RR) and mean difference (MD) was calculated as well as Peto time-to-event analyses to determine recurrence rate.

Results Five retrospective cohort studies ($n = 269$ STER versus $n = 319$ ESE) were included. There was no difference in rates of complete resection [RR: 1.01 (95% CI 0.94, 1.07)], *en bloc* resection [RR: 0.95 (95% CI 0.84, 1.08)], recurrence [OR: 1.18 (95% CI 0.33, 4.16)], and total adverse events [RR: 1.33 (95% CI 0.78, 2.27)]. Specific adverse events including rates of perforation [RR: 0.57 (95% CI 0.12, 2.74)] and bleeding [RR: 1.21 (95% CI 0.30, 4.88)] were not different between STER and ESE. There was a statistical difference when evaluating procedure time, with the STER group presenting significantly larger values [MD: 24.62 min (95% CI 20.04, 29.20)].

Conclusion STER and ESE were associated with similar efficacy and safety; however, ESE was associated with a significantly decreased time to complete the procedure.

Keywords Endoscopic resection · Submucosal tumor · Submucosal tunneling endoscopic resection · Endoscopic submucosal excavation

Submucosal tumors (SMTs), also known as subepithelial lesions (SELs) or subepithelial tumors (SETs), may be present throughout the entire gastrointestinal tract [1]. These types of lesions are commonly found during routine endoscopic investigation [2], most commonly identified as incidental findings [1, 3]. Submucosal tumors may appear as protrusions in the organ wall, with mucosa unaltered and equivalent to adjacent ones. The vast majority of these

patients are generally asymptomatic, though in a minority of cases, these lesions may cause pain, obstruction, or gastrointestinal hemorrhage [3, 4]. It remains pivotal to perform endoscopic ultrasonography (EUS) to more accurately evaluate these lesions and identify SMT topography and echogenicity, aiding the etiological diagnosis of these lesions [1, 5, 6].

The differential for SELs remains highly variable, depending on the layer of the organ wall from which the tumor has emerged [3, 7]. Endoscopy alone is insufficient for accurate diagnosis [6]. Among the potential etiologies include gastrointestinal stromal tumors (GISTs), which

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present malignant potential and should be resected if causing symptoms or larger than 2 cm, according to National Comprehensive Cancer Network guidelines [8]. Other potential etiologies include leiomyoma, lipoma, pancreatic rest, granular cell tumor, carcinoid, inflammatory gastric polyp, gastric varix, schwannoma, lymphangioma, or duplication cyst.

For years, surgical resection was the only therapeutic option for SMTs arising from the muscularis propria layer, due to its intimate contact with the serous membrane [9]. Conventional endoscopic resection techniques, such as endoscopic submucosal dissection (ESD), presented a considerable risk of perforations [10] and risk of incomplete resection for cases involving lesions larger than 2 cm [11, 12]. Aiming to provide a safe approach with impressive resection results, minimally invasive techniques such as submucosal tunneling endoscopic resection (STER) and endoscopic submucosal excavation (ESE) were developed [13].

Given the introduction of STER and ESE as available endoscopic resection techniques, we aimed to perform a structured systematic review and meta-analysis to compare the efficacy and safety of these modalities for resection of SMTs arising from the muscularis propria.

Materials and methods

Protocol and registration

This systematic review and meta-analysis was reported in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-analyses' (PRISMA) [14]. The study was submitted to the Prospective Register of Systematic Reviews (PROSPERO) and registered under number CRD42020185511. This study was approved by the Ethics-Scientific Committee of the Department of Gastroenterology at the University of Sao Paulo Medical School. Due to the study format, informed consent was not necessary.

Eligibility criteria and information sources

The initial search was conducted considering published studies with no restrictions concerning language or publication year. The selected studies followed the following criteria: (1) participants: patients with submucosal tumors from the muscularis propria at the esophagus or stomach; (2) intervention: submucosal tunneling endoscopic resection; (3) comparison: endoscopic submucosal excavation; and (4) results: complete resection, *en bloc* resection, recurrence, adverse events, perforation, bleeding, procedure time, and hospital stay.

Exclusion criteria were the following: (1) studies with non-human subjects; (2) studies including subjects younger than 18 years; (3) studies that assessed the analyzed

techniques only in other parts of the gastrointestinal tract; and (4) studies that did not discriminate outcomes according to each intervention group.

Search strategy and study selection

Searches were conducted electronically using on-line databases (MEDLINE, EMBASE and Cochrane Library), through December 31, 2020. The same search strategy was applied for all previous databases, namely: ((esophagus OR gastric OR stomach) AND (endoscopic mucosal resection OR submucosal tunneling resection techniques OR submucosal tunnel dissection OR microscopy scanning tunneling OR STER OR tunneling endoscopic muscularis dissection OR EFTR OR endoscopic full thickness resection OR endoscopic submucosal excavation)). The studies were selected based on the aforementioned exclusion and eligibility criteria. Two independent researchers conducted the screening following the eligibility conditions. Divergences were settled in consensus or after consulting a third reviewer.

Data collection process

After study selection, two reviewers extracted the required information and formatted the data into tables. Primary outcomes were complete resection (R_0), *en bloc* resection, total adverse events, and local recurrence. Secondary outcomes stratified adverse events such as bleeding and perforation as well as procedure time, and hospital stay. Due to the intrinsic risk of perforation as a result of resections of lesions at the muscularis propria, this outcome was defined as a discontinuity in the organ wall that required surgical interventions beyond endoscopy.

Risk of bias in individual studies

In order to assess the risk of bias in cohort studies, we employed the Risk of Bias in Non-randomized Studies (ROBINS-I) [15] (Table 1). This tool is structured into seven bias domains: (1) confounding; (2) selection of participants; (3) classification of interventions; (4) deviations from intended interventions; (5) missing data; (6) measurement of outcomes; (7) selection of the reported result. We analyzed the individual risk of bias for each included study.

Statistical analysis and quality of evidence

The analysis was conducted using the Review Manager software, version 5.4 (RevMan 5.4; Cochrane Collaboration, Oxford, UK). Risk ratio (RR) for dichotomous variables was calculated using a fixed-effects model. To appropriately determine rate of recurrence, a time-to-event analysis was utilized using the Peto Odds ratio according the Cochrane

Table 1 Risk of bias in non-randomized studies (ROBINS-I)

Study	D1	D2	D3	D4	D5	D6	D7	Overall
Hui Xiu <i>et al.</i> (2019)	●	●	●	●	●	●	●	●
Hong-wei Xu <i>et al.</i> (2019)	●	●	●	●	●	●	●	●
Chen Du <i>et al.</i> (2018)	●	●	●	●	●	●	●	●
Jiaoyang Lu <i>et al.</i> (2014)	●	●	●	●	●	●	●	●
Yingtong Chen <i>et al.</i> (2019)	●	●	●	●	●	●	●	●

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement:
Critical ●
Serious ●
Moderate ●
Low ●
No information. ?

Handbook working methodology. For continuous variables, expressed in absolute values, the differences between measures were calculated using the mean difference (MD)—employing the mean, the standard deviation, and the size of the sample for each group). In case of studies that failed to report mean and variance values, those were estimated from the median, the interval and the size of the sample [16]. We adopted a confidence interval of 95% and the level of statistical significance was established as a p -value lower than 0.05. To assess heterogeneity, we conducted heterogeneity level (I^2) analyses to identify publication bias and the percentage of variation across studies. We considered I^2 greater than 50% as high heterogeneity. Quality of evidence was assessed according to the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) (Table 2).

Results

A total of 3528 articles were identified, 3219 through our searches on MEDLINE via PubMed and other 309 found on EMBASE and Cochrane Library databases. Duplicates were removed. After applying the eligibility criteria, 7 studies of retrospective cohorts in full text were chosen; however, only 5 of which remained and were included in the meta-analysis [17–21]. The two excluded studies failed to present their data classified by intervention and comparison groups [22, 23]. The selection process is presented in Fig. 1 and Table 3 describes the individual characteristics of the selected studies. All 5 of the included retrospective cohort studies [17–21] specified

their inclusion and exclusion criteria, including and comparing 269 patients in the intervention group (STER) and 319 in the control group (ESE). One of the cohort studies presented additional data concerning endoscopic full thickness resection (EFTR) [17] that was not analyzed.

Risk of bias

All studies were assessed by ROBINS-I [15], with 3 studies classified as moderate risk [17, 19, 21] and 2 as serious risk [18, 20]. The detailed risk of bias for each included study is described in the complementary material (Table 1).

Individual results from studies

Complete resection (R_0)

All 5 studies [17–21] included in this meta-analysis reported the outcome of complete resection. A total of 588 patients were evaluated, of them 269 were in the STER group and 319 in the ESE group. There was no significant statistical difference between groups [RR: 1.01 (95% CI 0.94, 1.07); $I^2 = 58%$; $p = 0.87$] (Fig. 2). A low quality of evidence was defined (Table 2).

En bloc resection

Three studies [17, 19, 21] documented *en bloc* resection. In total, 411 patients were evaluated, with 180 in the STER

Table 2 Grading of recommendations, assessment, development, and evaluations (GRADE)

Certainty assessment		Summary of findings									
Participants (studies) followed up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Endoscopic submucosal excavation (ESE)	With Submucosal tunneling endoscopic resection (STER)			
Complete resection (R0)											
588 (5 observational studies)	Not serious	Serious ^a	Not serious	Not serious	Publication bias strongly suspected ^b	⊕⊕○○ LOW	297/319 (93.1%)	247/269 (91.8%)	RR 1.01 (0.94 to 1.07)	Risk with endoscopic submucosal excavation (ESE) 931 per 1,000 Risk difference with submucosal tunneling endoscopic resection (STER) 9 more per 1,000 (from 56 fewer to 65 more)	
En bloc resection											
411 (3 observational studies)	Not serious	Serious ^a	Not serious	Not serious	None	⊕⊕○○ MODERATE	208/231 (90.0%)	150/180 (83.3%)	RR 0.95 (0.84 to 1.08)	45 fewer per 1,000 (from 144 fewer to 72 more)	
Recurrence											
588 (5 observational studies)	Serious ^c	Not serious	Not serious	Very Serious ^d	None	⊕○○○ VERY LOW	6/319 (1.9%)	5/269 (1.9%)	RR 1.18 (0.33 to 4.29)	3 more per 1,000 (from 13 fewer to 62 more)	
Adverse events											
494 (4 observational studies)	Serious ^e	Serious ^a	Not serious	Not serious	All plausible residual confounding would reduce the demonstrated effect ^c	⊕⊕○○ MODERATE	87/269 (32.3%)	54/225 (24.0%)	RR 1.01 (0.78 to 1.32)	3 more per 1,000 (from 71 fewer to 103 more)	
Perforation											
431 (4 observational studies)	Extremely serious ^f	Not serious	Serious ^g	Very Serious ^d	None	⊕○○○ VERY LOW	4/205 (2.0%)	6/226 (2.7%)	RR 1.27 (0.39 to 4.16)	5 more per 1,000 (from 12 fewer to 62 more)	

Table 2 (continued)

Certainty assessment		Summary of findings										
Participants (studies) followed up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)			Relative effect (95% CI)	Anticipated absolute effects	
							With Endoscopic submucosal excavation (ESE)	With Submucosal tunneling endoscopic resection (STER)	With Endoscopic submucosal excavation (ESE)		Risk with endoscopic submucosal excavation (ESE)	Risk difference with submucosal tunneling endoscopic resection (STER)
Bleeding												
588 (5 observational studies)	Serious ^h	Not serious	Not serious	Very Serious ^d	All plausible residual confounding would reduce the demonstrated effect ^c	⊕⊕○○ LOW	3/319 (0.9%)	3/269 (1.1%)	RR 1.21 (0.30 to 4.88)	9 per 1,000	2 more per 1,000 (from 7 fewer to 36 more)	
Procedure time												
431 (4 observational studies)	Serious ⁱ	Not serious	Serious ^g	Not serious	None	⊕⊕○○ LOW	205	226	–	The mean procedure time was 0	MD 24.62 higher (20.04 higher to 29.2 higher)	
Length of hospital stay												
411 (3 observational studies)	Not serious	Very Serious ^j	Serious ^g	Not serious	Publication bias strongly suspected ^b	⊕○○○ VERY LOW	231	180	–	The mean length of hospital stay was 0	MD 0.61 higher (0.23 lower to 1.45 higher)	

CI confidence interval, RR risk ratio, MD mean difference

^aExplanations: Heterogeneity > 50%

^bOutlier presence

^cStudies with variable follow-up times

^dRR > 3 × CI

^eStudies evaluating variable adverse events

^fAbsence of standardization in the classification of perforation and difference in the execution of the endoscopic submucosal excavation (ESE) technique between studies

^gIntermediate outcome

^hAbsence of objective blood loss parameters

ⁱDifferences in lesion size between groups

^jHeterogeneity > 75%

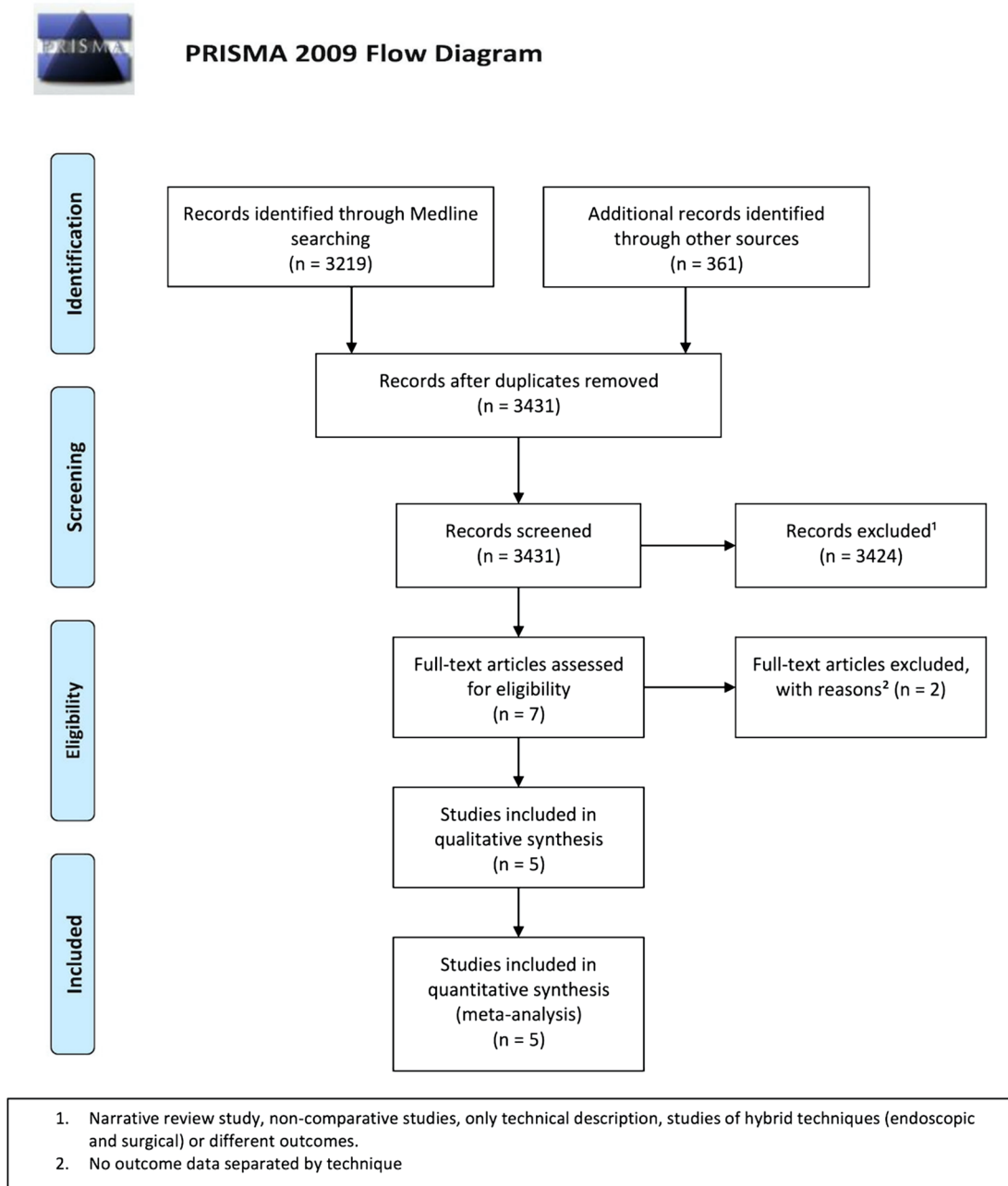


Fig. 1 Flow diagram showing study selection process for meta-analysis

group and 231 in the ESE group. There was no significant statistical difference between groups [RR: 0.95 (95% CI 0.84, 1.08); $I^2 = 51\%$; $p = 0.41$] (Fig. 3). A moderate quality of evidence was identified (Table 2).

Recurrence

All 5 selected studies [17–21] evaluated rates of local recurrence. A total of 588 patients were assessed, of these 269 were in the STER group and 319 in the ESE group.

According to the analysis (Fig. 4), there was no significant statistical difference between the two groups [OR: 1.18 (95% CI 0.33, 4.16); $I^2 = 0\%$; $p = 0.80$] and a very low quality of evidence was found (Table 2).

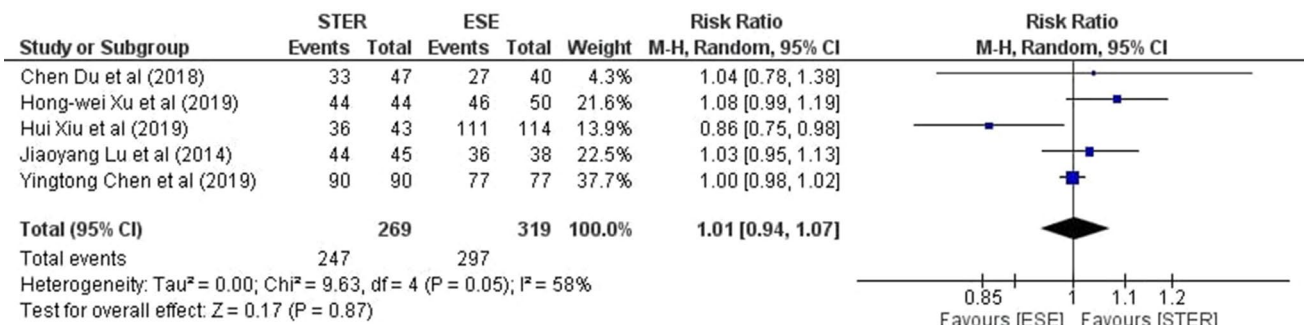
Adverse events

All 5 studies [17–21] presented data concerning adverse events. In a preliminary analysis, we verified the presence of high heterogeneity ($I^2 = 64\%$). In total, 588 patients were

Table 3 Characteristics of included studies

	Study	P: patients	I: interventions	C: control	O: outcome
Hui Xiu et al. (2019)	Retrospective cohort	STM Esophagus and stomach (n: 157)	ER-STER (n: 43)	ESE (n: 114)	Complete resection, en bloc resection, reoccurrence, perforation, bleeding, complications, and hospital stay
Hong-wei Xu et al. (2019)	Retrospective cohort	STM from cardia (1 cm–0–2 cm) (n: 94)	ER-STER (n: 44)	ESE (n: 50)	Complete resection, reoccurrence, perforation, bleeding, and procedure time
Chen Du et al. (2018)	Retrospective cohort	STM from cardia (n: 87)	ER-STER (n: 47)	ESE (n: 40)	Complete resection, en bloc resection, reoccurrence, perforation, bleeding, complete resection, hospital stay, and procedure time
Jiaoyang Lu et al. (2014)	Retrospective cohort	STM Esophagus and cardia (n: 83)	ER-STER (n: 45)	ESE (n: 38)	Complete resection, reoccurrence, perforation, bleeding, complications, and procedure time
Yingtong Chen et al. (2019)	Retrospective cohort	STM esophagus (n: 167)	ER-STER (n: 90)	ESE (n: 77)	Complete resection, en bloc resection, reoccurrence, perforation, bleeding, complete resection, hospital stay, and procedure time

STM submucosal tumor, ER endoscopic resection, STER submucosal tunneling endoscopic resection, ESE endoscopic submucosal excavation

**Fig. 2** Forest plot of complete resection (R_0)

evaluated, of them 269 were in the STER group and 319 in the ESE group. There was no significant statistical difference between groups [RR: 1.33 (95% CI 0.78, 2.27); $I^2 = 64\%$; $p = 0.30$] (Fig. 5). We next identified the presence of outlier study [20]. After removal of this outlier study, heterogeneity levels became very low ($I^2 = 0\%$). Afterward, 494 patients were evaluated, of which 225 were in the STER group and 269 in the ESE group, finding no significant statistical difference between groups [RR: 1.17 (95% CI 0.93, 1.47); $I^2 = 0\%$; $p = 0.19$] (Fig. 6). Therefore, 4 studies [17–19, 21] were included for this outcome. Quality of evidence was defined as moderate (Table 2).

Perforation

All 5 studies [17–21] presented data regarding perforation for this meta-analysis. A total of 588 patients were evaluated ($n = 269$ in the STER group and $n = 319$ in the ESE group). There was no significant statistical difference between groups [RR: 0.57 (95% CI 0.12, 2.74); $I^2 = 72\%$; $p = 0.49$] (Fig. 7). There was a very low quality of evidence defined (Table 2).

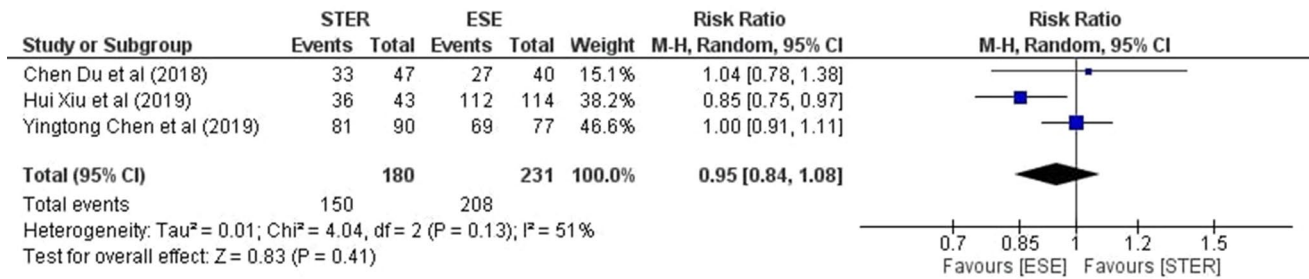


Fig. 3 Forest plot of en bloc resection

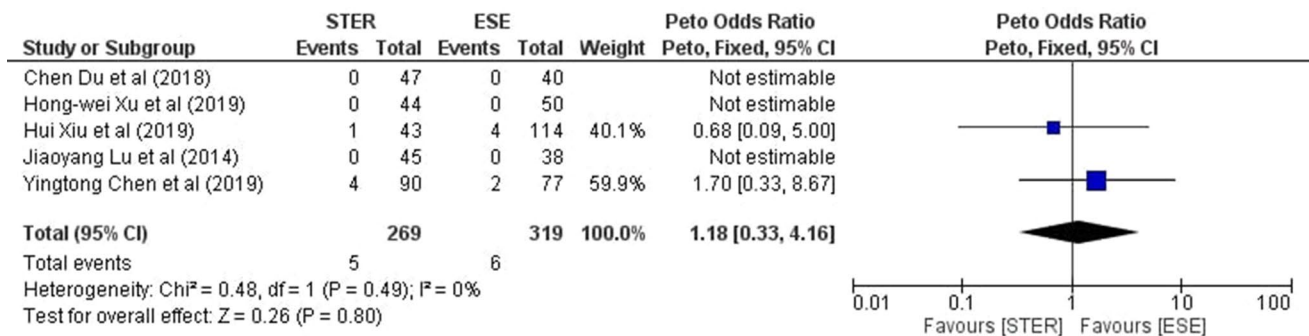


Fig. 4 Forest plot of recurrence

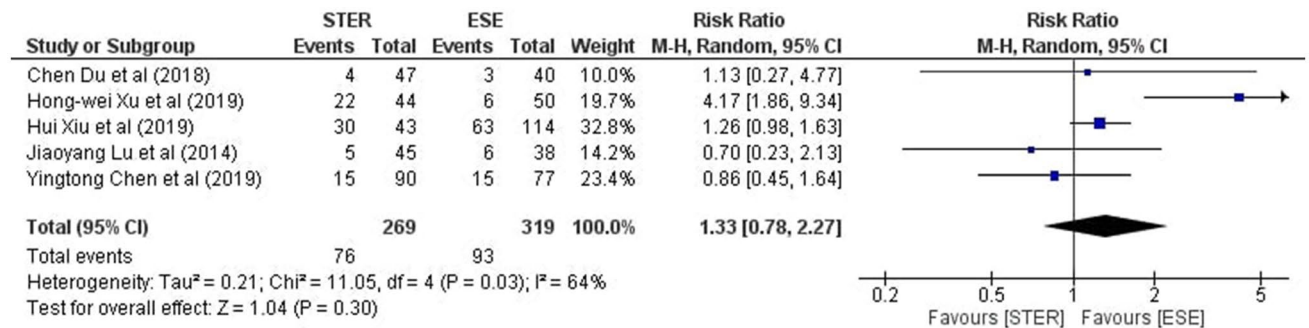


Fig. 5 Forest plot of adverse events

Bleeding

All 5 studies [17–21] reported post-resection hemorrhage outcomes. In total, 588 patients were assessed, with $n = 269$ in the STER group vs $n = 319$ in the ESE group. There was no significant statistical difference between groups [RR: 1.21 (95% CI 0.30, 4.88); $I^2 = 15%$; $p = 0.79$] (Fig. 8) and a low quality of evidence was found (Table 2).

Procedure time

Four studies [18–21] were considered in this outcome. In total, 431 patients were assessed, with $n = 226$ in the STER group and $n = 205$ in the ESE group. There was a statistical difference between groups, with significantly higher values in the STER group, which presented a mean difference of 24.62 min longer in comparison with ESE [MD: 24.62 min (95% CI 20.04, 29.20); $I^2 = 38%$; $p < 0.00001$] (Fig. 9). The quality of evidence for this outcome was defined as low (Table 2).

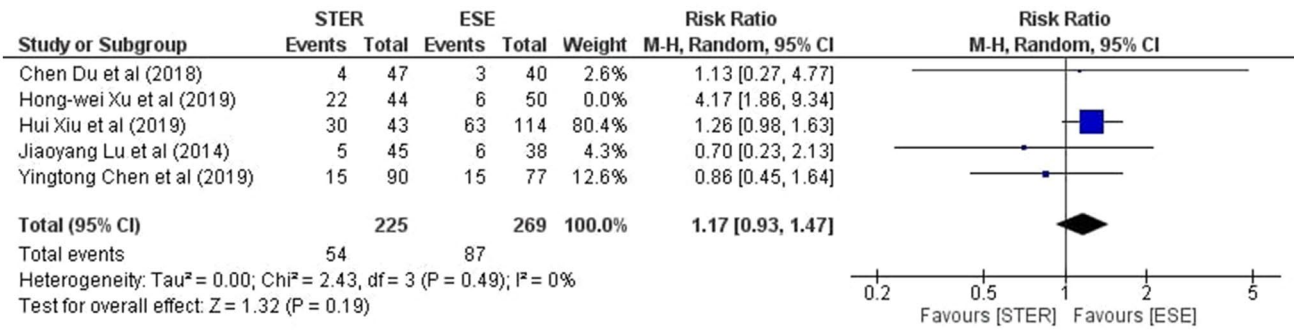


Fig. 6 Forest plot of adverse events after removal the outlier

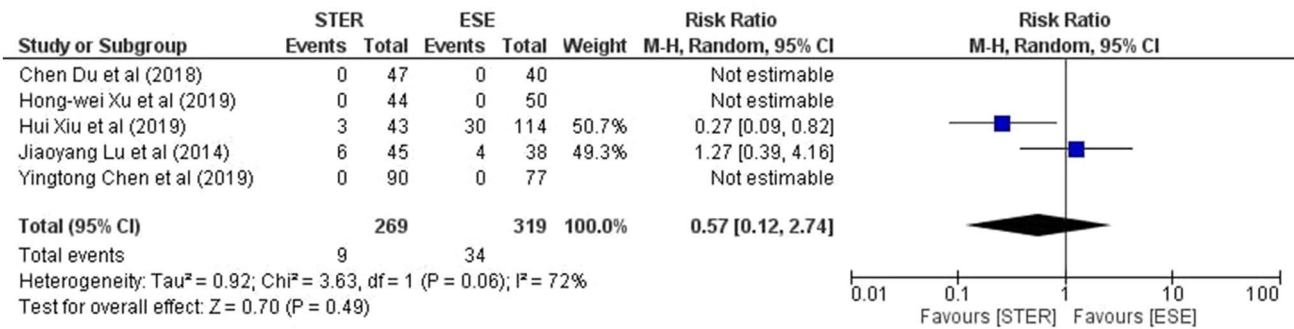


Fig. 7 Forest plot of perforation

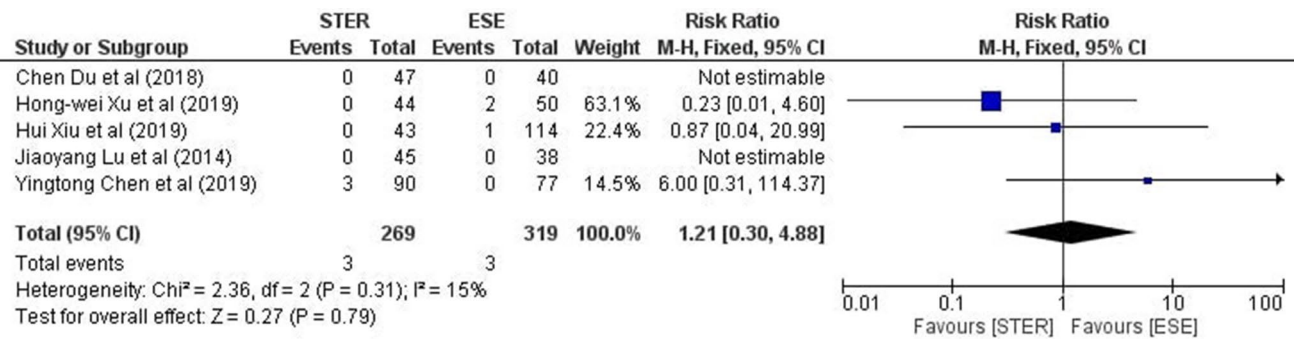


Fig. 8 Forest plot of bleeding

Length of hospital stay

Three studies [17, 19, 21] were included in this outcome. In total, 411 patients were evaluated, with 180 in the STER group and 231 in the ESE group. There was no significant statistical difference between groups [MD: 0.61 (95% CI -0.23, 1.45); I² = 95%; p = 0.15] (Fig. 10) and a very low quality of evidence was defined (Table 2).

Discussion

Although STER and ESE are considered safe and viable techniques [24] for the resection of submucosal tumors from the muscularis propria layer, it is not possible to define a technical superior procedure at this time due to the absence of robust data and incongruity of published data. In this systematic review and meta-analysis, we evaluated submucosal tunneling endoscopic resection (STER) and endoscopic submucosal excavation (ESE) techniques, currently the most

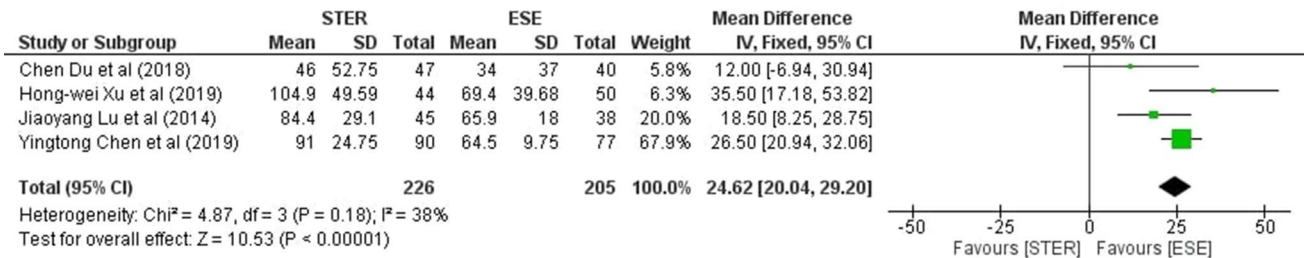


Fig. 9 Forest plot of procedure time

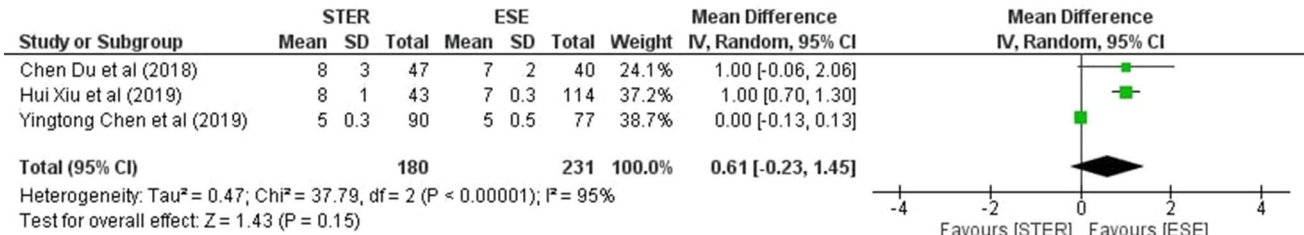


Fig. 10 Forest plot of length of hospital stay

widespread methods for the resection of esophageal and gastric SMTs originating from the muscularis propria. Both compared resection techniques appeared to be effective and safe; however, ESE was associated with a shorter procedure time. There was no difference in rates of complete resection, *en bloc* resection, recurrence, and total adverse events including rates of bleeding and perforation.

In 2012, Xu et al. first described the STER technique [25]. The technique involved a 2 cm longitudinal incision approximately 5 cm from the lesion, followed by the creation of a submucous tunnel until the exposure and removal of the lesion was complete [25]. The STER technique is similar to per-oral endoscopic myotomy (POEM) as utilized for the endoscopic treatment of achalasia. The SEL is then resected using a snare or a knife while in the submucosal tunnel and retrieved prior to closure of the defect using endoscopic clips or suture. Closure then improves post-resection healing, which decreases the risk of adverse events such as subcutaneous emphysema and pneumomediastinum [25, 26]. In 2017, Xiu-He et al. published a systematic review assessing SMT resection in the upper gastrointestinal tract by means of the STER technique, demonstrating that STER is a viable and safe option for treating these types of tumors [26].

In contrast to STER, the endoscopic submucosal excavation (ESE) technique is performed via a longitudinal or circular incision in the mucosa above the lesion, followed by the dissection of the layers until the tumor is found. Once this is accomplished and the lesion removed, the provider attempts to approximate the edges of the remaining mucosa with metal endoscopic clips [27]. ESE is derived and

perfected from an endoscopic submucous dissection (ESD) technique [10], which is a more widespread resection technique, but not suitable for lesions arising from deeper layers. Previous literature has shown ESE technique to be safe and effective for both esophageal [24] and gastric lesions [28, 29] at the muscularis propria.

When evaluating rates of complete resection (R_0) and *en bloc* resection we found no significant statistical difference between the patients that underwent STER vs ESE. Despite the groups being similar in many aspects, it should be noted that these groups were not homogenous throughout the included studies, with variation in regard to tumor topography and lesion size (Table 4). It remains important to acknowledge this may have influenced the results within these outcomes due to the anatomical variation at the resection site. In the included study, Xiu et al. [17] conducted an analysis utilizing subgroups categorized according to the location of the resected lesions, and showed that both STER and ESE presented no significant difference regarding complete and *en bloc* resection of esophageal lesions. An analysis concerning only gastric lesions was not possible due to the low number of SMTs resected by means of STER.

In a subgroup analysis, Xu et al. [20] demonstrated that tumors ≤ 15 mm had a complete resection rate with both ESE and STER of 100%. For tumors > 15 mm, the STER group had a higher rate of complete resection as well as adverse events compared to the ESE group. Xiu et al. [17] showed there is no significant difference between the rates of complete and *en bloc* resections of lesions < 20 mm and lesions between 20 and 40 mm.

Two previous systematic reviews, which considered only the STER technique, demonstrated complete (R_0) and *en bloc* resection rates of 97% and 94%, respectively [26, 30]. Another prospective study assessing only the ESE technique showed complete and *en bloc* resection rates of 95% and 96%, respectively [31]. These previous literature is in accordance with the results found in this present systematic review and meta-analysis. Individually, the studies suggest that lesions smaller than 10 mm to 15 mm may be safely resected by both techniques and that larger lesions may be preferably resected by STER, despite lower rates of *en bloc* resection of lesions of 4 cm or larger [17, 18, 20, 21].

With regard to rates of recurrence, there was no statistical difference between the techniques. However, it is important to acknowledge that the follow-up period varied among studies and the histologic etiology of each lesion was only defined in a post-procedure assessment of the resected tissue (Table 4). The most commonly found tumors were leiomyomas followed by GISTs, which are associated with higher recurrence risk [3]. Among the included studies, the study by Xu et al. [20] presented the largest sample of GIST lesions. Still, no patient in this study developed local recurrence after endoscopic resection, reinforcing the safety of both techniques, even among lesions with traditionally higher rates of recurrence. As our systematic review and meta-analysis has shown, other studies confirm that both STER [26, 30, 32–39] and ESE [28, 31] present low recurrence rates.

The assessment of perforation rate in our study also demonstrated no significant statistical difference between STER and ESE. The absence of a uniformly-established definition for all studies regarding this outcome, and the lack of information regarding the use of carbon dioxide (CO₂) flow applied in the procedures, compromise its level of evidence. It is important to highlight that the ESE technique presents alternative variations regarding the incision performed in the mucosa, namely the longitudinal [31] and circumferential [27] incisions. Among the studies selected in our analysis, 2 presented circumferential incisions [17,

19] while 3 utilized a longitudinal incision [18, 20, 21]. The latter allowed an easier approximation of the mucosa with metal clips at the end of the procedure, which has been associated with a decreased risk of a clinically significant perforation. Furthermore, our study showed no significant statistical difference concerning bleeding rate between the groups. Post-procedure hemorrhage was associated with a low incidence for both techniques, occurring in only 3 cases among all patients submitted to STER (3/269) and 3 events among patients undergoing ESE (3/319).

As for the safety of the techniques, Lu et al. [18] performed subgroup analyses among lesions of different sizes, and showed that lesions < 10 mm reached 100% of complete resection rate, and there was no perforation or adverse symptoms related to the procedure. For lesions > 10 mm, despite the high rate of complete resection (ESE: 92%, STER: 97%), the perforation rate was also high (ESE: 16%, STER: 18.2%). Both STER and ESE had a similar perforation rate (3%, $p < 0.05$).

Not surprisingly, the length of hospital stay was also similar—both being endoscopic treatments with reduced length of stay compared to traditional surgical resection. Importantly, however, ESE was associated with a shorter procedure time compared to STER. The STER technique may demand a longer execution time possibly because it requires the formation of a tunnel by dissection until the lesion is exposed [40]. This occurs in contrast to ESE, which dissects the organ wall layers at a place equivalent to the lesion site. Despite all studies being retrospective, and there being a need for more high quality data, we believe that this meta-analysis provides important information that may help in decision-making. We acknowledge that the average size of the lesions removed by the STER technique is slightly higher in all studies included in the meta-analysis, and thus, may be a form of selection bias that makes the time to perform the procedure longer.

When evaluating the individual studies, respective authors attempted to reduce this bias. Du et al. reported in their study that no difference was found between the groups when assessing the size of the lesions ($p < 0.05$). The study

Table 4 Characteristics of resected tumors

	Tumor size (mean ± SD)		Pathological diagnosis, <i>n</i>						Localization	
	STER	ESE	Leiomyoma		GIST		Others		<i>n</i> (E/C/S) ^a	
			STER	ESE	STER	ESE	STER	ESE	STER	ESE
Chen Du	34 ± 21.38	25.75 ± 15.89	14	10	0	2	0	1	14 (0/14/0)	13 (0/13/0)
Jiaoyang Lu	12.1 ± 3.9	11.5 ± 3.7	42	32	3	6	0	0	45 (29/16/0)	38 (27/11/0)
Hong-wei Xu	22.05 ± 7.67	15.32 ± 7.77	31	34	10	14	3	2	44 (14/14/16)	50 (6/6/38)
Hui Xiu	22.25 ± 4.34	15 ± 2.89	38	57	3	39	2	18	43 (23/10/10)	114 (12/3/99)
Yingtong Chen	21.1 ± 12.7	16.8 ± 15.4	87	73	1	4	2	0	90 (90/0/0)	77 (77/0/0)

^aE/C/S esophagus, cardia, stomach

by Lu et al. performed a detailed assessment by subgroups, confirming that to resect lesions > 10 mm, performing STER requires more time. In an analysis of subgroups, Xu et al. confirmed that the mean time of operation was longer with STER than with ESE for tumors ≤ 15 mm and that both groups had a similar time for lesions > 15 mm. Contrary to the other meta-analyzed studies, Chen et al. showed that tumors ≥ 20 mm have similar operating time for both STER and ESE ($p > 0.05$) and that for tumors < 20 mm, STER was performed in a shorter time ($p < 0.05$).

It is important to acknowledge this systematic review and meta-analysis is not without other limitations. Chiefly, this study included only observational studies—which is not surprising given the novelty of the endoscopic techniques. Despite this, it is possible the decision to perform one technique over the other may result in significant selection bias and inability to control for unmeasured confounders. Additionally, given the complexity of these procedure, it is likely these results will not translate to a broader clinical practice, and will continue to be performed by a small group of endoscopists in a few centers with expertise. As such, the well-designed randomized clinical trials or prospective studies among these institutions as well as registry databases are needed. Furthermore, adoption of a rigorous definition concerning the criteria for lesion selection, measured outcome assessment, and implementation are required.

Conclusion

Overall, STER and ESE are both considered safe and effective techniques for the resection of esophageal and gastric SMTs arising from the muscularis propria. The choice between STER and ESE should thus follow the particularities of each institution, prioritizing the technique for which the endoscopist is more skilled and trained, as well as availability of resources. Ultimately, the ESE technique was associated with a shorter procedure time compared to STER. However, there was no significant difference between the techniques with regard to rates of complete resection (R_0), en bloc resection, adverse events, local recurrence, and length of hospital stay.

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E.; revising the article and english; WMB: analysis and interpretation of data, drafting the article, final approval; EGHM analysis and interpretation of data, drafting the article, revising the article, final approval.

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