

Short versus long esophageal myotomy during peroral endoscopic myotomy: A systematic review and meta-analysis of comparative trials

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Abstract

Background: Peroral endoscopic myotomy (POEM) is an established modality of treatment for achalasia cardia. Considerable variations exist in the technique of POEM with respect to the length and orientation of the myotomy. In this systematic review and meta-analysis, we compared the outcomes of short versus long myotomy during POEM.

Methods: We searched multiple databases from January 2010 to March 2021 to identify studies reporting on POEM. We selected studies that reported on comparative outcomes of POEM using short versus long myotomy. We performed a comparative analysis of clinical success, procedural duration, gastroesophageal reflux disease (GERD), and adverse events with short and long myotomy in POEM by meta-analysis.

Results: A total of 521 patients from five studies in which 241 patients were treated with short and 280 patients with long myotomy approaches were analyzed. The pooled rate for clinical success gave an odds ratio (OR) of 1.27 (95% confidence interval [CI] 0.50–3.26; $I^2 = 0$; $P = 0.62$); for hospital stay OR 0.22 (95% CI – 0.03 to 0.46; $I^2 = 0$; $P = 0.08$); for GERD by esophagogastroduodenoscopy (EGD) OR 0.58 (95% CI 0.31–1.07; $I^2 = 0$; $P = 0.08$), and for adverse events OR 0.67 (95% CI 0.29–1.53; $I^2 = 51$; $P = 0.34$). Abnormal esophageal acid exposure was less frequent with OR 0.45 (95% CI 0.22–0.90; $P = 0.02$; $I^2 = 0$) and the procedure duration was significantly shorter in the short myotomy group with OR – 0.76 (95% CI – 1.00 to – 0.52; $I^2 = 43$; $P = 0.001$).

Conclusion: Short myotomy and long myotomy in POEM seem comparable with each other in terms of clinical success and adverse events. Short myotomy is associated with significantly shorter procedural duration and possibly reduced esophageal acid exposure compared with long myotomy.

Keywords: Achalasia, endoscopy, esophagus, myotomy, outcomes

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INTRODUCTION

Peroral endoscopic myotomy (POEM) has established its place as a safe and effective treatment modality for achalasia cardia. Since its inception a decade ago, several modifications

in the technique of POEM have evolved primarily involving the orientation and the length of myotomy. Of these, the length of esophageal myotomy during POEM has garnered

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attention in recent studies.^[1-6] Traditionally, the length of esophageal and gastric myotomy varies from 7 to 10 cm and 2 to 3 cm, respectively. Adequate gastric myotomy has been shown to prevent recurrent dysphagia in cases with achalasia.^[7] On the other hand, there is no strong evidence for performing long esophageal myotomy.

In this systematic review and meta-analyses, we aim to evaluate the outcomes of short versus long esophageal myotomy in cases with idiopathic achalasia.

MATERIALS AND METHODS

The present systematic review and meta-analysis were performed according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines.^[8] The databases used for searching the studies included Medline, Embase, Cochrane, and Google Scholar. In addition, abstracts published in the major conference proceedings were also screened. The search was limited to the English language. Since the first study on POEM in achalasia was published in the year 2010, the search was restricted to the studies published from January 2010 to March 2021. The following key terms were used in different combinations: “achalasia” OR “esophagus achalasia” AND “peroral endoscopic myotomy” OR “per-oral endoscopic myotomy” OR “POEM” AND “short myotomy” OR “shorter myotomy” OR “modified myotomy.” The search, data extraction, and assessment of the quality of the studies were performed by two independent investigators (ZN and HM). Any discrepancy between the two investigators was sorted out by consensual discussion and the opinion of the third investigator (RT).

Criteria for study inclusion and exclusion

All the studies were assessed for eligibility by two independent investigators (ZN and HM). The studies included in this meta-analysis had to be randomized controlled trials (RCT) or retrospective, published as full text or abstract, and had to fulfill the following inclusion criteria: age >18 years, comparison of short versus long or standard myotomy during POEM, outcome defined by clinical success at ≥ 6 months. The following types of studies were excluded: fewer than 50 participants, follow-up <6 months, animal model studies, published in a language other than English, case reports, editorials, and reviews. The full texts of all the published studies were reviewed in an independent manner by two investigators (ZN and HM). In case multiple studies were published by the same authors on the same cohort as suggested by overlapping study periods, the latest study was considered eligible for inclusion in the review.

Data abstraction and quality assessment

The following parameters were recorded from the selected studies: study characteristics (design, year of publication, sample size), POEM procedure-related parameters (procedural duration, adverse events), demographic characteristics of the study population (mean/median age in years, gender, previous treatment, type of achalasia), mean or median follow-up duration in months, clinical success as defined by Eckardt score of ≤ 3 or < 4 , gastroesophageal reflux disease (GERD) after POEM (symptoms, erosive esophagitis, pH monitoring), and duration of hospital stay. The data obtained from the included studies were systematically recorded in a database (Microsoft Excel[®] 2021, Version 16.48, Microsoft Corporation).

The risk of bias was assessed with respect to the main outcome using the Cochrane Risk of Bias assessment tool.^[9]

Outcomes assessed

The main outcome measured included clinical success as defined by Eckardt score ≤ 3 or < 4 . Other outcomes measured were procedure duration, adverse events, gas-related adverse events, post-POEM GERD as evaluated by symptoms, increased esophageal acid exposure and reflux esophagitis, and hospital stay. Procedure duration and hospital stay were recorded as continuous variables, whereas the other outcome measures were recorded as dichotomous variables. Any disagreement was resolved by consensus among the two investigators involved in the process of abstraction.

Statistical analysis

The effect sizes for the outcomes of interest were expressed as the standardized mean difference with 95% confidence interval (CI) for numerical or continuous variables and odds ratios (ORs) with 95% CI for categorical data. Numerical data, available as a range, were transformed to standard deviation before analysis using the method described by Hozo *et al.*^[10] Data available as percentages were transformed to numbers prior to analysis. Heterogeneity among the studies was determined by inspection of forest plots, the Cochrane Q test, and the I^2 statistic, and classified as low ($I^2 = 0\%–30\%$), moderate (31%–60%), substantial (61%–75%), and considerable (76%–100%) heterogeneity. Random effects models (Der Simonian and Laird) were used for analysis when there was heterogeneity among the studies.^[11] Fixed-effect model (Mantel–Haenszel) was used when there was no heterogeneity. Forest plots were constructed for the primary and secondary outcomes. All the analyses were performed using Review Manager 5.4 (RevMan).

RESULTS

Baseline characteristics of the studies

The preliminary literature search revealed 1,168 records. After screening for eligibility, a total of five studies including three RCTs and two retrospective studies were included in the review.^[2-6] All the included studies were published between 2018 and 2021. The details of the selection process according to the PRISMA guidelines and the summary of included studies are presented in Figure 1 and Table 1, respectively. The assessment for risk of bias is summarized in Suppl. Figure 1.

Patient characteristics

Overall, the studies involved a total of 521 patients including 241 and 280 patients in the short and long myotomy groups, respectively. Demographic characteristics were available in four studies, including 401 patients (males 199, mean age 42.9 ± 13.4 years).^[3-6] The subtypes of achalasia were reported in four studies, including type I ($n = 88$), type II ($n = 309$), and type III ($n = 4$).^[3-6] One of the included studies enrolled exclusively cases with type II achalasia.^[5] A history of prior treatment was noted in a total of 84 patients in three studies.^[3,4,6] One study (Gu *et al.*)^[5] included only treatment-naïve cases, whereas the

data regarding prior treatment were not available in another study (Familiari *et al.*).^[2]

Definition of short myotomy

The definition of short and long myotomies was variable in all five studies. Two studies defined short/long esophageal myotomy as $\leq 3/\geq 6$ cm (Nabi *et al.*)^[6] and 3–4/7–8 cm (Gu *et al.*).^[5] In the other two studies, a total myotomy length of $\leq 7/>7$ cm (Huang *et al.*)^[4] and 7/12 cm (Familiari *et al.*)^[2] was used to define short and long myotomies, respectively. One study (Li *et al.*)^[3] used the term short (6–8 cm) and long tunnel (10–14 cm) to define the two groups. The final (actual) length of esophageal myotomy was available from three studies and was significantly smaller in the short myotomy group with significant heterogeneity: OR = 3.24 (95% CI = 5.05 to 1.42; $P = 0.0005$; $I^2 = 96\%$)^[3,4,6] [Suppl. Figure 2].

Clinical success

The data on clinical success defined as Eckardt score of ≤ 3 or <4 were available in 501 (96.2%) study participants involving all the five studies included in the review. The outcomes were presented at predefined follow-up durations in the three randomized studies including 6 months in one and 12 months in two studies,^[2,5,6] whereas follow-up

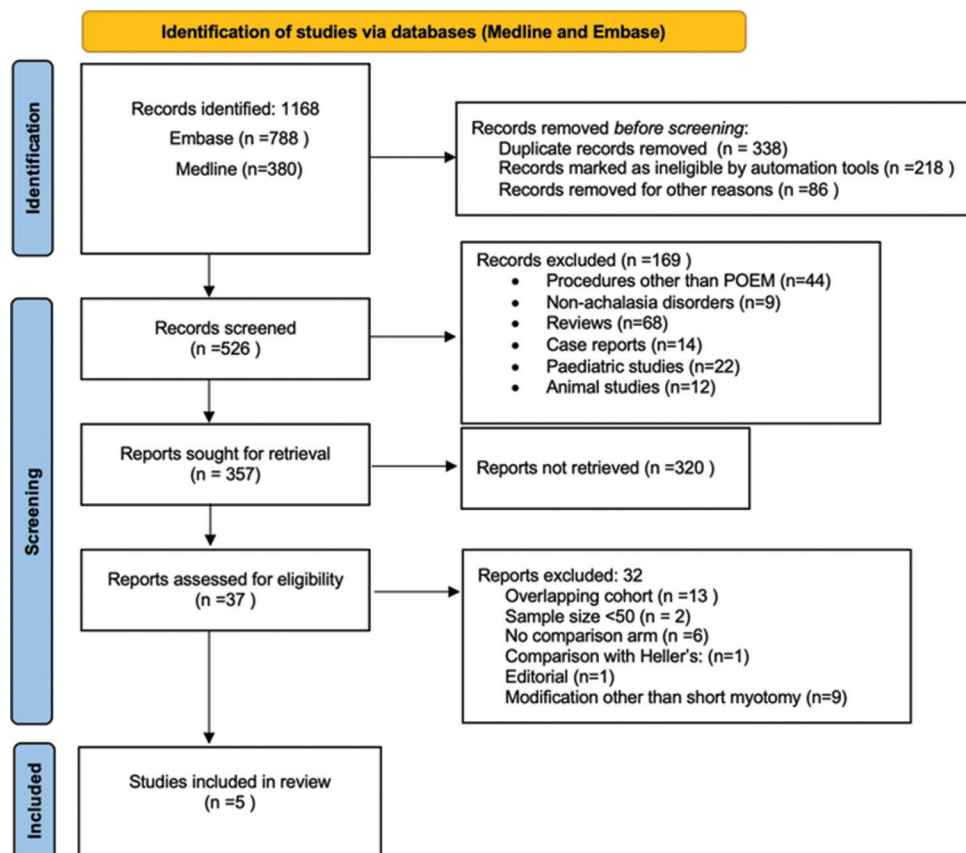


Figure 1: PRISMA diagram showing the flow of study selection

Table 1: Clinical characteristics of studies comparing short versus long esophageal myotomy

Study	Study design	n (S vs. L)	Gender (M/F)	Age, Mean (SD/range)	Achalasia subtype; I, II, III	Disease duration (years)	Prior therapy (%)	Myotomy length, cm	Procedure duration, mean (SD/range)	Adverse events (%)	Mucosal injury (%)	Insufflation adverse events (%)
Familiari et al. ^[2]	RCT	62	NA	NA	NA	NA	NA	7 (Total)	43.6 (17.0)	35%	NA	NA
Li et al. ^[3]	R	63	24/39	49.3 (19-79)	16, 45, 2	9.4 (0.1-40)	23 (36.5)	6-8 (Tunnel)	54.8 (17.3)	33.9%	4 (6.3)	2 (3.2)
		63	30/33	45.9 (16-72)	9, 52, 0	9.4 (0.3-30)	19 (30.1)	10-14	49.2 (23-120)	21 (33.3)	5 (7.9)	6 (9.5)
Huang et al. ^[4]	R	36	19/17	40.8 (11.1)	12, 24, 0	8.8 (5.5)	9 (25)	≤7 (Total)	46.6 (18.5)	3 (8.3)	0 (0)	1 (2.8)
		74	40/34	37.7 (13.0)	26, 48, 0	8.9 (5.8)	12 (16.2)	>7	62.1 (25.2)	6 (8.1)	1 (1.3)	2 (2.7)
Gu et al. ^[5]	RCT	46	21/25	43.6 (11.4)	Only II	5 (0.3-34)	Excluded	3-4 (esophageal)	31.2 (15.3)	0 (0)	0 (0)	0 (0)
		48	23/25	42.8 (10.2)		4.1 (0.1-31)		7-8	45.6 (16.2)	1 (2.2)	1 (20.8)	0 (0)
Nabi et al. ^[6]	RCT	34	18/16	40.1 (16.8)	12, 22, 0	3 (1.5-4.7)	12 (35.3)	≤3 (esophageal)	44.03 (13.78)	4 (11.8)	1 (2.9)	3 (8.8)
		37	24/13	41.3 (14.4)	13, 24, 0	3 (1-5)	9 (24.3)	≥6	72.43 (27.28)	4 (10.8)	1 (2.7)	3 (8.1)
Study	n (S vs. L)	Hospital stay, mean (SD)	Erosive esophagitis (%)	Reflux symptoms (%)	pH GERD (%)	Post-POEM LES, mmHg	Post-POEM IRP, mmHg	Eckardt score (post-POEM)	Success (%)	Follow-up, months (range)		
Familiari et al. ^[2]	62	NA	35% vs. 33.9% (not known how assessed)			16.1 (10.1)	7.8 (5.3)	NA	100%	6		
	58					19.6 (11.1)	8.7 (4.8)		98%	6		
Li et al. ^[3]	63	NA	6 (9.5)	6 (9.5)	NA	15.6 (1.5-35.7)	NA	1.1 (0-4)	56 (98.2)	20.1 (6-48)		
	63		8 (12.7)	8 (12.7)		17.7 (3-38.8)		1 (0-4)	55 (98.2)	23.6 (6-48)		
Huang et al. ^[4]	36	9.9 (2.4)	1 (2.8)	NA	NA	15.9 (3.2)	NA	1.3 (1.2)	34 (94.4)	26.8 (8-54.3)		
	74	9.3 (2.9)	4 (5.4)			13.3 (5.7)		1.6 (1.3)	68 (91.9)	29.5 (6-58.8)		
Gu et al. ^[5]	46	7 (0.9)	4 (8.7)	7 (15.2)	11 (23.9)	11.8 (4.4)	10.1 (2.4)	0.76 (0.51)	44 (95.6)	12		
	48	6.5 (1.6)	7 (14.6)	11 (22.9)	21 (43.8)	12.1 (3.9)	9.7 (2.6)	0.72 (0.42)	45 (93.8)	12		
Nabi et al. ^[6]	34	2.82 (0.67)	11 (32.3)	NA	7 (25.9)	NA	8.6 (1.3)	0.93 (0.93)	29 (93.5)	12		
	37	2.81 (0.70)	18 (48.6)		12 (40)		7.4 (1.3)	0.82 (0.98)	32 (96.9)	12		

RCT, randomized controlled trial; R, retrospective; S, short; L, long; GERD, gastroesophageal reflux disease; POEM, per oral endoscopic myotomy; LES, lower esophageal sphincter pressure; IRP, integrated relaxation pressure; SD, standard deviation

duration was presented as mean (range) in two studies.^[3,4] The minimum follow-up duration was 6 months in all the included studies. Clinical success was similar in the short and long myotomy groups with no heterogeneity among the included studies (OR 1.27; 95% CI 0.50–3.26; $P = 0.62$; $I^2 = 0$) [Figure 2a]. A subanalysis of randomized trials also revealed similar clinical success in both the groups (OR 1.20; 95% CI 0.34–4.26; $I^2 = 0$).

Objective evaluation of success

An objective measure of clinical success (Eckardt score) was reported in four studies.^[3-6] There was no significant difference in the mean post-POEM Eckardt scores between short and long myotomy groups: OR 0.02 (95% CI – 0.18 to 0.21; $P = 0.88$; $I^2 = 0\%$) [Figure 2b].

The mean lower esophageal sphincter (LES) pressures after POEM was reported in four studies involving 307 (58.9%) participants.^[2-5] Postoperative LES pressures were not significantly different in both the groups: OR – 0.07 (95% CI – 0.41 to 0.27; $P = 0.70$; $I^2 = 49\%$). Postoperative integrated relaxation pressure (IRP) measures were available in three studies and did not differ significantly between the two groups: OR 0.28 (95% CI – 0.33 to 0.89; $P = 0.37$; $I^2 = 84$).^[2,5,6] Significant heterogeneity was noted between the studies with respect to both the post-POEM manometry parameters [Figure 3a and b].

Procedural duration

The procedural duration was defined by all the studies in 521 (100%) participants. Pooled mean procedure duration in the short and long myotomy groups was 40.3 and 53.9 minutes, respectively. The procedure duration was significantly shorter in the short myotomy group with moderate heterogeneity between the studies: OR – 0.76 (95%CI – 1.0 to – 0.52; $P < 0.001$; $I^2 = 43$). The difference in the procedure duration remained significant after performing sensitivity analysis and removing the outlier study by Nabi et al.: OR – 0.66 (95% CI – 0.85 to – 0.47; $P < 0.001$; $I^2 = 0$) [Figure 4a and b].^[6]

Gastroesophageal reflux

The data on erosive esophagitis, symptomatic GERD, and pH-positive reflux were provided by four,^[3-6] two,^[3,5] and two studies,^[5,6] respectively. Erosive esophagitis was less frequent in the short myotomy group with no heterogeneity among the studies: OR 0.58 (95% CI 0.31–1.07; $P = 0.08$; $I^2 = 0$). However, the difference was not statistically significant [Figure 5a]. Increased esophageal acid exposure was reported in two studies and significantly less in the short myotomy group: OR 0.45 (95% CI 0.22–0.90; $P = 0.02$; $I^2 = 0$) [Figure 5b]. Symptomatic GERD was not significantly different between the two groups: OR 0.66 (95% CI 0.31–1.41; $P = 0.28$; $I^2 = 0$).

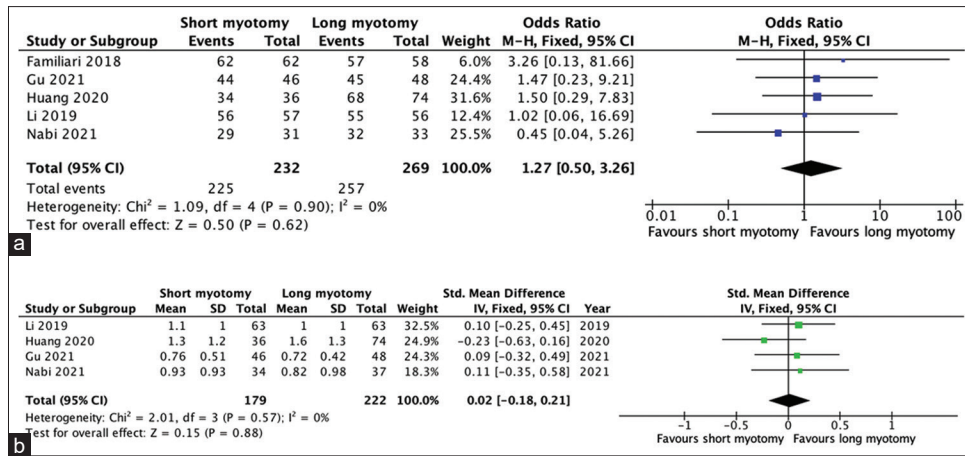


Figure 2: (a) Forest plot showing the comparison of clinical success in short versus long myotomy groups, (b) Forest plot showing the comparison of post-POEM Eckardt scores in short versus long myotomy groups

Other outcomes

Adverse events were reported in all the studies and were not significantly different between the short and long myotomy groups: OR 0.67 (95% CI 0.29–1.53; P = 0.34; I² = 51). The difference remained nonsignificant after performing sensitivity analysis and excluding one outlier study by Li *et al.*^[3]: OR 1.08 (95% CI 0.58–2.01; P = 0.81; I² = 0) [Suppl. Figure 3a].

Other outcomes were not significantly different between the two groups including gas-related adverse events: OR 0.64 (95% CI 0.22–1.85; P = 0.41; I² = 0); mucosal injury: OR 0.74 (95% CI 0.25–2.17; P = 0.58; I² = 0). Pooled mean hospital stay in short and long myotomy groups were 4.8 and 4.0 days with no significant difference in the two groups: OR 0.22 (95% CI - 0.03 to 0.46; P = 0.08; I² = 0) [Suppl. Figures 3b and c, 4].

DISCUSSION

In this systematic review and meta-analysis, the clinical success with short myotomy was found similar to long or standard myotomy during POEM, in cases with idiopathic achalasia cardia. In addition, short myotomy is associated with shorter procedural duration and reduced esophageal acid exposure.

POEM is an established endoscopic modality of treatment for achalasia and other nonachalasia spastic esophageal motility disorders of the esophagus.^[12-14] The safety and efficacy of POEM have been confirmed in multiple studies, and the updated societal guidelines have incorporated POEM into the management algorithm for achalasia.^[15-18] Since its introduction a decade ago, several modifications have been evaluated with regard to the technique of POEM. The prominent among these include the orientation (anterior or posterior) and the length (short or long) of myotomy. Several randomized trials and systematic reviews have confirmed that the orientation of myotomy, anterior or posterior, has no substantial impact on the outcomes of POEM.^[19-22] More recently, the need for a long (7–10 cm) esophageal myotomy has been questioned in several studies.^[1-6]

In this systematic review and meta-analysis, we analyzed the studies that compared short and long myotomies during POEM. In these studies, short myotomy was variably defined according to the length of esophageal myotomy (two studies),^[5,6] the length of total myotomy (two studies),^[2,4] and the length of submucosa tunnel (one

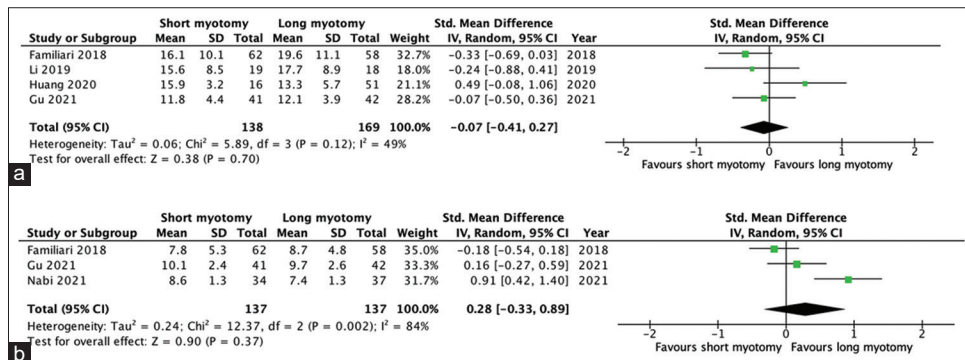


Figure 3: (a) Forest plot showing the comparison of post-POEM lower esophageal sphincter pressures in short versus long myotomy groups, (b) Forest plot showing the comparison of post-POEM integrated relaxation pressures in short versus long myotomy groups

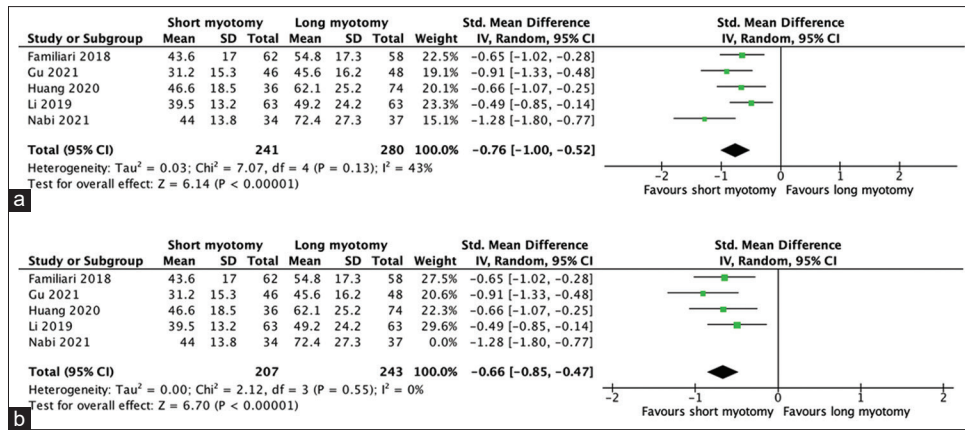


Figure 4: (a) Forest plot showing the comparison of procedure duration in short versus long myotomy groups, (b) Forest plot showing the comparison of procedure duration in short versus long myotomy groups after exclusion of outlier study

study).^[3] Consequently, there was marked heterogeneity in the final length of esophageal myotomies reported in three studies.

The main objective of the review was to compare clinical success in both groups. There was no difference in the clinical efficacy and postoperative Eckardt scores between the two groups at a minimum follow-up of 6 months. The findings are substantiated by the fact that postprocedure LES pressures and IRP were also similar in both the groups. This suggests that short myotomy is equally effective in achalasia at least for a short-term follow-up. However, caution is advised while applying the results to all the subtypes of achalasia as only one of the studies included cases with type III achalasia, that too had a small sample size ($n = 4$).^[3] Similarly, none of the studies included nonachalasia spastic esophageal motility disorders. Therefore, the results cannot be extrapolated to type III achalasia and nonachalasia spastic esophageal motility disorders, including Jackhammer esophagus and distal esophageal spasm, where long esophageal myotomies are recommended for optimal outcomes.^[23,24]

The procedural duration was significantly shorter in the short myotomy group. This finding was consistent across all the included studies. Procedural duration is a function of the operator’s expertise as well as technical difficulty during the POEM procedure. Therefore, it appears logical to assume that short myotomy may be associated with fewer adverse events especially those related to insufflation.^[25] On the contrary, the present review did not find a significant difference in the rate of total adverse events, mucosal injuries, and gas-related adverse events. One possible reason may be the small number of study participants in the included studies and the operator’s expertise limiting the overall rate of adverse events.

Post-POEM reflux esophagitis and esophageal acid exposure were lower in the short myotomy group. However, the difference was significant only for esophageal acid exposure. Of note, the results of the pH study were available in only two of the five studies included in the review.^[5,6] The pH-positive reflux was significantly lower in the short myotomy group in one (Gu *et al.*)^[5] and similar in the other study (Nabi *et al.*)^[6] Therefore, caution is advised

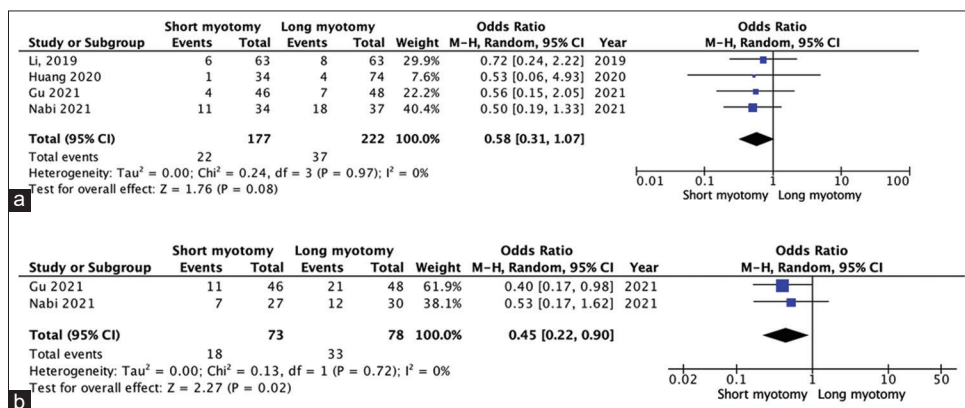


Figure 5: (a) Forest plot showing the comparison of post-POEM erosive esophagitis in short versus long myotomy groups, (b) Forest plot showing the comparison of post-POEM abnormal esophageal acid exposure in short versus long myotomy groups

while interpreting the results, and the true impact of short myotomy on post-POEM reflux remains to be unraveled in well-designed future studies.

There are several strengths of this systematic review and meta-analysis. The review adds to our current understanding regarding the impact of the technical modification on the outcomes of POEM. Of the studies included in this review, three studies were randomized trials. However, we acknowledge certain limitations pertaining to this review. One of the randomized studies was available in abstract form only. The data regarding objective evaluation including high-resolution manometry parameters and pH study details were not available in all the trials. Symptomatic GERD was reported in only two studies, and a standard questionnaire for the assessment of GERD was used in only one study. Lastly, none of the studies included compared esophago-gastric junction distensibility using EndoFLIP.

In conclusion, short myotomy appears to be equally effective with the advantage of reduced operating time and possibly less esophageal acid exposure compared with standard or long myotomy.

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Nil.

Conflicts of interest

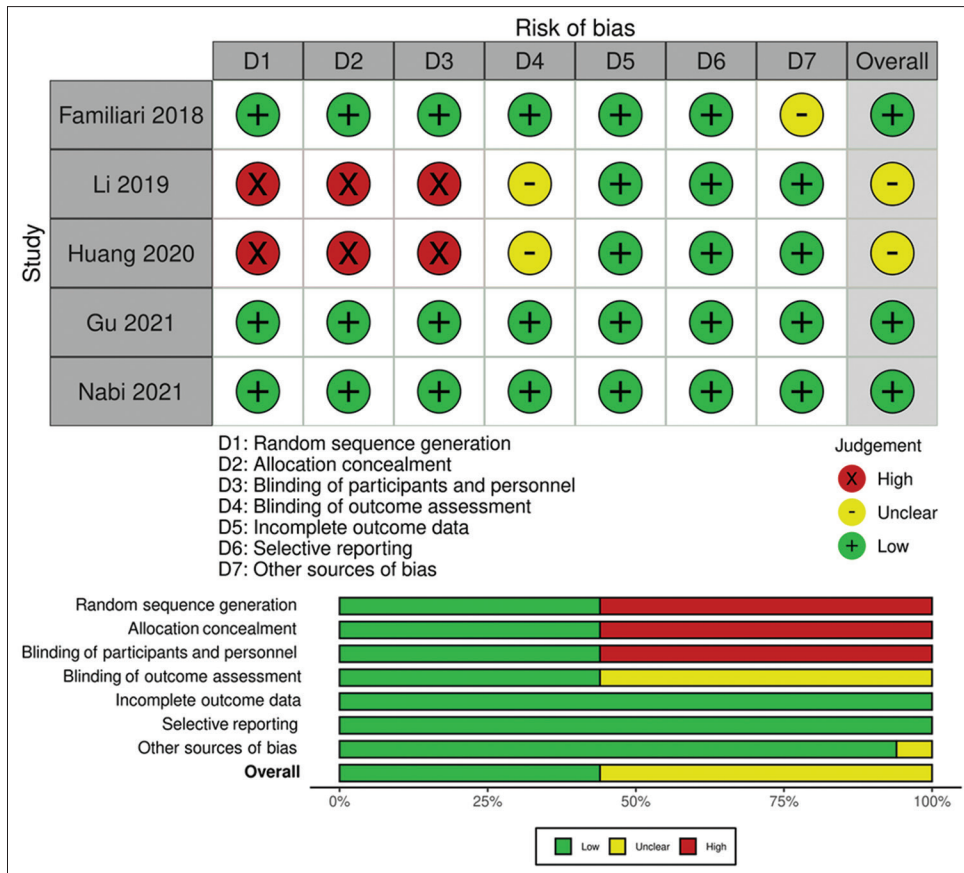
There are no conflicts of interest.

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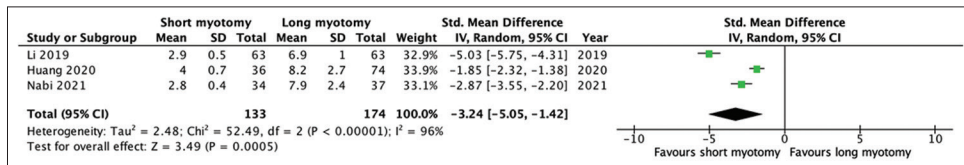
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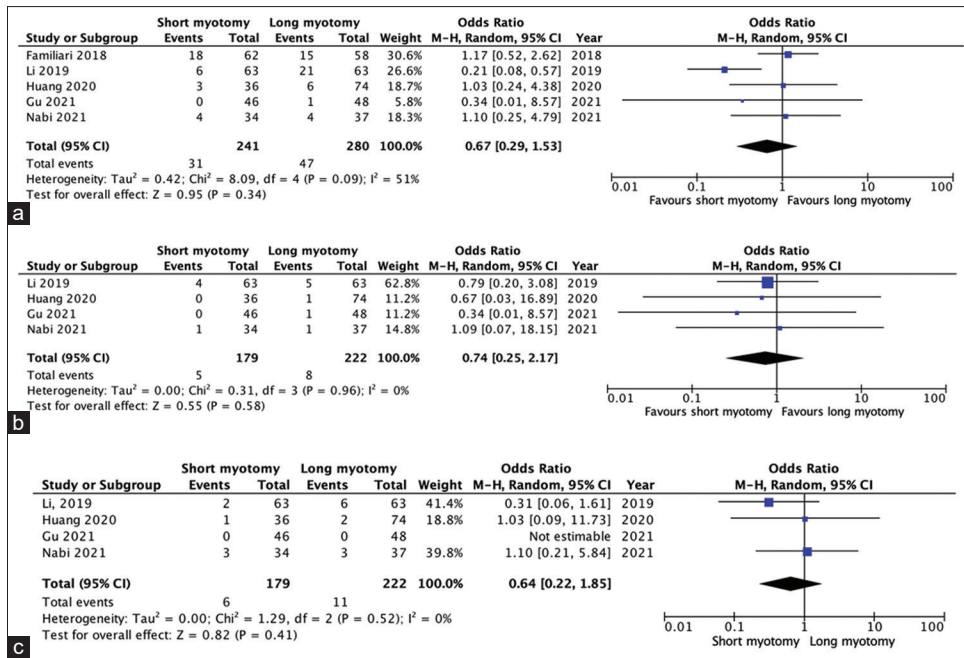
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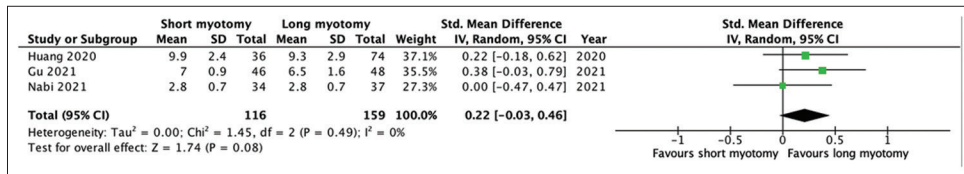
Suppl. Figure 1: Risk of bias in the included studies



Suppl. Figure 2: Forest plot showing the comparison of esophageal length of myotomy in short versus long myotomy groups



Suppl. Figure 3: (a) Forest plot showing the comparison of POEM procedure related adverse events in short versus long myotomy groups, (b) Forest plot showing the comparison of mucosal injuries in short versus long myotomy groups, (c) Forest plot showing the comparison of insufflation related adverse events in short versus long myotomy groups



Suppl. Figure 4: Forest plot showing the comparison of duration of hospital stay in short versus long myotomy groups