Gastroenterology Research and Practice

Peroral Endoscopic Myotomy for Achalasia

Lead Guest Editor: Xiao-Wei Tang
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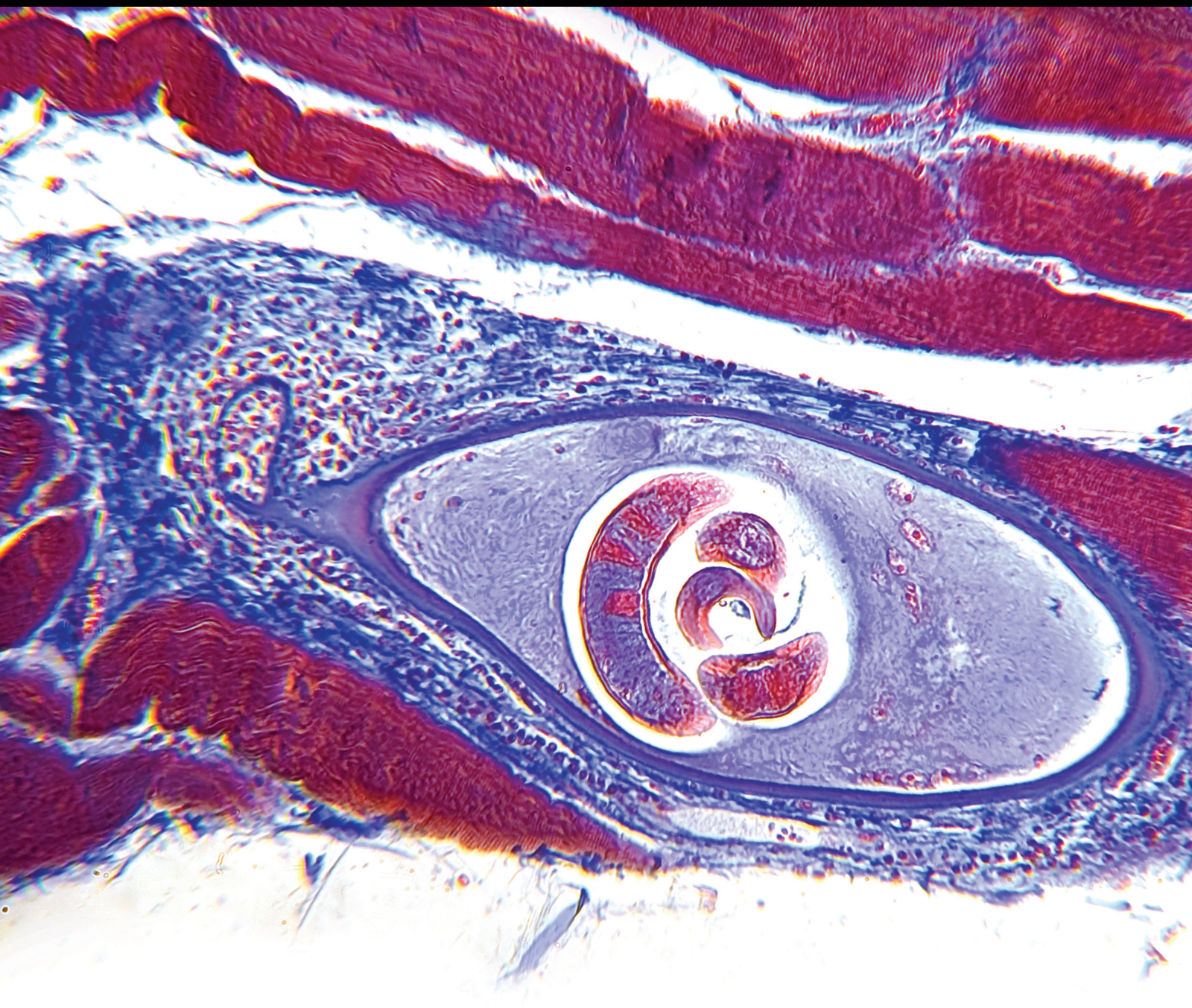

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Research Article

Safety and Efficacy of the Supine Position with the Right Shoulder Raised versus the Left Lateral Position in Peroral Endoscopic Myotomy for Achalasia: A Large-Sample Retrospective Study

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Background. The correct surgical position is very important in the treatment of peroral endoscopic myotomy (POEM) for achalasia, which can make the procedure safer and more efficient. Currently, there are two commonly used positions: the supine position with the right shoulder raised and the left lateral position. This study aims to evaluate the differences in the safety and efficacy of these two positions. *Methods*. We conducted a retrospective study of 702 patients with achalasia undergoing POEM from December 2010 to December 2020. These patients were divided into the supine position with the right shoulder raised group ($n = 579$) and the left lateral position group ($n = 123$). The efficacy of POEM and adverse events were analyzed. *Results*. The clinical characteristics were similar in both groups, and there were no significant differences between the two groups in the Eckardt score change, lower esophageal sphincter (LES) basal pressure or residual pressure after POEM (all $p > 0.05$). The mean operative time in the supine position with the right shoulder raised group was significantly shorter than that in the left lateral position group (43.5 min vs. 54.6 min, respectively, $p < 0.001$). In addition, the differences between the two groups in terms of gas-related complications, such as pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema were statistically significant (all $p < 0.05$). *Conclusions*. The efficacy of POEM was comparable between the two groups. However, the supine position with the right shoulder raised significantly reduced the operative time and the rate of procedure-related adverse events, especially gas-related complications.

1. Introduction

Achalasia is a functional disease that involves esophageal dynamic dysfunction of unknown cause. It is characterized by aperistalsis of the esophageal body and failure of the lower esophageal sphincter (LES) to relax, with various symptoms, including dysphagia, regurgitation, chest pain, and weight loss [1, 2]. Nowadays, peroral endoscopic myotomy (POEM) is widely used as a safe and efficient therapy for achalasia [3, 4]. The clinical remission rate can be as high as 89–100% [5, 6]. During POEM, correct patient positioning is very important for a safer and easier procedure. At present, the positions commonly used during endoscopy are the left lateral position, supine position, and the supine position with the right shoulder raised. However, there are no reports on which position is the most appropriate for POEM, and endoscopists usually select the position according to their own operating habits.

The left lateral position is the conventional position for endoscopic diagnosis and treatment, and many endoscopists also routinely use this position for POEM. The supine position facilitates selection of the proximal posterior esophageal wall for surgery; however, due to the twisted degree of the patient's head, it may be difficult to advance the endoscope; thus, this position is rarely used in POEM. In recent years, we have gradually used the supine position with the right shoulder raised to perform POEM. This position falls in between the left lateral and supine position, with the patient's

(a) (b)

Figure 1: (a) The patient's right shoulder was raised by a cushion. (b) The recommended elevation angle of the right shoulder was about 30°.

head less twisted. We usually use a cushion or pillow to raise the patient's right shoulder and the recommended elevation angle of the right shoulder is about 30° (Figure 1).

No study has reported the safety and efficacy of using different positions in POEM for the treatment of achalasia. Therefore, we designed this retrospective study to compare the safety and efficacy of POEM in the left lateral position and supine position with the right shoulder raised to promote further development of POEM.

2. Methods

2.1. Patients. The records of 702 consecutive patients who received POEM to treat achalasia at the First Medical Center of Chinese PLA General Hospital between December 2010 and December 2020 were reviewed in this single-center retrospective study. Before the operation, we explained the relevant procedures in detail to each patient, including possible perioperative complications, treatment plans and postoperative follow-up, which were fully understood by all patients. The study was approved by the Ethics Committee of the Chinese PLA General Hospital, and all patients voluntarily participated in the study and signed written informed consent forms.

2.2. Ling Classification. Endoscopic classification of achalasia is defined by the Ling classification, which includes three types [7]: Ling I, dilated esophagus, wall of the esophagus is straight and smooth; Ling II, dilated tortuous esophagus, with a circular or semicircular structure; and Ling III, esophageal cavity dilates, with a diverticular structure. Ling II was further classified into three subtypes: IIa (with a thin circular structure), IIb (with a semicircular structure and the midpoint within one-third of the cavity), and IIc (with a semicircular structure and the midpoint beyond one-third of the cavity). Ling III was also further classified into three subtypes: IIIl (diverticular structure mainly in the left wall of the esophagus), IIIr (diverticular structure mainly in the right wall of the esophagus), and IIIlr (diverticular structure in both the left and right walls of the esophagus).

2.3. Indicators Monitored. In this study, the main indicators monitored included the efficacy of POEM, perioperative complications and gas-related adverse events. The efficacy mainly depended on the evaluation of symptomatology, which was concluded by comparing the preoperative and postoperative Eckardt score [8] and high-resolution manometry (HRM) [9]. Perioperative complications mainly included bleeding and perforation, while gas-related adverse events included pneumothorax, pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema.

2.4. Instruments and POEM. A gastroscope and a high-frequency generator were used during POEM. A disposable injector with a normal saline solution was used for submucosal injections. The Triangle tip knife was used to establish the submucosal tunnel and myotomy. Hemostatic forceps and clips were used to prevent hemorrhage and perforation. Carbon dioxide gas was used for insufflation with a CO_2 insufflator during all procedures.

All patients receiving POEM were required to fast for 48 hours before the operation and complete esophageal cleansing by gastroscopy. The surgical steps in POEM have been reported previously [10], and they include three main steps: establishment of a submucosal tunnel, myotomy, and sealing the tunnel entrance (Figure 2). All procedures were performed by two experienced endoscopists (Enqiang Linghu and Ningli Chai), who are very skilled in operating on patients in two body positions without significant differences. It is worth mentioning that five types of myotomy methods were used, which were an inner circular muscle incision, circular muscle incision combined with balloon shaping, glasses-type muscle incision, progressive full-thickness myotomy, and full-thickness muscle incision [11]. After the operation, all patients were required to stay in bed and fasted for 3 days. Proton pump inhibitors (PPIs) were administered intravenously and antibiotics were used prophylactically to avoid infection. In addition, if perioperative bleeding, perforation, and other complications occurred, the patients received active symptomatic treatment such as drug hemostasis, endoscopic hemostasis, and endoscopic closure of the perforation,

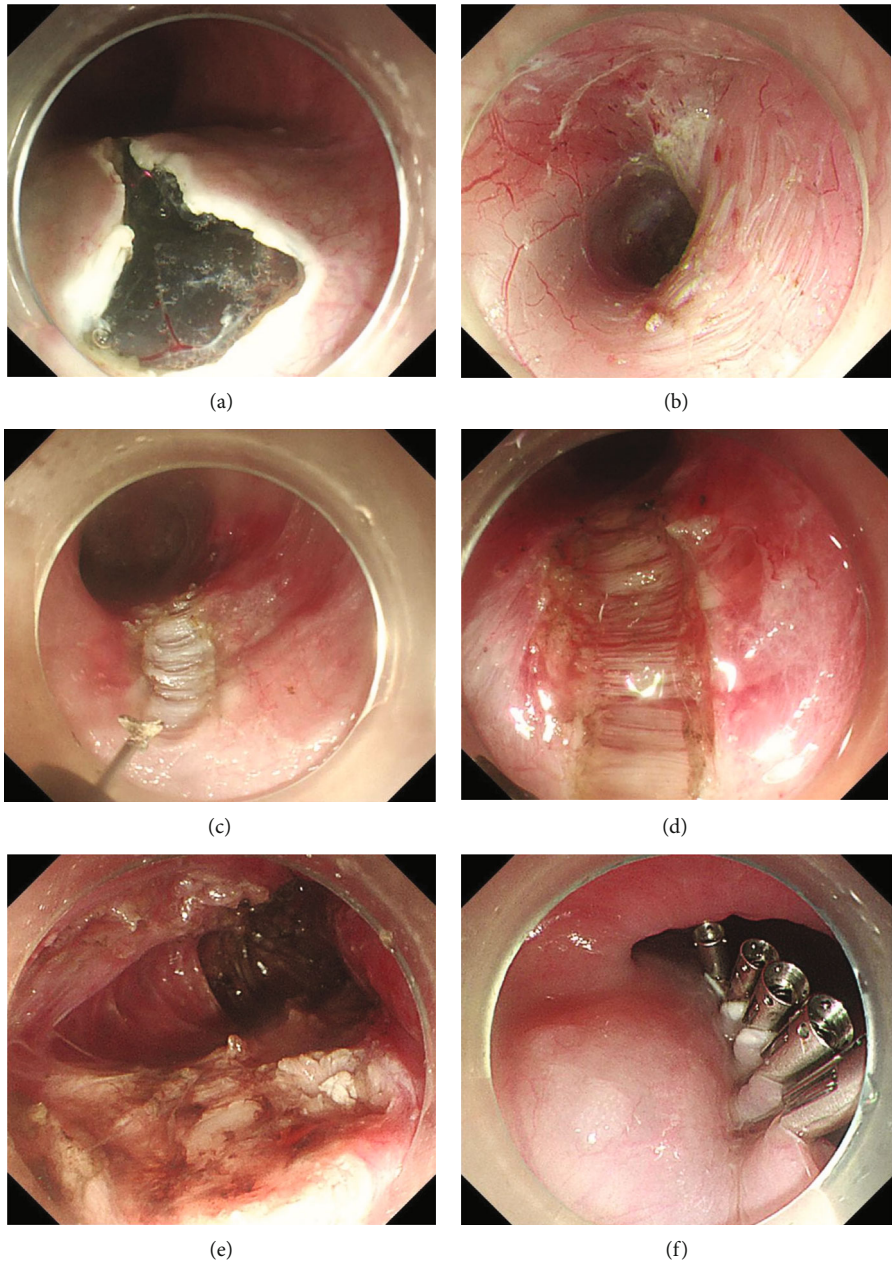

Figure 2: Peroral endoscopic myotomy procedures. (a) A reverse T entry incision was performed. (b) The submucosal tunnel was established. (c) and (d) Partial circular muscle was cut at the starting point of the myotomy. (e) The end of the myotomy. (f) Closure of the tunnel entry with clips.

as well as interventional embolization for hemostasis and surgery. Other treatments were also administered when necessary. Patients were followed up at 3 months, 6 months, and 1 year after POEM, including endoscopy, 24-hour esophageal pH monitoring, and HRM. Thereafter, annual follow-up was strongly recommended.

2.5. Statistical Analysis. For the data related to this study, we designated special personnel to record, manage, and assist with statistical analysis. Measurement data are expressed as the mean value ± standard deviation or median with range, whereas numerical data are described by frequency and percentage and were compared using the χ^2 or Fisher's exact test. The measurement data were analyzed by t-test and one-way analysis of variance or rank-sum test according to whether the data conformed to a normal distribution. Chi-square tests were used to compare categorical variables. Multiple regression analysis or logistics regression analysis is used to explore the relationship between multiple variables. $p < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical Characteristics of the Two Groups. A total of 702 patients were enrolled in the study, including 309 males and 393 females, aged from 18 to 85 years (mean 44.6 years). 579 patients were placed in the supine position with the

Table 1: Clinical characteristics of the two groups.

	Supine position with the right shoulder raised group ($n = 579$)	Left lateral position group ($n = 123$)	p value
Sex, male/female (n)	249/330	60/63	0.241
Age, mean (range) (years)	45.7 (18–85)	43.3 (19–77)	0.088
Duration of symptoms, mean (range) (years)	7.1 (0.1–45)	5.4 (0.2–33)	0.069
Previous treatment [n (%)]	112 (19.3)	34 (27.6)	0.636
Balloon dilation	57 (9.8)	20 (16.3)	—
Botox injection	33 (5.7)	10 (8.1)	—
Temporary stenting	3 (0.5)	2 (1.6)	—
Heller myotomy	8 (1.4)	0 (0)	—
Balloon dilation + Botox injection	3 (0.5)	0 (0)	—
Balloon dilation + temporary stenting	1 (0.2)	0 (0)	—
Botox injection + temporary stenting	1 (0.2)	0 (0)	—
Temporary stenting + Heller myotomy	1 (0.2)	1 (0.8)	—
Peroral endoscopic myotomy	5 (0.9)	1 (0.8)	—
Ling classification [n (%)]			0.116
I	69 (11.9)	23 (18.7)	—
IIa	157 (27.1)	32 (26.0)	—
IIb	148 (25.6)	32 (26.0)	—
IIc	180 (31.1)	28 (22.8)	—
IIIl	8 (1.4)	5 (4.1)	—
IIIr	7 (1.2)	1 (0.8)	—
IIIlr	10 (1.7)	2 (1.6)	—
Chicago subtype of achalasia [n (%)]			0.877
I	113 (19.5)	26 (21.1)	—
II	428 (73.9)	90 (73.2)	—
III	38 (6.6)	7 (5.7)	—

right shoulder raised, while the other 123 patients were placed in the left lateral position. The average disease course of the patients in the supine position with the right shoulder raised group was 7.1 years (range 1 month to 45 years) and that in the left lateral position group was 5.4 years (range 2 months to 33 years). Before undergoing POEM, 112 patients (19.3%) in the supine position with the right shoulder raised group had received previous treatments (57 treated with balloon dilation, 33 with Botox injection, 3 with temporary stenting, 8 with Heller myotomy, 3 with balloon dilation + Botox injection, 1 with balloon dilation + temporary stenting, 1 with Botox injection + temporary stenting, 1 with temporary stenting + Heller myotomy, and 5 POEM), whereas 34 patients (27.6%) in the left lateral group had received previous treatments (20 with balloon dilation, 10 with Botox injection, 2 with temporary stenting, 1 with temporary stenting + Heller myotomy, and 1 with POEM). The Ling classification in the supine position with the right shoulder raised group included 69 Ling type I patients, 485 Ling type II patients, and 25 Ling type III patients; the Ling classification in the left lateral group included 23 Ling type I patients, 92 Ling type II patients, and 8 Ling type III patients, respectively. Chicago II was the most common type of achalasia in both groups (73.9% vs. 73.2%). There were no statistically significant differences between the two groups in terms of gender, age, duration of symptoms, previous treatment, Ling classification or Chicago classification (all $p > 0.05$). The clinical characteristics of the two groups are shown in Table 1.

3.2. Comparison of POEM-Related Parameters. All patients in both groups successfully underwent POEM, and the detailed data are shown in Table 2. In the supine position with the right shoulder raised group, the mean lengths of the tunnel and myotomy were 10.6 cm (4–20 cm) and 7.0 cm (3–15 cm), respectively, while those in the left lateral position group were 11.9 cm (7–26 cm) ($p = 0.297$), and 6.6 cm (2–23 cm) ($p = 0.103$), respectively. Progressive full-thickness myotomy was performed in 85.3% (494 cases) of patients in the supine position with the right shoulder raised group and in 75.6% (93 cases) of patients in the left lateral position group. The types of myotomy in the remaining patients in the two groups included inner circular muscle incision (14 vs. 4 cases), circular muscle incision combined with balloon shaping (19 vs. 6 cases), glasses-type muscle incision (14 vs. 5 cases), and full-thickness muscle incision (38 vs. 15 cases). Although the types of myotomy differed among the patients, there were no statistically significant

Table 2: Comparisons of POEM-related parameters and adverse events between the two groups.

	Supine position with the right shoulder raised group ($n = 579$)	Left lateral position group ($n = 123$)	p value
Types of myotomy [n (%)]	—	—	0.087
Inner circular muscle incision	14 (2.4)	4 (3.2)	—
Circular muscle incision + balloon shaping	19 (3.3)	6 (4.9)	—
Glasses-type muscle incision	14 (2.4)	5 (4.1)	—
Progressive full-thickness myotomy	494 (85.3)	93 (75.6)	—
Full-thickness muscle incision	38 (6.6)	15 (12.2)	—
Operating time, mean (range) (min)	43.5 (17–180)	54.6 (22–170)	<0.001
Tunnel length, mean (range) (cm)	10.6 (4–20)	11.9 (7–26)	0.297
Myotomy length, mean (range) (cm)	—	—	—
Esophageal	5.0 (0–13)	4.7 (0–21)	0.108
Gastric	2.0 (0–4)	1.9 (0–3)	0.937
Total	7.0 (3–15)	6.6 (2–23)	0.103
All intraoperative adverse events [n (%)]	53 (9.2)	26 (21.1)	<0.001
Mucosal injury	9 (1.6)	2 (1.6)	1.000
Pneumothorax	6 (1.0)	2 (1.6)	0.927
Pneumoperitoneum	16 (2.8)	9 (7.3)	0.027
Pneumomediastinum	2 (0.3)	3 (2.4)	0.040
Subcutaneous emphysema	20 (3.4)	10 (8.1)	0.020
Fever (temperature > 38.0°C) [n (%)]	14 (2.4)	2 (1.6)	1.000

differences between the two groups ($p = 0.087$). However, the mean operative time in the supine position with the right shoulder raised group [43.5 min (range 17–180 min)] was significantly shorter than that in the left lateral position group [54.6 min (range 22–170 min)] ($p < 0.001$).

3.3. Symptom Relief and HRM Outcomes. As shown in Table 3, 532 patients (91.9%) in the supine position with the right shoulder raised group received a symptom score during follow-up, with a mean follow-up time of 23.5 months (3–60 months), while the follow-up time in the left lateral position group was 25.4 months (3–66 months). Based on a postoperative Eckardt score of ≤3, which was defined as successful treatment, there was no significant difference in the therapeutic success between the two groups (96.8% vs. 95.3%, $p = 0.394$). Both groups of patients showed a significant improvement in the post-treatment Eckardt score. However, there was no statistically significant difference in the Eckardt score between the two groups before and after POEM [5.8 (range 0–12) vs. 5.8 (range 0–10)] ($p = 0.850$).

During follow-up, postoperative gastroesophageal reflux occurred in 83 patients, including 68 in the supine position with the right shoulder raised group and 15 in the left lateral position group. There was no statistically significant difference in the incidence of reflux between the two groups ($p = 0.728$). All patients had effective relief of symptoms following oral administration of PPIs. Due to the obvious improvement in clinical symptoms and discomfort during manometry, 182 patients in the supine position with the right shoulder raised group and 31 patients in the left lateral position group completed postoperative manometry, respectively. The basal and residual pressure of the LES in both groups decreased significantly after POEM; however, the difference in the degree of decreased residual pressure of the LES between the two groups was not statistically significant ($p = 0.105$, $p = 0.086$).

3.4. Comparison of POEM-Related Adverse Events. Adverse events occurred in 53 (9.2%) patients in the supine position with the right shoulder raised group and in 26 (21.1%) patients in the left lateral position group, representing a significant difference ($p < 0.001$). In the supine position with the right shoulder raised group, 9 (1.6%) patients developed mucosal injury and 6 (1.0%) patients developed pneumothorax, compared with 2 (1.6%) and 2 (1.6%) patients in the left lateral position group, respectively, and the difference between the two groups was not statistically significant ($p = 1.000$, $p = 0.927$). Mucosal injury was closed with tissue clips or porcine fibrin glue. One patient with serious pneumothorax in the left lateral position group, whose right lung was 80% compressed, was instantly relieved after exhausting approximately 1400 ml of gas, and the remaining patients with mild pneumothorax gradually recovered spontaneously. However, the incidence of pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema was 2.8%, 0.3%, and 3.4%, respectively, in the supine position with the right shoulder raised group and 7.3%, 2.4%, and 8.1%, respectively, in the left lateral position group, and the differences were statistically significant between the two groups ($p = 0.027$, $p = 0.040$, $p = 0.020$). All patients with pneumoperitoneum were treated by abdominocentesis with a 10 ml syringe, and 4 of the 10 patients with subcutaneous emphysema in the left lateral position group required puncture decompression. The

Table 3: Comparisons of Eckardt scores and HRM between the two groups.

	Supine position with the right shoulder raised group ($n = 579$)	Left lateral position group ($n = 123$)	p value
Follow-up period, mean (range) (months)	23.5 (3–60)	25.4 (3–66)	0.106
Symptom score follow-up rate [n (%)]	532 (91.9)	107 (87.0)	0.085
Treatment success (Eckardt score ≤3) [n (%)]	515 (96.8)	102 (95.3)	0.394
Eckardt score, mean (range)	—	—	—
Pre-treatment	7.0 (4–12)	7.2 (4–12)	0.266
Post-treatment	1.2 (0–4)	1.4 (0–5)	0.092
Pre-post	5.8 (2–10)	5.8 (2–10)	0.850
Gastroesophageal reflux [n (%)]	68 (12.8)	15 (14.0)	0.728
HRM follow-up rate [n (%)]	182 (31.4)	31 (25.2)	0.172
LES basal pressure, mean (range) (mm Hg)	—	—	—
Pre-treatment	37.6 (0.7–100.6)	35.6 (6.2–73.9)	0.396
Post-treatment	15.6 (0.6–56.2)	17.2 (0.5–52.7)	0.247
Pre-post	22.0 (–9.4 to 79.1)	18.4 (–4.9 to 46.5)	0.105
LES residual pressure, mean (range) (mm Hg)	—	—	—
Pre-treatment	29.1 (1–83.2)	27.3 (6.5–74.2)	0.318
Post-treatment	11.1 (0.7–28.9)	12.1 (0.5–36.2)	0.266
Pre-post	18.0 (–5 to 64)	15.1 (–4.3 to 47.7)	0.086

Table 4: Multivariate regression analysis of operative time on course of disease, whether full-thickness myotomy, tunnel length and operative position.

	B	Beta	F	R^2 (adjusted R^2)	t	p
Constant	36.515	—	13.320^{***}	0.071 (0.066)	5.403	<0.001
Disease duration	0.278	0.102			2.770	0.006
Full-thickness myotomy	−6.472	−0.123			−2.964	0.003
Tunnel length	1.036	0.112			3.008	0.003
Operative position	6.480	0.123			2.922	0.004

Notes: $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

Table 5: Binary logistic regression analysis of the occurrence of gas-related complications on course of disease, whether full-thickness myotomy, tunnel length and operative position.

	B	SE	Wald	v	p	Exp(B)	95% CI of Exp(B)	
							Lower limit	Upper limit
Constant	−4.694	1.211	15.016	1	<0.001	0.009	—	—
Disease duration	0.012	0.020	0.348	1	0.555	1.012	0.973	1.051
Full-thickness myotomy	−0.214	0.383	0.312	1	0.577	0.807	0.381	1.711
Tunnel length	0.108	0.067	2.629	1	0.105	1.114	0.978	1.270
Operative position	0.966	0.369	6.874	1	0.009	2.629	1.276	5.413

remaining patients with pneumomediastinum and subcutaneous emphysema did not require specific clinical interventions. No massive hemorrhage occurred during the procedure, and no delayed bleeding occurred in either group.

In addition, 14 (2.4%) patients in the supine position with the right shoulder raised group and 2 (1.6%) patients in the left lateral position group developed fever after POEM, but the difference between the two groups was not statistically significant ($p = 1.000$). Among them, 1 patient in the left lateral position group experienced bacteremia due to *Propionibacterium acnes*, and this patient's temperature gradually returned to normal after taking third-generation cephalosporin. The POEM-related adverse events are also listed in Table 2.

3.5. Multivariate Regression Analysis and Logistics Regression Analysis. The results of multivariate regression analysis and logistics regression analysis that affect the operative time and occurrence of gas-related complications are shown in Tables 4 and 5. Multivariate regression analysis showed that

the longer disease duration, left lateral position, longer tunnel length, and full-thickness myotomy were associated with longer operative time, with statistically significant differences ($p = 0.006, 0.004, 0.003$, and 0.003, respectively). However, in logistics regression analysis, only the left lateral position was more prone to gas-related complications ($p = 0.009$), while the course of disease, tunnel length, and whether full-thickness myotomy was performed did not present correlation with gas-related complications for the time being ($p = 0.555, 0.105, 0.577$, respectively).

4. Discussion

Since the Japanese scholars Inoue et al. first reported the POEM used to treat achalasia in 2010 [10], research on POEM has continuously increased [12–17]. Some of these studies are conducive to the further improvement and development of POEM, and our exploration of the operative position is based on this intention. Many endoscopists use the conventional left lateral position to perform POEM. However, in our clinical practice and investigations, we have found that the supine position with the right shoulder raised seems to be more advantageous in some aspects. Therefore, we designed this study to clarify the influence of surgical position on POEM.

It should be noted that we also initially used the supine position to perform POEM. However, we only completed this in a few cases as the patient's head was too twisted, the endoscopic propulsion was difficult, and fluids remained in the rear esophageal cavity due to gravity, which might soak the tunnel incision during the procedure and affect the endoscopic field. Therefore, the purpose of this study was to compare the difference between the conventional left lateral position and the supine position with the right shoulder raised which is increasingly being used clinically.

In our study, 579 patients were enrolled in the supine position with the right shoulder raised group and 123 in the left lateral position group, respectively. There were no significant differences between the two groups in clinical baseline data, such as age, sex, disease course, previous treatment history, Ling classification, and Chicago subtype of achalasia. In the comparison of procedure-related parameters, there was no significant difference in tunnel length, myotomy length (including esophageal myotomy length, gastric myotomy length, and total myotomy length), and types of myotomy between the two groups. However, the operating time in the supine position with the right shoulder raised group was significantly shorter than that in the left lateral position group ($p < 0.001$). Based on this, we performed further multivariate regression analyses for several factors that may influence the operative time, and the results showed that prolonged disease duration, long intraoperative tunnel construction, and full-thickness myotomy, and left lateral position increased the operative time. In general, patients with a longer course of disease may have more pronounced dilatation and distortion of the esophagus and higher pressure of LES, which may require more complex surgical procedures and increase the operative time. Similarly, building a longer tunnel and performing a full-thickness myotomy during the operation also complicates the operation and naturally takes more time. The influence of the above factors on the operative time is relatively easy to understand, while the influence of different operative positions has not been reported before, which is also the focus of our attention.

The left lateral position is the routine position for endoscopic examinations, which helps the endoscopist to identify the anatomic orientation of the esophageal wall because the common direction to operate a device under endoscopy is the 6 o'clock position; however, it is necessary to rotate the endoscope to adjust the correct direction for a tunnel to be established in the right rear esophageal wall. By contrast, the supine position with the right shoulder raised retains the advantages of the supine position in favor of the selection of the proximal posterior esophageal wall for surgery, while the patient's head is less twisted so that the device can be withdrawn in a naturally relaxed way to the proximal rear esophageal wall under endoscopy, facilitating the approach and withdrawal of the endoscope as well as the whole operation. In addition, as reported in the relevant literature [18], the supine position with the right shoulder raised is advantageous with respect to no fluid retention at the right rear esophageal wall (because it is not the lowest point in this position), with no effect on the surgical field. All of these factors contribute to the faster completion of POEM in the supine position with the right shoulder raised.

POEM-related adverse events reported in previous studies were also the focus of our attention [19–21]. Differences in gas-related complications were observed between the two groups in the present study. By comparing the distribution differences between two groups and conducting further logistics regression analysis, the results showed that the left lateral position group was more prone to gas-related complications than the supine position with the right shoulder raised group. Specifically, the incidence of pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema was significantly lower in the supine position with the right shoulder raised group than in the left lateral position group. In terms of pneumothorax, although the difference between the two groups was not statistically significant, the incidence was higher in the left lateral position group, and 1 patient with severe pneumothorax and 4 patients with subcutaneous emphysema requiring puncture decompression were all in the left lateral position group. Overall, the supine position with the right shoulder raised was superior in controlling gas-related complications. Anatomically, the esophagus is located behind the trachea and heart and in front of the spine. It is relatively safe to establish a submucosal tunnel at the proximal posterior wall of the esophagus away from major organs. This also coincides with the direction in which the supine position with the right shoulder raised establishes the tunnel. On the other hand, in the left lateral position group, the operation required more time, and the gas had more time to diffuse through the tunnel cavity to the outer esophageal space before the tunnel reached below the relative plane of the diaphragm. These were the two main reasons for the higher

incidence of gas-related complications in the left lateral position group.

In addition to gas-related complications, intraoperative mucosal injury and postoperative fever occurred in a small number of patients. The differences in these complications were not significant between the two groups. However, it is worth noting that 1 patient with postoperative fever developed bacteremia in the left lateral position group. During POEM, the esophageal cavity is not completely sterile, and some small blood vessels are inevitably exposed in the process of establishing the submucosal tunnel and myotomy, which creates conditions for bacteria to enter the blood. As mentioned above, the left lateral position group had a longer operation duration, which increased the potential risk of bacteremia. This also demonstrates another advantage of the supine position with the right shoulder raised.

During follow-up, treatment efficacy was satisfactory in both groups, with symptom relief rates reaching over 95%, and there was no significant difference between the groups. Postoperative follow-up HRM data showed that the pressure of the LES (including basal pressure and residual pressure) in both groups was significantly relieved compared with that before surgery, which was also one of the manifestations showing the efficacy of POEM. These results were similar to those in previous studies [5, 6]. We also noted that a small number of patients developed reflux after POEM. Some of these patients had higher Eckard scores due to the discomfort caused by reflux, despite the fact that their dysphagia symptoms were generally relieved. This suggests that further research on the effective control of reflux after POEM may be needed in the future.

The present study had several limitations. One limitation was its retrospective design and potential selection bias, as our hospital is a tertiary referral center. Other limitations of the study included a lack of HRM, 24-hour pH testing, and timed-barium swallow after POEM in some patients. Therefore, prospective multicenter, randomized clinical trials with long-term follow-up periods should be carried out in the future.

5. Conclusion

POEM is a safe and efficient treatment for patients with achalasia, irrespective of whether it is performed in the supine position with the right shoulder raised or left lateral position. Therapeutic success was achieved in 96.6% of cases. No significant differences between the two groups were observed in terms of the changes in the Eckardt score, LES basal pressure or residual pressure after POEM. Compared to the left lateral position group, the supine position with the right shoulder raised group had a shorter operating time and fewer procedure-related adverse events, especially gas-related complications.

Abbreviations

POEM: Peroral endoscopic myotomy
LES: Lower esophageal sphincter
HRM: High-resolution manometry
PPI: Proton pump inhibitor.

Data Availability

All data obtained or analyzed during this work are included within the article.

Conflicts of Interest

The authors declare that there is no conflict of interest.

Authors' Contributions

Nanjun Wang and Ningli Chai initiated the study design and drafted the manuscript, and they are the co-first authors. Longsong Li, Yawei Bi, and Shengzhen Liu contributed to software and data curation. Wengang Zhang and Shasha Wang contributed to supervision, review, and editing. Enqiang Linghu contributed to methodology, review, and editing. All authors read and approved the final manuscript.

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Review Article

An Updated Meta-analysis: Similar Clinical Efficacy of Anterior and Posterior Approaches in Peroral Endoscopic Myotomy (POEM) for Achalasia

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Introduction. Currently, there are few studies on the efficacy of peroral endoscopic myotomy (POEM) in the anterior or posterior approach; however, limited studies have shown contradictory findings. Thus, the goal was to obtain more quantitative and objective outcomes and further compare the clinical efficacy of these two approaches in this meta-analysis. *Methods*. A comprehensive search of PubMed, Embase, Cochrane Library, and Web of Science was conducted to find studies relevant to POEM. The retrieval time was from database inception to September 2021. Studies reporting the effects of POEM according to the anterior or posterior approach were included. STATA 16.0 was used to perform statistical analysis, mainly comparing the quantitative objective indicators (lower esophageal sphincter (LES) pressure and Eckardt scores, etc.) in anterior and posterior approaches by meta-analysis. *Result*. A total of 19 studies with 1261 patients were finally included. Except for shorter procedure time in the posterior approach, other factors (pooled difference of LES pressure, Eckardt scores, clinical success, length of total myotomy, hospital stays, gastroesophageal reflux (GERD), and adverse event) were compared, and all above confirmed that there is no difference between anterior and posterior approaches, and the safety of POEM is ensured. In addition, both anterior and posterior myotomy can improve LES pressure and Eckardt scores, and the difference in anterior and posterior myotomy was unconspicuous. *Conclusion*. The terms of the pooled difference in LES pressure, Eckardt scores, and other factors (clinical success, length of total myotomy, hospital stays, GERD, adverse events, and procedure time) seemed to be similar for the anterior and posterior approaches. However, the further prognosis after POEM via anterior and posterior approaches needs to be answered in the future.

1. Introduction

Achalasia (AC), which means "nonrelaxing" in Greek, is a primary disorder of esophageal motility with the main features of lower esophageal sphincter (LES) relaxation disorder and reduced esophageal peristalsis [1]. Its typical clinical manifestations, including severe dysphagia, regurgitation, retrosternal pain, and weight loss, affect the quality of life of patients. Previous epidemiology suggested that it was a rare disease affecting only 1 in 100,000 people [2, 3]; nevertheless, the incidence rate in recent years has increased to 2 to 3 times [4].

The current treatments for achalasia include pneumatic dilation (PD), botulinum toxin injection (BTI), laparoscopic

Heller myotomy (LHM), and peroral endoscopic myotomy (POEM). Because it is an incurable disease, the aim of the treatment is to remit LES relaxation disorder and lower LES pressure to relieve the symptoms of obstruction [5]. As recurrent dysphagia of PD and BTI often requires repeated treatment, LHM and POEM have become the main treatment methods because of their better efficacy [6–9].

POEM has been used more widely over the past decade because of its confirmed safety and efficiency [10, 11]. However, recent data showed that the incidence of postprocedure gastroesophageal reflux (GERD) of POEM can be up to 40%, which was higher than that of LHM [12]. Some studies have indicated that the myotomy length, achalasia subtype, and history of previous treatment had no effect on the occurrence of postprocedure GERD in POEM. A circular myotomy of the anterior approach might lessen the postprocedure GERD of POEM [13]. Through theoretical analysis, the anterior approach, in the 2-3 o'clock position, is easier than the posterior approach and has a lesser risk of damage to sling muscle fibers and the angle of His, which might be more beneficial to the antireflux mechanism of the esophagus [5, 14]. Nevertheless, a prior study showed that the rate of postprocedure GERD of POEM, clinical success, and adverse events were almost the same in both anterior and posterior approaches [14], which was contradicted by other studies.

This prior study [14], as a currently available estimate in the literature with respect to the clinical outcomes of anterior and posterior myotomy in POEM, compared clinical success, GERD, and adverse events between anterior and posterior myotomy. Nevertheless, these outcomes had more subjectivity since they were not based on quantitative objective indicators, such as LES pressure and Eckardt score.

Therefore, based on a previous study [14], the purpose of this study was to analyze objective indicators to obtain more quantitative and objective outcomes and update the analysis data through a meta-analysis of studies grouping POEM according to anterior and posterior approaches and to further compare the clinical efficacy of these approaches.

2. Methods

2.1. Search Strategy. For this meta-analysis, a comprehensive search of several databases, including PubMed, Embase, Cochrane Library, and Web of Science, from database inception to September 2021 was conducted. The search string consisted of the following keywords: "Achalasia", "Achalasia, Esophageal", "POEM", and "peroral endoscopic myotomy", as detailed in Appendix 1. In addition, references to the evaluated articles were checked to identify additional studies.

2.2. Selection Criteria. In this meta-analysis, the two authors (WNJ and XYL) screened the articles that needed to be evaluated together, and the screening process was carried out strictly according to the following procedures and standards. All conflicts between the two researchers were resolved by conference. First, irrelevant literature was eliminated by title and abstract. Then, according to the inclusion and exclusion criteria, studies were included through full-text reading. The inclusion criteria were as follows: (1) adults (participants aged ≥18 years) diagnosed with achalasia by clinical symptoms, barium contrast, or esophageal manometry; (2) POEM in the anterior or posterior approach; (3) outcomes included Eckardt score, LES pressure, clinical success rate, incidence of complications, and incidence of GERD; and (4) original study. The exclusion criteria were as follows: (1) the effect of POEM was not analyzed according to the approach; (2) the study population was less than 20 patients; (3) animal studies; (4) the study data were not available; and (5) studies not published in English. If there were multiple studies from the same cohort for the same experiment, data from the most recent and/or most appropriate comprehensive single report were included.

2.3. Data Extraction and Quality Evaluation. According to a standardized data extraction form that had been previously formulated, the following information was independently extracted by two authors (WNJ and XYL): first author, year of publication, country, journal, study design, study period, site of myotomy, range of ages, number of patients, gender ratio, follow-up duration (months), type of achalasia, course of disease (months), prior treatment/intervention, pre- and postoperative LES pressures (mmHg), pre- and post-POEM Eckardt scores, procedure time (minutes), length of myotomy (cm), hospital stays (day), number of clinical successes after POEM at 12 months and >12 months, postprocedure GERD evidenced by esophagogastroduodenoscopy (EGD), and adverse events.

The Newcastle–Ottawa Scale (NOS) for cohort studies was used to assess the quality of cohort studies [15], while the Jadad score was used to assess the quality of randomized controlled trials (RCTs) [16]. The NOS quality score contained 8 questions, and the Jadad score consisted of 4 questions, as detailed in Supplementary Table 1-2. Two authors (WNJ and XYL) independently evaluated the eligibility of the included studies. In case of disagreement, a third author (KD) would participate in the discussion.

2.4. Data Analysis. In this meta-analysis, a random-affects model was used to calculate the pooled estimates in each case according to the methods suggested by Der Simonian and Laird [17]. Before statistical analysis, if the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases [18].

2.5. Outcomes Assessed

2.5.1. Primary Outcome. Quantitative indicator consists of pooled difference in LES pressure and Eckardt scores before and after POEM in the anterior approach and posterior approach.

2.5.2. Secondary Outcomes

(1) Length of total myotomy in the anterior approach and posterior approach

(2) Hospital stays in the anterior approach and posterior approach

(3) Overall clinical success after POEM at 12 months and >12 months in the anterior approach and posterior approach

(4) Pooled occurrence of adverse events after POEM in the anterior approach and posterior approach

(5) Pooled occurrence of GERD events after POEM in the anterior approach and posterior approach (according to EGD findings)

(6) Procedure time in the anterior approach and posterior approach

The assessment methodology and definitions are as follows:

(1) The pooled difference in LES pressure is calculated by subtracting the pre-POEM LES pressure from the post-POEM LES pressure

(2) Pooled difference of Eckardt scores is calculated by post-POEM Eckardt scores minus pre-POEM Eckardt scores

(3) In the included studies, clinical success was defined as achieving an Eckardt score ≤ 3 postprocedure [19],

(4) Adverse events were defined as mild, moderate, or severe events, as reported by the American Society for Gastrointestinal Endoscopy (ASGE) lexicon [20]

(5) Postprocedure GERD was evaluated by EGD findings based on the Los Angeles classification of esophagitis (> A) [21]

Metaregression analyses were used to evaluate whether the length of total myotomy, proportion of type II achalasia, prior treatments (PBD, EBTI, and Heller's myotomy), course of disease, and length of follow-up time had any effect on the primary outcomes.

2.6. Validation of Meta-analysis Results

2.6.1. Heterogeneity. The I^2 measure from the netmeta statistical package was used to investigate the heterogeneity. I^2 values <30% are low, values of 30-60% are moderate, values of 61%-75% are substantial, and values >75% indicate considerable heterogeneity [22].

2.6.2. Publication Bias. The funnel plot and the Egger test were used to identify publication bias qualitatively and quantitatively [23]. If there was any publication bias, the trim and fill method of Duval and Tweedie was used to perform the adjustment [24]. Publication bias for the RCTs was not ascertained separately, since the number of studies was <10.

P values < 0.05 on both tails were considered statistically significant in all tests. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25] were followed to perform analysis and reporting, and the PRISMA checklist is shown in Appendix 2. All statistical procedures were performed using Stata (version 16.0).

3. Results

3.1. Study Selection and Quality of Included Studies. A total of 3958 studies were identified in this literature search after removing 2324 duplications. After screening the titles and abstracts, 3883 irrelevant studies were excluded. The remaining 76 full-length articles were identified, and 57 studies were excluded. Finally, 19 studies were included in this meta-analysis. These studies were published between 2016 and 2020. Six studies only reported the outcomes of POEM in the anterior approach [26–31], and nine studies only reported the outcomes of POEM in the posterior approach [32–40], while four studies compared outcomes of POEM via the anterior approach and posterior approach [41–44]. This meta-analysis included ten studies reporting outcomes with POEM via anterior myotomy and thirteen studies reporting outcomes with POEM via posterior myotomy. The flow chart of this literature search and final inclusions is illustrated in Figure 1. Seven studies were replicated in the cohort, and the most comprehensive recent studies were included [45–50].

This meta-analysis included three RCTs [41–43], of which two were considered low quality and one was considered high quality. Of the remaining 16 studies, 12 studies were considered high quality, while 4 studies were considered medium quality. Overall, 13 of 19 studies (68.4%) were considered high quality. The details of the NOS quality scores and Jadad scores are shown in Supplementary Table 1-2.

3.2. Population Characteristics. This meta-analysis finally included a total of 1261 patients in this analysis (606 patients in the anterior approach and 655 patients in the posterior approach). The age range was 33-63 years in the anterior approach and 38-68 years in the posterior approach. The male proportion was 55% in the anterior approach and 51% in the posterior approach. The follow-up duration of patients after POEM ranged from a minimum of 6 months to a maximum of 46.2 months. The baseline characteristics of the anterior approach and posterior approach were comparable, and the detailed characteristics of the included studies are summarized in Table 1.

4. Outcomes

4.1. Pooled Difference in LES Pressure. The meta-analysis for the pooled difference in LES pressure comprised 10 studies with 574 patients (218 patients in the anterior approach and 356 patients in the posterior approach). The pooled difference in LES pressure via the anterior approach was -24.56 mmHg (95% confidence interval (CI) -31.29 to -17.82 mmHg; $n = 5$; I^2 96.25%) and that via the posterior approach was -20.14 mmHg (95% CI -23.44 to -16.85 mmHg; $n = 7$; I^2 94.72%), which showed no

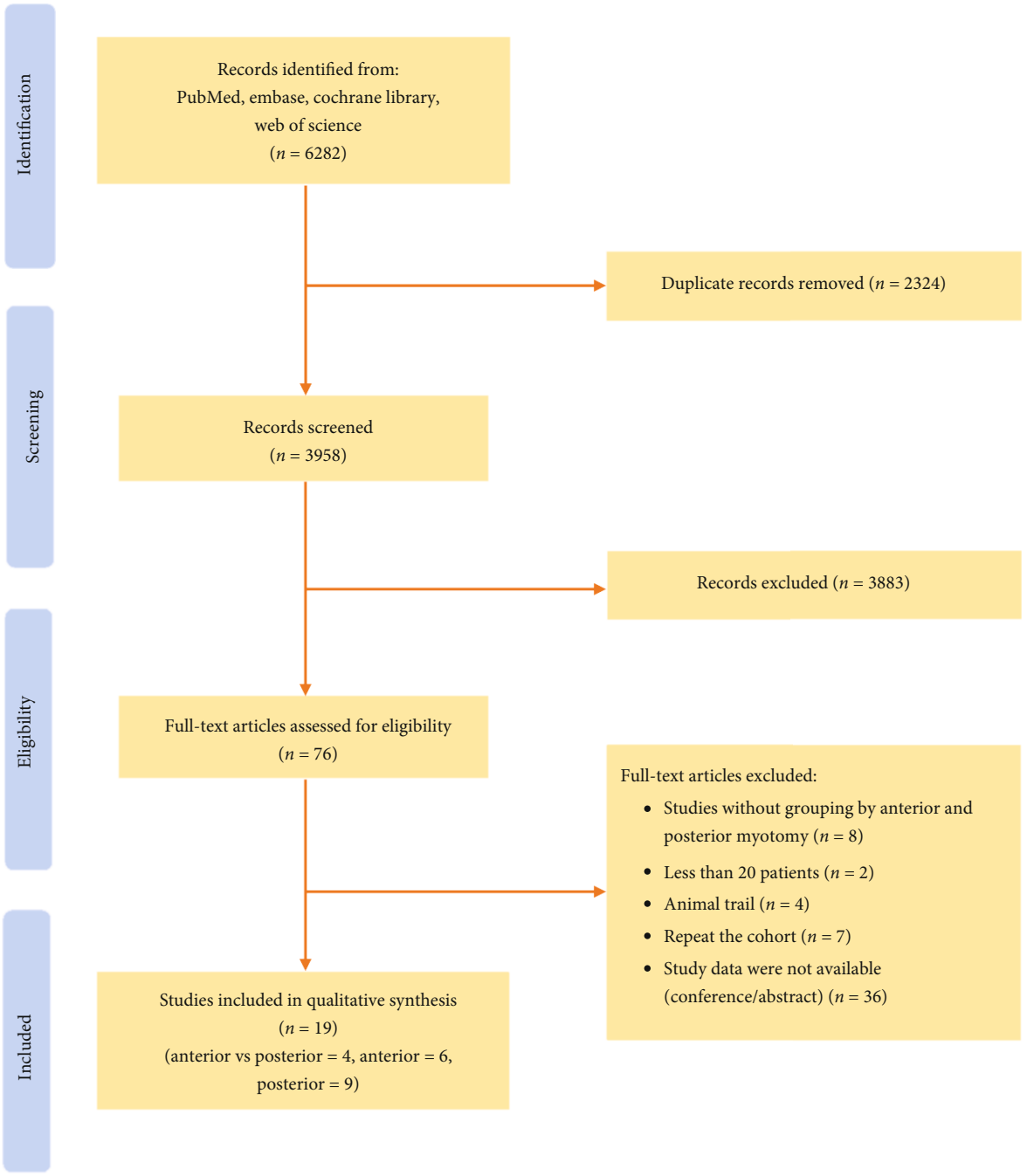

Figure 1: Study selection flow chart.

significant difference between anterior myotomy and posterior myotomy ($P = 0.25$) (Figure 2(a)). However, significant heterogeneity was observed ($I^2 = 96.58\%$; $n = 10$). Thus, metaregression analysis and sensitivity analysis were performed to determine the sources of heterogeneity. In the metaregression analysis based on length of total myotomy, the proportion of type II achalasia, prior treatments (PBD, EBTI, and Heller's myotomy), course of disease, and length of follow-up time did not show any effect on the previous outcome, as none of the two-tailed P values was less than 0.05 (Table 2). In the subsequent sensitivity analysis, none of the included studies was relevant to the heterogeneity, which shows the robustness of our results (Supplementary Fig. 6).

To eliminate the interference of baseline differences between studies on the results, better baseline level control was needed. Thus, further analysis was conducted in studies with a direct comparison between anterior and posterior approaches. Among all the included studies, 3 studies met the conditions of direct comparison because the patients were divided into anterior and posterior groups for comparison in these studies (including two RCTs [41, 43] and one cohort [44]). The analysis after balancing baseline showed

Table 1: Characteristics of included studies.

Study	Country	Type of study	Site of myotomy	Age, mean/median (range/SD)	Patients(n)	Gender (male/female)	Follow-up (months)	Achalasia(I/II/III)	Course of disease (months)
Hungness et al. [26]	USA	Retrospective (cohort)	Anterior	52.9 (18)	112	68/44	29 (11)	25/58/20	NA
Shiwaku et al. [27]	Japan	Prospective (cohort)	Anterior	48.8 (18.8)	70	41/29	NA	6/55/9	NA
Tang et al. [28]	China	Retrospective (cohort)	Anterior	34.9 (7.7)	22	14/8	12	5/17/0	6.4 (5.4)
				38.5 (11.3)	39	20/19		13/26/0	6.5 (4.8)
Ward et al. [29]	USA	Prospective (cohort)	Anterior	63.0 (17.9)	41	25/16	12	NA	81.6 (117.6)
Werner et al. [30]	Germany, etc.	Retrospective (cohort)	Anterior	44.9 (9–88)	80	43/37	29 (24–41)	24/48/5	NA
Zheng et al. [31]	China	Retrospective (cohort)	Anterior	32.5 (8.36)	26	14/12	12	11/15/0	22.31 (8.31)
de Pascale et al. [32]	Italy	Retrospective (cohort)	Posterior	56 (18–83)	32	20/12	23.7 (12–46.2)	0/31/1	36 (6.0–312)
Duan et al. [33]	China	Retrospective (cohort)	Posterior	43 (14)	70	33/37	30 (24-46)	12/51/7	60.0 (6.0–396.0)
				41 (13)	53	30/23		9/39/5	54.0 (6.0–240.0)
Farias et al. [34]	Brazil	Retrospective (cohort)	Posterior	53.70 (11.74)	20	9/11	12	NA	NA
				44.61 (14.80)	31	15/16	12	NA	NA
Guo et al. [35]	China	Retrospective (cohort)	Posterior	40.7 (15.3)	67	36/31	40.1 (2.8)	13/50/4	94.7 (95.5)
Meng et al. [36]	China	Retrospective (cohort)	Posterior	44.8 (11.6)	32	13/19	25 (11)	5/18/9	24 (12–60)
Peng et al. [37]	China	Retrospective (cohort)	Posterior	37.5 (13.0)	13	8/5	46.2 (4.1)	NA	46.8 (33.6)
Tyberg et al. [38]	USA, etc.	Prospective (cohort)	Posterior	54.2	51	24/27	24.4 (12–52)	13/29/6	134.4
Wang et al. [39]	China	Retrospective (cohort)	Posterior	67.9 (4.3)	21	12/9	21.8	5/16/0	166.8 (140.4)
Zhang and Linghu [40]	China	Retrospective (cohort)	Posterior	43.3 (16–79)	32	16/16	27 (24–51)	0/0/32	24.0 (2.4–336.0)
Ramchandani et al. [41]	India	RCT	Anterior	38 (13.5)	30	15/15	6	5/21/4	22.2 (28.1)
			Posterior	43.9 (15.7)	30	18/12		6/21/3	35.6 (37.6)
Stavropoulos et al. [42]	USA	RCT	Anterior	54.2 (2)	101	52/49	NA	22/58/21	NA
			Posterior	54.8 (1.8)	114	60/54	NA	36/56/22	NA
Tan et al. [43]	China	RCT	Anterior	45.8 (12.2)	31	15/16	15.8 (3.8)	4/26/1	80.4 (80.4)
			Posterior	42.4 (13.3)	32	14/18	15.1 (3.9)	3/28/1	74.4 (86.4)
Ichkhanian et al. [44]	USA, etc.	Prospective (cohort)	Anterior	52.3 (21)	54	29/25	34.5 (6.9)	13/33/8	53.3 (61.4)
			Posterior	51.2 (18)	57	23/34	32.5 (5.2)	4/42/11	50.5 (59.9)

that the pooled weighted mean difference (WMD) was -1.56 mmHg (95% CI -3.09 to 0.78 mmHg; I^2 0.00%; $n = 3$; $P = 0.19$) (Figure 2(b)), which still showed no significant difference between these two groups, and the significant heterogeneity disappeared.

4.2. Pooled Difference in Eckardt Scores. The meta-analysis for the pooled difference of Eckardt scores comprised 15 studies with 937 patients (479 patients in the anterior approach and 458 patients in the posterior approach). The pooled difference in Eckardt scores via the anterior approach was -5.83 (95% CI -6.22 to -5.45; $n = 8$; I^2 83.15%) and that via the posterior approach was -6.07 (95% CI -6.52 to -5.62; $n = 10$; I^2 88.93%), which showed no significant difference between anterior myotomy and posterior myotomy ($P = 0.44$) with high heterogeneity (Figure 3(a)). To determine the sources of heterogeneity, metaregression analysis and sensitivity analysis were performed. Similarly, the metaregression analysis based on length of total myotomy, proportion of type II achalasia, prior treatments (PBD, EBTI, and Heller's myotomy), course of disease, and length of follow-up time showed no relevance between them and the heterogeneity, as shown in Table 2. The sensitivity analysis did not show any study relevant to the heterogeneity (Supplementary Fig. 6).

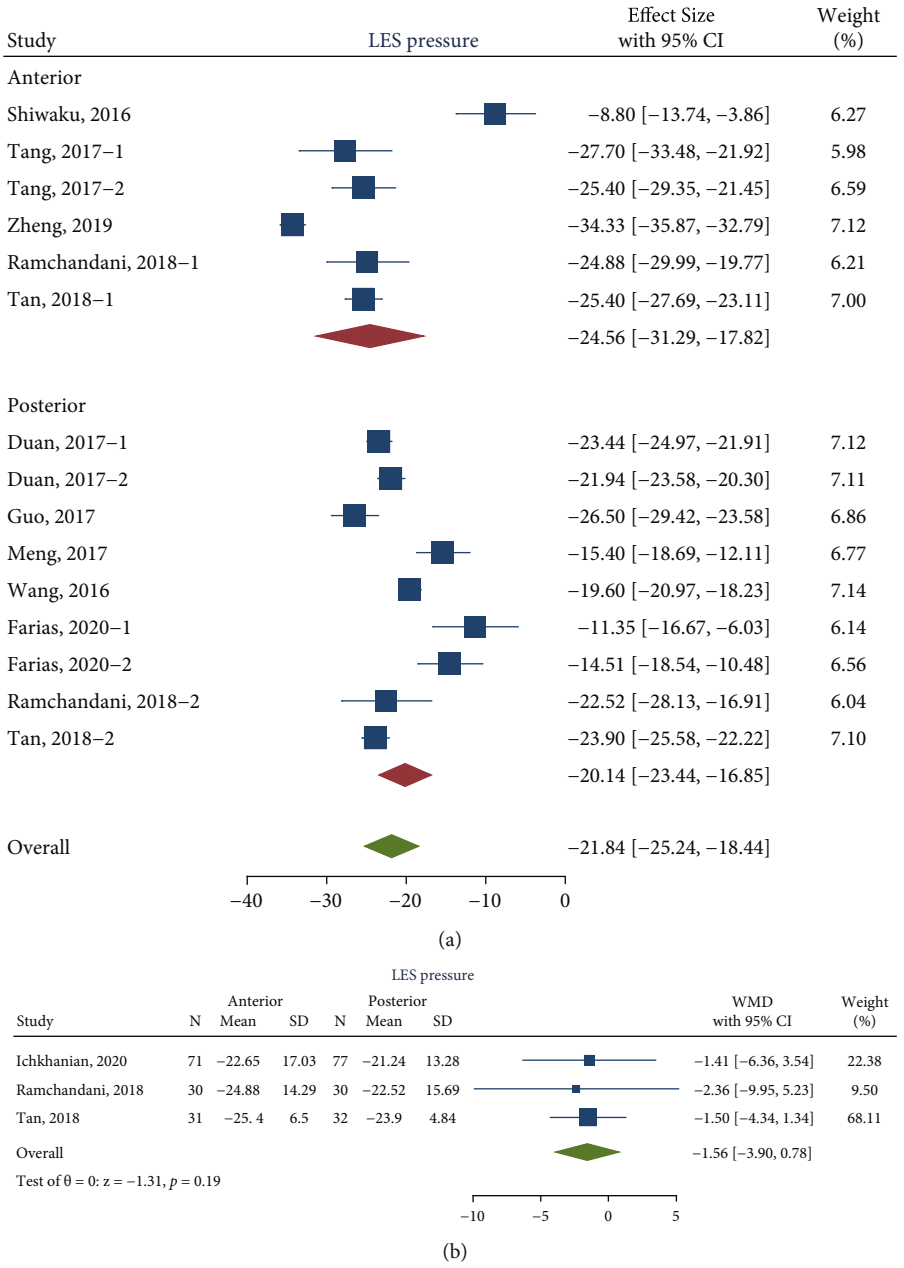

Figure 2: (a) Forest plot, difference in pre- and postoperative LES pressure before balancing baseline; (b) Forest plot, pre- and postoperative LES pressure difference between anterior and posterior approaches after balancing baseline Labels 1 and 2 were sectionalizations inside the study. They grouped these factors as follows: preoperative intervention/non-preoperative intervention (Tang, 2017), FTM/CM (Duan, 2017), Chagas/idiopathic (Farias, 2020), and anterior/posterior (Ramchandani, 2018; Tan, 2018).

Table 2: Metaregression with differences in pre- and postoperative Eckardt scores/LES pressure.

Variate	Meta regression (two-tailed P value)	
	Eckardt scores	LES pressure
Length of total myotomy	0.377	0.231
Follow up time	0.678	0.935
Type II proportion in AC	0.058	0.639
Course of disease	0.412	0.297
Prior treatment	0.351	0.279

Likewise, a better balancing of the baseline characteristics was needed, and then, analysis of directed comparison was performed. The analysis of Eckardt scores after balancing baseline revealed that the pooled WMD was 0.08 (95% CI -0.28 to 0.44; I^2 0.00%; $n = 3$; $P = 0.66$), without heterogeneity (Figure 3(b)).

4.3. Length of Total Myotomy and Hospital Stays. With the meta-analysis of 11 studies including 741 patients (368 patients in the anterior approach and 373 patients in the posterior approach), the length of total myotomy was 12.30 cm (95% CI 10.04 to 14.56 cm; $n = 6$; I^2 97.70%) in the anterior approach

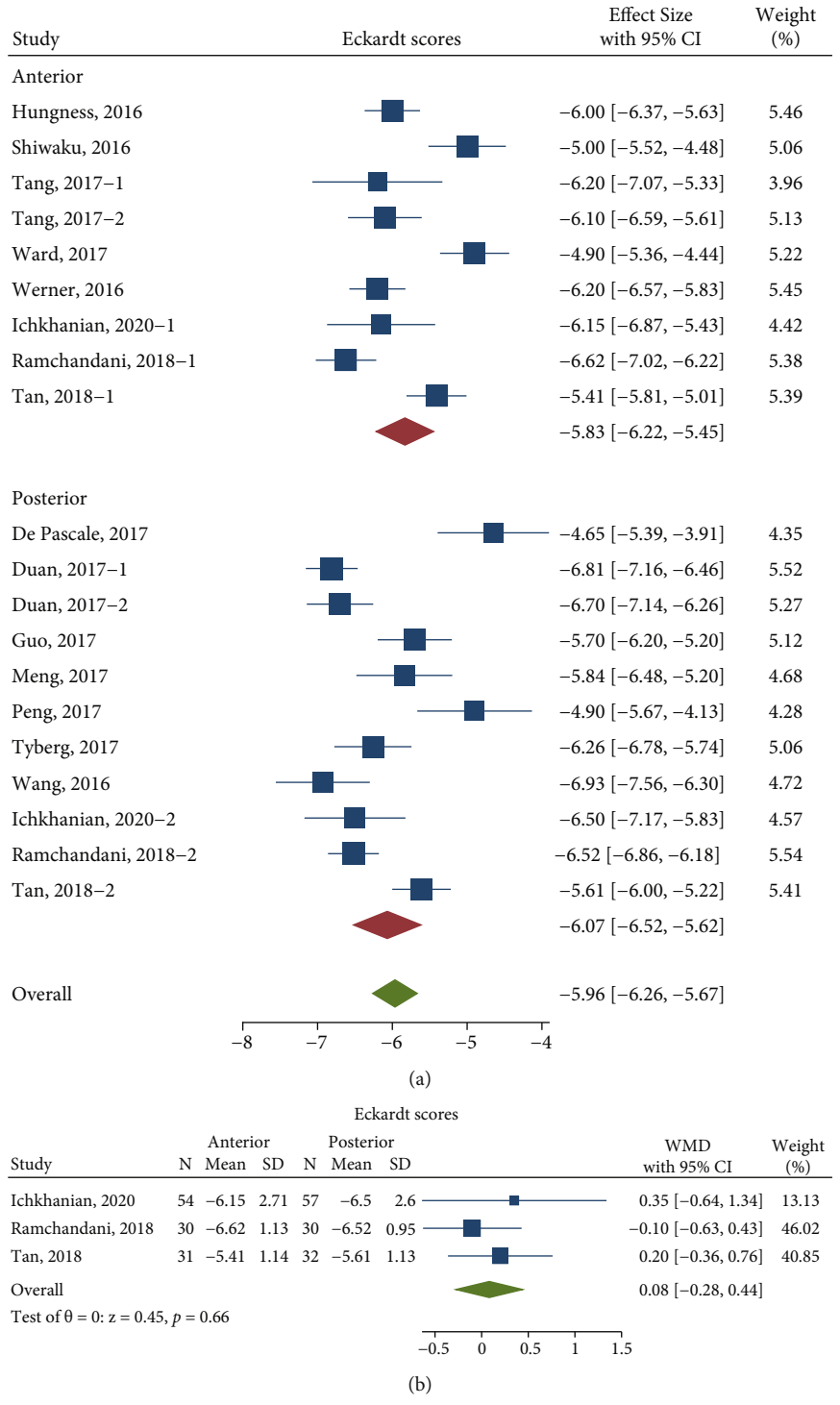

Figure 3: (a) Forest plot, difference in pre- and postoperative Eckardt scores before balancing baseline; (b) Forest plot, Differences in the pre- and postoperative Eckardt scores of the anterior and posterior approaches after balancing baseline Labels 1 and 2 were sectionalizations inside the study. They grouped these factors as follows: preoperative intervention/non-preoperative intervention (Tang, 2017), FTM/CM (Duan, 2017), Chagas/idiopathic (Farias, 2020), and anterior/posterior (Ramchandani, 2018; Tan, 2018).

and 10.81 cm (95% CI 9.86 to 11.76 cm; $n = 7$; I^2 97.80%) in the posterior approach. There was no significant difference between them ($P = 0.23$) (Figure 4(a)). After balancing the baseline characteristics of the studies by direct comparison, the pooled WMD was 0.36 cm (95% CI -0.60 to 1.31 cm; I^2 67.14%; $n = 2$; $P = 0.46$), which still showed no significant difference between these two groups (Figure 4(b)).

With the meta-analysis of 9 studies including 536 patients (303 patients in the anterior approach and 233 patients in the posterior approach), the hospital stays of the anterior

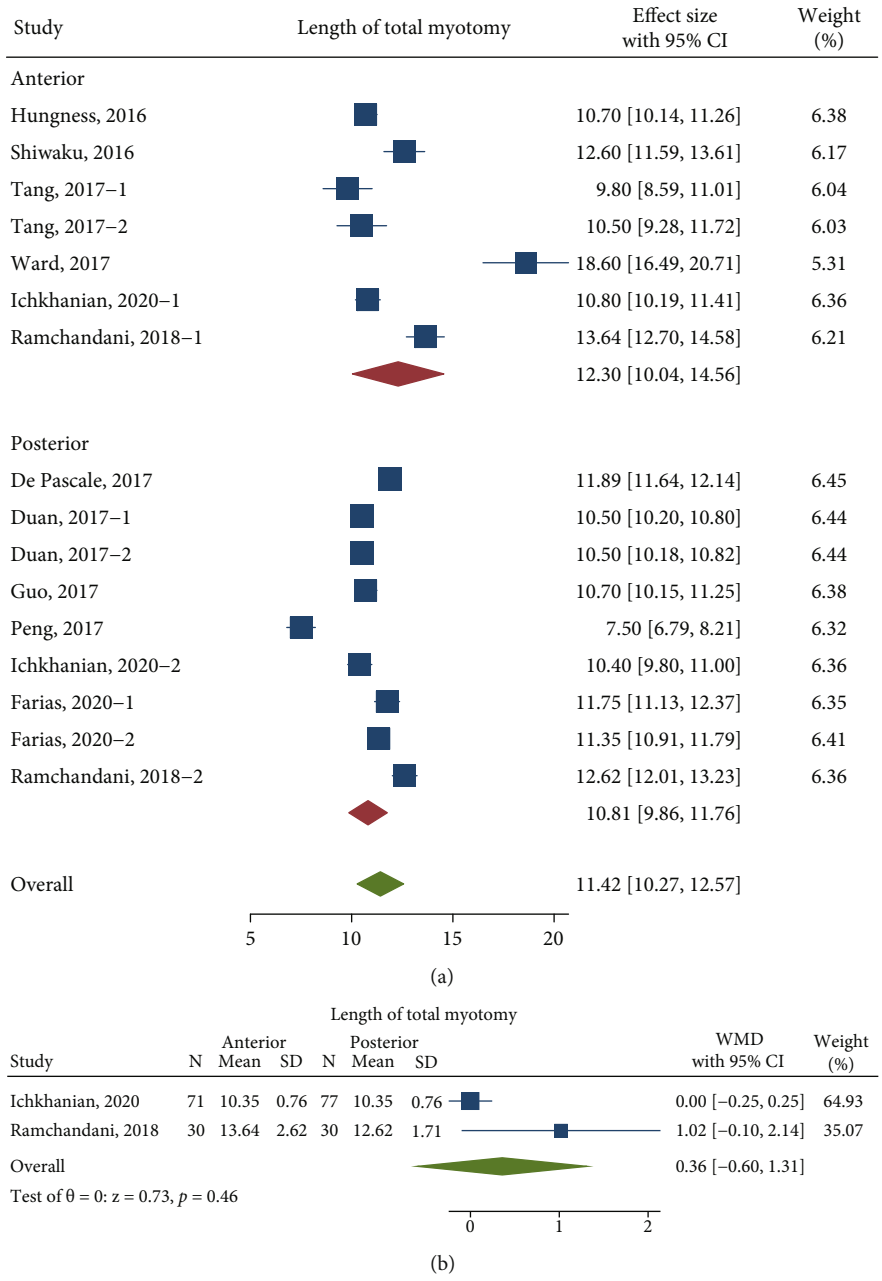

Figure 4: (a) Forest plot, Comparison of the length of total myotomy before balancing baseline; (b) Forest plot, Length of total myotomy difference between anterior and posterior approaches after balancing baseline Labels 1 and 2 were sectionalizations inside the study. They grouped these factors as follows: preoperative intervention/non-preoperative intervention (Tang, 2017), FTM/CM (Duan, 2017), Chagas/idiopathic (Farias, 2020), and anterior/posterior (Ramchandani, 2018; Tan, 2018).

approach was 4.95 days (95% CI 3.29 to 6.60 days; $n = 6$; I^2 99.23%) and that of the posterior approach was 4.65 days (95% CI 3.09 to 6.22 days; $n = 6$; I^2 99.07%), which showed no significant difference ($P = 0.80$) (Figure 5(a)). After balancing the characteristics of the studies, the pooled WMD was -0.24 days (95% CI -0.55 to 0.07 days; I^2 30.85%; $n = 3$; $P = 0.13$), which still showed no significant difference between these two groups (Figure 5(b)).

Compared to the previous study, there were several new studies included in our meta-analysis, and we updated these indexes mentioned above as supplements. In particular, we analyzed the difference between pre- and post-POEM (LES pressure and Eckardt scores), which would be more precise. Additionally, the outcomes as follows were analyzed, and the results are consistent with the previous study: the overall clinical success after POEM with a follow-up time at 12 months and >12 months both showed no obvious difference between the anterior approach and posterior approach, as detailed in Tables 3 and 4 and Supplementary Fig. 1-2. The pooled occurrence of GERD events after POEM and the

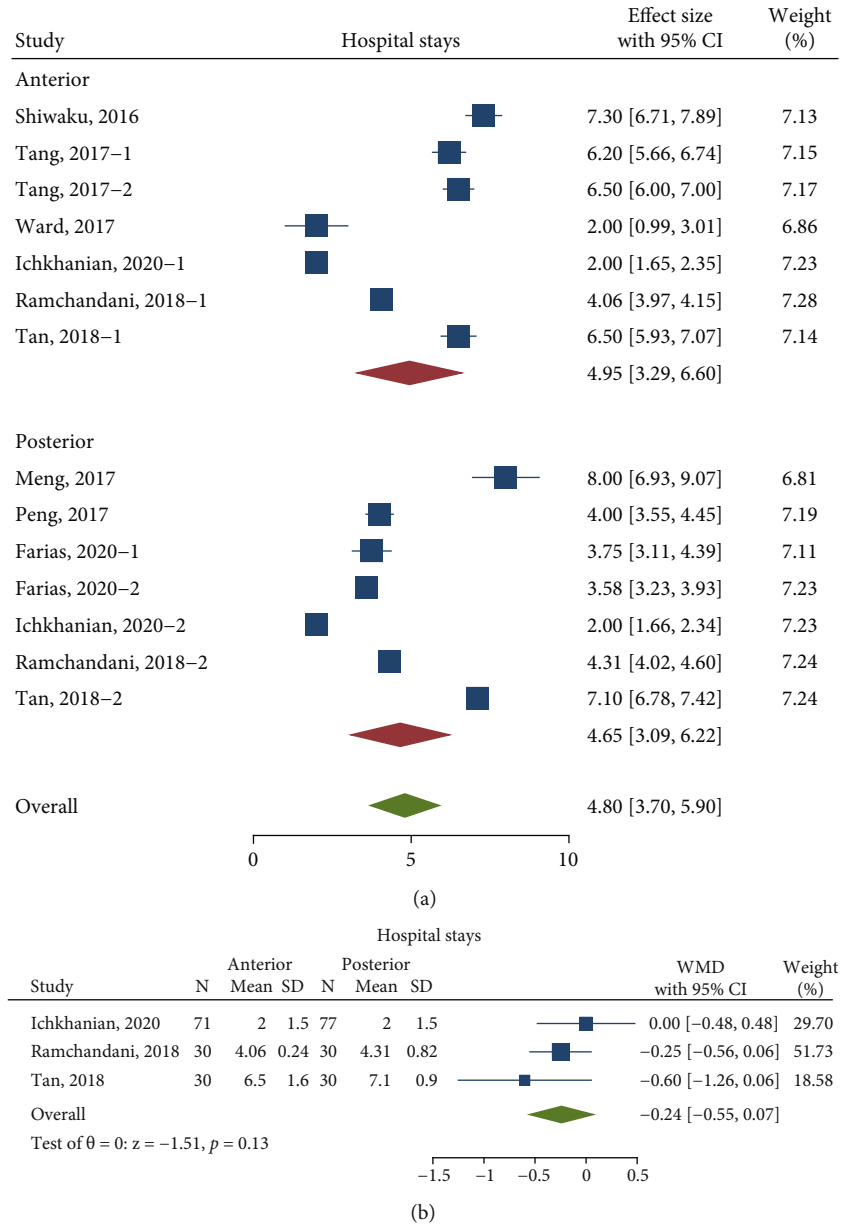

Figure 5: (a) Forest plot, Comparison of hospital stays before balancing baseline; (b) Forest plot, hospital stays difference between anterior and posterior approaches after balancing baseline Labels 1 and 2 were sectionalizations inside the study. They grouped these factors as follows: preoperative intervention/non-preoperative intervention (Tang, 2017), FTM/CM (Duan, 2017), Chagas/idiopathic (Farias, 2020), and anterior/posterior (Ramchandani, 2018; Tan, 2018).

pooled occurrence of adverse events after POEM did not show a difference between the anterior approach and posterior approach in our analysis. Additionally, it seemed that the procedure time of the posterior approach did not differ from that of the anterior approach in statistics (anterior vs. posterior: 78.33 vs. 70.46 mins; $P = 0.53$). All results are summarized in Tables 3 and 4 and Supplementary Fig. 3-5.

Publication bias was evaluated for the included studies. A funnel plot was used to perform the analysis for our primary outcomes (Supplementary Fig. 7). No publication bias was identified in the results of Eckardt scores and clinical success at 12 months. However, we found publication bias in the results of LES pressure and clinical success > 12 months. Further analysis was conducted by the trim and fill method and confirmed that the trend of pooled effects was similar.

5. Discussion

POEM has been more widely used over the past decade in the treatment of achalasia. Several studies have confirmed the safety and efficiency of POEM [10, 11]. A prior study showed that the rate of postprocedure GERD of POEM, clinical success, and adverse events was almost the same in both

Table 3: Summary of the results before balancing baseline.

Outcome	Effective size (95% CI; n; I^2)		P value[a]
	Anterior	Posterior	
LES pressures[b] (mmHg)	-24.56 (-31.29, -17.82; $n = 5$; 96.25%)	-20.14 (-23.44.-16.85; $n = 8$; 94.72%)	0.25
POEM Eckardt[b]	-5.83 (-6.22, -5.45; $n = 8$; 83.15%)	-6.07 (-6.52, -5.62; $n = 10$; 88.93%)	0.44
Clinical success at 12 months[c] (%)	94 (90, 97; $n = 8$; 46.74%)	95 (92, 98; $n = 9$; 22.00%)	-
Clinical success > 12 months[c] (%)	86 (78, 94; $n = 3$; 69.24%)	92 (87, 97; $n = 7$; 72.59%)	0.19
Procedure time[d] (min)	78.33 (56.44, 100.22; $n = 7$; 98.72%)	70.46 (59.05, 81.87; $n = 10$; 98.47%)	0.53
Length of total myotomy[d] (cm)	12.30 (10.04, 14.56; $n = 6$; 97.70%)	10.81 (9.86, 11.76; $n = 7$; 97.80%)	0.23
Hospital stays[d] (day)	4.95 (3.29, 6.60; $n = 6$; 99.23%)	4.65 (3.09, 6.22; $n = 6$; 99.07%)	0.80
GERD by EGD[c] (%)	22 (17, 27; $n = 9$; 58.27%)	16 (12, 21; $n = 11$; 51.38%)	0.11
Adverse events[c] (%)	2 (0, 7; $n = 9$; 84.88%)	5 (1, 9; $n = 13$; 74.76%)	-

[a]P value of subgroup analysis between anterior and posterior approaches. [b]Differences in the pre- and postoperative mean of the anterior/posterior approach in the subgroup analysis. [c]Pooled rate of clinical success at 12 months, clinical success > 12 months, GERD by EGD, and adverse events in subgroup analysis. [d]Pooled mean procedure time, length of total myotomy, and hospital stays in the subgroup analysis.

Table 4: Summary of the results in direct comparison.

Outcome	Effective size (95% CI; n; I^2)	P value
LES pressures (mmHg)	WMD: -1.56 (-3.90, 0.78; $n = 3$; 0.00%)	0.19
POEM Eckardt	WMD: 0.08 (-0.28, 0.44; $n = 3$; 0.00%)	0.66
Clinical success at 12 months	lnOR: 0.03 (-0.67, 0.74; $n = 4$; 0.00%)	0.92
Procedure time (min)	WMD: 3.41 (-1.14, 7.95; $n = 4$; 0.00%)	0.14
Length of total myotomy (cm)	WMD: 0.36 (-0.60, 1.31; $n = 2$; 67.41%)	0.46
Hospital stays (day)	WMD: -0.24 (-0.55, 0.07; $n = 3$; 30.85%)	0.13
GERD by EGD	lnOR: -0.12 (-0.55, 0.31; $n = 4$; 0.00%)	0.59
Adverse events	lnOR: 0.33 (-0.53, 1.18; $n = 4$; 0.00%)	0.46

anterior and posterior approaches [14]. However, these outcomes are quantitative objective indicators. This study analyzed objective indicators to obtain more quantitative and objective outcomes and update the analysis data.

In this study, with a total of 1261 patients from 19 studies, no significant differences between the anterior group and posterior group in terms of the pooled difference in LES pressure before and after POEM, the pooled difference in Eckardt scores before and after POEM, overall clinical success after POEM at 12 months and >12 months, the length of total myotomy, hospital stays, the pooled occurrence of GERD events after POEM, and the pooled occurrence of adverse events were identified.

From this study, the pooled differences in LES pressure of the anterior approach and posterior approach were -24.56 mmHg and -20.14 mmHg, respectively, with a pooled WMD of -1.56 mmHg ($P = 0.19$). In addition, the pooled differences in Eckardt scores of the anterior approach and posterior approach were -5.83 and -6.07, respectively, with a pooled WMD of 0.08 ($P = 0.66$). There was no heterogeneity with the pooled WMD for the pooled difference in LES pressure and Eckardt scores.

As in a previous study [14], the overall clinical success after POEM at the 12-month follow-up and >12-month follow-up, occurrence of GERD events after POEM, and adverse events were similar in anterior myotomy and posterior myotomy. In addition, the length of total myotomy (anterior vs. posterior: 12.30 cm vs. 10.81 cm), hospital stays (anterior vs. posterior: 4.95 vs. 4.65 days), and procedure time (anterior vs. posterior: 78.33 min vs. 70.46 min) in the anterior approach seemed to be comparable to those in the posterior approach. This study further confirms the safety of POEM, and the influence of anterior and posterior approaches on POEM is not significant.

At present, only 2 meta-analyses comparing POEM via the anterior approach and posterior approach have been published [14, 51]. The results reported in this study differed from the results in the latest meta-analysis [14]. Compared with the latest study, two new articles were included in this study [34, 44]. One of the new articles was a follow-up study of the RCT [46]. Additionally, LES pressure and Eckardt scores were added as the primary outcomes, which were quantified indicators. Thus, the results would be more objective. Furthermore, the length of total myotomy and hospital stays were also compared between the anterior and posterior approaches because these two indicators may affect the choice of approach.

For the other meta-analysis [51], the methods and reported outcomes in this meta-analysis are obviously different from those in this study. The earlier meta-analysis only included four RCTs with 488 patients to compare the efficiency of anterior and posterior myotomy. The clinical

success, incidence of GERD after POEM, LES pressure, and total operation time did not differ between anterior and posterior myotomy, which was consistent with the findings of this study. However, this meta-analysis indicated that anterior myotomy was associated with a shorter hospital stays, while posterior myotomy had fewer adverse events, lower risk, and shorter incision closure time, which were different from the outcomes in this study. In this study, the length of total myotomy, hospital stays, pooled occurrence of GERD events after POEM, and pooled occurrence of adverse events did not show significant differences between the anterior and posterior approaches. These different results may be attributed to the different quantities and types of included articles. This study included 1261 patients from 19 studies consisting of 3 RCTs and 16 cohorts, which contained a larger population, and the result might be more convincing.

There was no significant difference in procedure time between the anterior and posterior approaches. However, according to theoretical analysis, the endoscope in the posterior approach can fit the working channel better and shorten the incision closure time [14]. Nevertheless, it seems that the length of total myotomy is not affected by the anterior or posterior approach, although the posterior approach provides a better alignment of the endoscopic accessories with the channel of the endoscope. Thus, the hospital stays would not be influenced by the shorter procedure time. However, these outcomes may be influenced by factors such as operator experience, level of health care facility, and patient age, as the heterogeneity is high.

Regarding postprocedure GERD, both this study and a previous study found no difference between the anterior approach and the posterior approach, which is inconsistent with a theoretical analysis: the anterior approach has a lower risk of damage to sling muscle fibers and the angle of His, which might be more beneficial to the antireflux mechanism of the esophagus [5, 14]. This may be due to different skill levels of operators, different lifestyles of patients, and partial or full thickness myotomy. Thus, more studies with head-to-head comparisons between anterior and posterior myotomy are needed.

There are several strengths of this study. A systematic literature search was conducted, with clear inclusion criteria, careful exclusion of redundant studies, inclusion of good-quality studies, detailed extraction of data, and strict evaluation of study quality. This is also the first meta-analysis to compare the difference in LES pressure and Eckardt scores, length of total myotomy, and hospital stays between anterior and posterior approaches.

There are limitations in this study, and some of these are unavoidable. First, most of the studies were observational studies, although 4 of them were performed using a prospective cohort, and 3 RCTs were included. None of the studies were representative of the general population or community practice. These factors have affected the quality of evidence. Second, heterogeneity was identified in several comparisons, including the pooled difference in LES pressure and Eckardt scores. However, there was no heterogeneity with the pooled WMDs in the direct comparison, and it revealed the same outcomes. Thus, the result could be confirmed. The reason for the observed heterogeneity based on the metaregression analysis and sensitivity analysis was not found. Thus, the observed heterogeneity may be related to the difference in the operators' experience and the institutional policy. Since then, studies with large samples and multicenter RCTs have been excluded.

Despite these limitations, this meta-analysis demonstrates that the terms of the pooled difference in LES pressure and Eckardt scores, clinical success, length of total myotomy, hospital stays, GERD, adverse events, and procedure time seemed to be similar for both the anterior and posterior approaches. Further prognosis after POEM via anterior and posterior approaches needs to be studied in the future.

Data Availability

Supplementary Tables 1–2, Supplementary Figs. 1–7, and Appendices 1–2 are available online only (Supplementary Material).

Consent

This study did not require patient consent.

Conflicts of Interest

The authors have declared that no competing interests exist.

Authors' Contributions

Weina Jing performed the analysis and drafted the original manuscript; Xinyue Luo performed the analysis and edited the manuscript; Jinlin Yang, Junchao Wu, and Yuxiang Chen revised the manuscript. Kai Deng conceived and designed the article and revised the manuscript. Weina Jing and Xinyue Luo contributed equally.

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Supplementary Materials

Supplementary 1. Supplementary Table 1: the NOS quality scores (evaluating the quality of cohort studies).

Supplementary 2. Supplementary Table 2: the Jadad scores (evaluating the quality of RCTs).

Supplementary 3. Supplementary Fig. 1: forest plot and bubble plot and clinical success after POEM at 12 months. (A) Meta-analysis of clinical success at 12 months with the anterior/posterior approach. (B) Metaregression of clinical success after

POEM at 12 months with the anterior/posterior approach. (C) Meta-analysis of clinical success after POEM at 12 months in direct comparison with the anterior/posterior approach.

Supplementary 4. Supplementary Fig. 2: forest plot and bubble plot and clinical success after POEM > 12 months. (A) Meta-analysis of clinical success after POEM > 12 months in indirect comparison between anterior and posterior approaches. (B) Metaregression of clinical success after POEM > 12 months and the anterior/posterior approach.

Supplementary 5. Supplementary Fig. 3: forest plot, bubble plot, and procedure time. (A) Meta-analysis of procedure time in indirect comparison between anterior and posterior approaches. (B) Metaregression of the procedure time and anterior/posterior approach. (C) Meta-analysis of procedure time in direct comparison with anterior/posterior approach.

Supplementary 6. Supplementary Fig. 4: forest plot and bubble plot and pooled occurrence of GERD events associated with POEM. (A) Meta-analysis of pooled occurrence of GERD events associated with POEM in indirect comparison between anterior and posterior approaches. (B) Metaregression of pooled occurrence of GERD events and anterior/posterior approach. (C) Meta-analysis of the pooled occurrence of GERD events associated with POEM in direct comparison with the anterior/posterior approach.

Supplementary 7. Supplementary Fig. 5: forest plot and bubble plot and pooled occurrence of adverse events associated with POEM. (A) Meta-analysis of the pooled occurrence of adverse events associated with POEM in the anterior/posterior approach. (B) Metaregression of pooled occurrence of adverse events and anterior/posterior approach. (C) Meta-analysis of the pooled occurrence of adverse events associated with POEM in direct comparison with the anterior/posterior approach.

Supplementary 8. Supplementary Fig. 6: sensitivity analysis for heterogeneous studies in the meta-analysis.

Supplementary 9. Supplementary Fig. 7: funnel plot for publication bias in the meta-analysis (LES pressure, Eckardt scores, and clinical success at 12 months and >12 months).

Supplementary 10. Appendix 1: search strategy.

Supplementary 11. Appendix 2: PRISMA checklist.

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Review Article

Safety and Efficacy of Peroral Endoscopic Shorter Myotomy versus Longer Myotomy for Patients with Achalasia: A Systematic Review and Meta-analysis

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Background and Aims. The adequate myotomy length during peroral endoscopic myotomy (POEM) is still controversial. We performed this systematic review and meta-analysis to determine the efficacy and safety of the modified POEM with shorter myotomy (SM) and compare the outcomes between SM and longer myotomy (LM) in achalasia patients. *Methods*. A comprehensive literature search was conducted in PubMed, EMBASE, Cochrane Library, and Web of Science databases from inception to May 28, 2021. The primary outcome was clinical success rate and incidence of reflux-relative adverse events (AEs). Fixed- or random-effect models were adopted for the analysis according to the heterogeneity. *Results*. Five studies involving 225 patients in SM group and 222 patients in LM group were included. The overall clinical success of SM was 96.6% (95% confidence interval (CI) 92.7 to 98.4%). SM showed noninferior response as compared to LM (risk ratio (RR) 1.02, 95% CI 0.98 to 1.06, $P = 0.41$, $I^2 = 0\%$). Based on the abnormal acid reflux by pH monitoring, its incidence was significantly lower in the SM group than that in the LM group (RR 0.58, 95% CI 0.36 to 0.94, $P = 0.03$, $I^2 = 0\%$). With respect to procedure-related parameters, the total procedure time of SM was significantly shorter than that of LM (mean difference (MD) -16.30, 95% CI -23.10 to -9.49, $P < 0.001$, $I^2 = 68\%$). *Conclusions*. SM and LM are comparable in providing treatment efficacy for achalasia patients, whereas less operation time and lower incidence of post-POEM abnormal esophageal acid exposure are observed in SM.

1. Introduction

Achalasia is a relatively rare motility disorder of the esophagus characterized by insufficient lower esophageal sphincter (LES) relaxation and abnormal peristalsis, resulting in progressive dysphagia to liquids and solids, regurgitation of undigested food, noncardiac chest pain, and different degrees of weight loss [1]. Achalasia is incurable because the underlying etiology remains unknown. It has been reported that the primary cause of achalasia may be the selective loss of inhibitory neurons in the myenteric plexus of the distal esophagus and LES [2]. As a result, all available therapeutic options of achalasia currently are palliative and aimed to lower LES pressure to improve esophageal emptying, including medical managements such as oral pharmacological therapy, endoscopic botulinum toxin injection, endoscopic pneumatic dilatation, laparoscopic Heller myotomy, and peroral endoscopic myotomy (POEM) [3].

POEM was first performed by Inoue et al. in 17 patients with achalasia nearly a decade ago [4]. For the first seven patients in their study, a relatively shorter myotomy (SM) (mean 4.9 cm) was used, while for the last ten patients, a longer myotomy (LM) (mean 10.4 cm) was used, and it was found that the latter group experienced better symptom improvement [4]. Since then, thousands of POEM procedures with LM have been adopted worldwide for patients with achalasia, and a large number of clinical studies and meta-analyses have reported its excellent efficacy and safety

with a reported mean myotomy length range from 8.2 to 14.4 cm [5–7]. However, achalasia is a LES dysfunction disorder and the length of LES is reported just 3.6 cm (range from 3.3 to 4.3 cm) in achalasia patients [8]. Hence, modified POEM with SM might be able to provide the same benefits on patients with achalasia as the LM. Another key point is that lowering LES pressure not only leads to symptom relief but also increases lower esophageal acid exposure, with the high risk of post-POEM gastroesophageal reflux disease (GERD) [9]. Meanwhile, a previous study has demonstrated that gastric myotomy > 2.5 cm resulted in increased rates of moderate esophagitis [10].

Presently, the optimal myotomy length remains unknown due to the lack of evidence, but a few papers have reported the promising clinical outcomes of the modified POEM with SM for achalasia patients [8, 11–14]. To provide more practical recommendations for endoscopists, we performed this systematic review and meta-analysis to determine the efficacy and safety of the modified POEM with SM (myotomy length ≤ 7 cm) [4] and compare the clinical success rate and incidence of reflux-relative adverse events (AEs) between SM and LM (myotomy length > 7 cm) in achalasia patients [4].

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [15] was followed in this systematic review and meta-analysis [15]. We stated that the protocol of this review was not registered. As it was studied based on the published summary data, written consent from patients and ethical approval from an institutional review board were not required.

2.1. Eligibility Criteria. Prespecified inclusion criteria were as follows: (1) population: adult individuals (age greater than 18 years) who were diagnosed with achalasia based on symptoms, endoscopy, barium swallow, and high-resolution manometry (HRM) [1]; (2) intervention: the modified POEM with SM (total myotomy length ≤ 7 cm with about 2 cm incision at the gastric side) [4]; (3) comparison: no comparison or conventional POEM with LM (total myotomy length > 7 cm) [4]; (4) outcomes: provided data on primary outcomes, including clinical success (Eckardt score ≤ 3) and/or reflux-related adverse events [16]; and (5) study type: all controlled, uncontrolled, prospective, and retrospective articles.

Prespecified exclusion criteria were as follows: (1) meta-analysis, reviews, case reports, case series, experimental studies in animal models, conference abstracts, editorials, letters to the editor, and expert comments; (2) studies with incomplete data or ongoing trials without reported clinical outcomes; and (3) duplicate studies with overlapped patients except for the most recent publication with the largest population.

2.2. Information Sources and Search Strategy. Two authors (Shu Huang and Huifang Xia) independently conducted a comprehensive literature search in PubMed, EMBASE, Cochrane Library, and Web of Science [v.5.35] databases from inception to May 28, 2021, without language restriction. The following search keywords were adopted: "POEM" and "achalasia". Disagreements were resolved by consensus. The detailed search strategies and identified items in each database are presented in Supplementary Table 1. Additionally, we examined the references of the screened records and searched significant articles manually to identify additional studies.

2.3. Selection Process. After using an automated tool to remove duplicates, the authors (Shi Lei and Xia Huifang) independently screened all titles and abstracts with retained records found in a literature search. Irrelevant studies were excluded. The steps so far have been done in the EndNote software. The authors then independently reviewed the full text of the remaining records and identified eligible studies according to our inclusion and exclusion criteria items. Mismatched studies were excluded. Differences of opinion on the choice of research at the level of title/abstract or full text should be resolved through consensus and discussion with the third author (Zhang Han). To summarize the study selection process, we used a modified PRISMA flowchart [15].

2.4. Data Collection Process and Data Items. Two authors (Jiao Jiang and Wensen Ren) independently used a standardized spreadsheet that had been developed in advance to extract the data from the eligible studies. Disagreements were resolved by consensus and discussion with a third author (Han Zhang). When an included study failed to supply us with relevant information, we contacted the authors of the paper by email to seek extra details.

The primary outcomes were as follows: (1) the overall clinical success rate in SM group and the difference of clinical success rate between SM and LM groups. We restricted the Eckardt score as a measure of clinical success in our analysis. The Eckardt score consists of four symptoms (dysphagia, regurgitation, chest pain, and weight loss) that are graded according to severity, and the clinical success is defined as a score ≤ 3 [16]. (2) Postoperative reflux-related events including symptomatic reflux, reflux esophagitis on endoscopy, and abnormal acid reflux based on pH monitoring. The secondary outcomes were as follows: (1) the difference of the perioperative outcomes including total procedure time and hospital stay between the SM and LM groups; (2) the difference between pre- and postoperative outcomes including Eckardt score, lower esophageal sphincter pressure (LESP), integrated relax pressure (IRP), and diameter of barium column (DBC) in the SM group; (3) the difference of postoperative outcomes between SM and LM including Eckardt score, LESP, and IRP; and (4) the overall technical success and the number of various types of perioperative adverse events (AEs) in the SM group.

The following data were extracted from each article: (1) study characteristics: first author, year of publication, study design, study period, study location, and follow-up duration; (2) patients' demographics in both the SM and LM groups: sample size, age, sex, symptoms duration,

Chicago classification, and previous treatments; (3) POEM procedure details in both the SM and LM groups: total procedure time, myotomy direction, tunnel length, myotomy length, and hospital stay; and (4) reported primary and secondary outcomes. The data that support the results of this study are available from Dr. Han Zhang (443191590@qq.com) upon reasonable request.

2.5. Study Risk of Bias Assessment. Two authors (Jiao Jiang and Wensen Ren) independently identified and evaluated the risk of bias of the included studies. The methodological quality of the observational studies was assessed using the Newcastle-Ottawa scale (NOS) [17], which assesses selection (4 items), comparability (2 items), and outcomes (3 items). A study can be awarded a maximum of one star for each item within the selection and outcome categories while a maximum of two stars can be given for comparability. Generally, studies with no less than six stars were considered of high quality. The methodological quality of the randomized controlled trials (RCTs) was assessed using the Cochrane Collaboration's tool [18], which covers six domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. A judgment of high, low, or unclear risk of material bias was given to each item. Any discrepancies were resolved by consensus and discussion with a third author (Han Zhang) during the quality assessment.

2.6. Reporting Bias Assessment. To detect outcome reporting bias, we examined the trial protocols to see if the specified outcomes were reported in the corresponding trial publications. When trial protocols were not available, we compared the outcomes reported in the methods and results sections of the trial publications. We did not statistically perform funnel plot asymmetry test and Egger's test to assess publication bias because there were only five papers included.

2.7. Certainty Assessment. Two reviewers (Yan Peng and Muhan Lü) independently assessed the quality of the evidence for results from the meta-analysis using the Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE) system [19]. The system classifies the overall quality of evidence as high, moderate, low, or very low four levels. Firstly, the rating of the estimate from observational studies begins with low-quality evidence, while the rating of the estimate from randomized controlled trials begins with high-quality evidence. Then, it can decrease based on the five considerations that include the study limitations, inconsistency of results, indirectness of evidence, imprecision, and reporting bias, whereas it can increase based on large effect, plausible confounding, and dose response. During this process, any disagreements were resolved by consensus and discussion with a third author (Han Zhang).

2.8. Statistical Analysis. We performed a meta-analysis if data were available for more than one study. For meta-analyses of continuous variables (total procedure time, hospital stay, Eckardt score, LESP, IRP, and DBC), the mean differences (MD) between pre- and post-POEM data or between SM and LM data were calculated with 95% confidence intervals (CIs). All continuous data reported as mean/median (range) values were converted to mean ± SD before analysis according to the method of Hozo et al. [20]. For meta-analyses of dichotomous variables (technical success, clinical success, and reflux-related AEs), the pooled event rate in SM and the risk ratio (RR) between SM and LM data were calculated with 95% CIs. Heterogeneity among studies was qualitatively and quantitatively assessed using two methods: the χ^2 test ($P < 0.10$ indicated the presence of heterogeneity) and I^2 statistic. I^2 values of 0-50%, 51-74%, and 75% or more were considered to indicate a low, moderate, and high degree of heterogeneity, respectively. In the presence of substantial heterogeneity ($I^2 > 50\%$), a random-effect model was used as a pooling method; otherwise, a fixed-effect model was adopted. We were unable to perform subgroup analyses of characteristics such as symptom duration, achalasia subtype, and previous treatments owing to insufficient data. Sensitivity analyses were also conducted by using the leave-one-out method to test the influence of each individual study on pooled estimates. All P values were 2-tailed, and P values < 0.05 were considered statistically significant in all tests except for the χ^2 test. All statistical procedures were conducted using the statistical software Review Manager 5.3 with the exception of the pooled event rate, which was performed in Comprehensive Meta-Analysis software.

3. Results

3.1. Study Selection. The initial literature databases search yielded 4254 potential related records, of which 930 on PubMed, 2048 on EMBASE, 138 on Cochrane Library, and 1138 on Web of Science. The records were transferred to the EndNote for screening, and 1973 duplicates were removed using automation tools. Then, out of the 2281 remaining studies, 2249 irrelevant studies were eliminated after assessing their title and abstract. Finally, out of the 32 remaining studies, 27 studies were excluded after the examination of their full text based on the inclusion and exclusion criteria. No additional study was retrieved from the references of the screened records. The reasons and references for the excluded studies after full text review were available in Supplementary Table 2. Five studies [8, 11–14] involving 225 patients in SM and 222 patients in LM were included in final qualitative analysis and quantitative synthesis. The adapted flow diagram of the study selection is presented in Figure 1.

3.2. Study Characteristics. The main characteristics of the included studies and patients are described in Table 1. Five studies [8, 11–14] with a total of 447 patients were included, of which four studies [11–14] compared the clinical outcomes between SM and LM (225 patients in the SM group and 222 patients in the LM group). Two RCTs [13, 14], one prospective cohort study [8], and two retrospective cohort studies [11, 12] were analyzed with a short-term follow-up. All studies were performed in the East Asia, including 4 in China and 1 in India. The period of patient

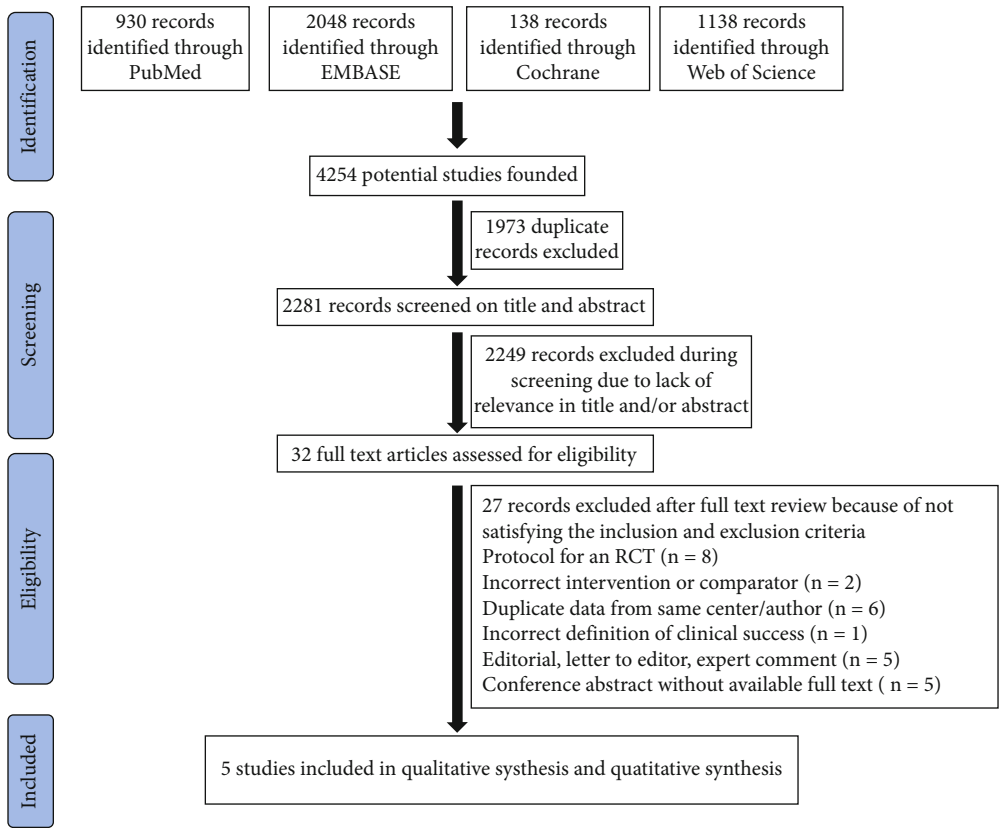

Figure 1: Adapted Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

enrollment was between 2011 and 2019. The sample size varied from 34 to 63 in the SM group and from 37 to 74 in the LM group. The mean age ranged from 36 to 49.3 years in the SM group and from 37.7 to 45.9 years in the LM group. The male proportion ranged from 37% to 53% in the SM group and from 48% to 65% in the LM group. The symptom duration varied widely from 0.7 to 9.4 years in both the SM and LM groups. Based on Chicago classification, there were 66 type I, 156 type II, and 3 type III achalasia in the SM group and 48 type I, 172 type II, and 2 type III achalasia in the LM group. The detailed characteristics of the POEM procedures are presented in Table 2. The mean total procedure time ranged from 31.2 to 52 minutes in the SM group and from 45.6 to 72.43 in the LM group. The mean length of hospital stay ranged from 2.82 to 9.9 days in the SM group and from 2.81 to 9.3 days in the LM group. The detailed outcomes reported in the included studies are summarized in Table 3. All POEM procedures were performed successfully, and no surgery intervention was required. The reported clinical success rate ranged from 94.4% to 100% in the SM group and from 91.9% to 98% in the LM group.

3.3. Risk of Bias in Studies. NOS was used to assess the risk of bias for 3 cohort studies. All cohort studies were given a score of 6-7 stars, representing the high quality of studies. Cochrane Collaboration's tool was used to assess the risk of bias for 2 RCTs, and only other bias was unclear in both two studies, representing that all RCTs were of high quality. The results of NOS and Cochrane Collaboration's tool quality assessment are summarized in Supplementary Table 3 and Supplementary Table 4, respectively.

3.4. Overall Clinical Success and Technical Success in the SM Group. Five studies that included a total of 225 patients were available to estimate the overall clinical success rate of SM. We used a fixed-effect model due to insignificant heterogeneity ($I^2 = 0\%$, $P = 0.775$), and the pooled clinical success rate of POEM with SM for achalasia patients was estimated at 96.6% (95% CI 92.7 to 98.4%) (Figure 2(b)). For technical success, the estimated pooled event rate was 98.9% (95% CI 96.2 to 99.7%; $I^2 = 0\%$, $P = 0.998$, Figure 2(a)).

3.5. Pre-POEM versus Post-POEM in the SM Group. Five studies involving 225 patients in the SM group compared pre-POEM with post-POEM outcomes. As the heterogeneity among studies was significant in Eckardt score, LESP, and DBC ($I^2 = 87\%$, $P < 0.001$; $I^2 = 87\%$, $P < 0.001$; $I^2 = 0\%$, $P = 0.005$, respectively), we used random-effect model for the analysis. While the heterogeneity among studies was low in IRP ($I^2 = 44\%$, $P = 0.17$), we used fixed-effect model for the analysis. In terms of the Eckardt score, achalasia patients treated with SM showed significant response as compared to pre-POEM (4 studies, $n = 225$ in the pre-POEM arm and $n = 225$ in the post-POEM arm, MD 6.07, 95% CI 5.34 to 6.20, Figure 3(a)). Based on the LESP, achalasia patients treated with SM showed significant improvement as compared to pre-POEM (4 studies, $n = 191$ in the pre-POEM

Table 1: General characteristics of the studies and patients.

Study	Wang et al., 2015	Li et al., 2018		Huang et al., 2020		Gu et al., 2020		Nabi et al., 2020	
Study design	Prospective cohort	Retrospective cohort		Retrospective cohort		RCT		RCT	
Study period	Jan 2012 to Feb 2013	Jan 2013 to Dec 2016		Jul 2011 to Sep 2017		Feb 2018 to Feb 2019		Jun 2017 to Mar 2019	
Study location	Guangzhou, China	Beijing, China		Shenzhen, China		Changsha, China		Hyderabad, India	
Patients group	SM	SM	LM	SM	LM	SM	LM	SM	LM
Total patients (*n*)	46	63	63	36	74	46	48	34	37
Mean age (years)	36	49.3	45.9	40.8	37.7	43.6	42.8	40.1	41.3
Male, *n* (%)	17 (37)	24 (38)	30 (48)	19 (53)	40 (54)	21 (46)	23 (48)	18 (53)	24 (65)
Symptoms duration (years)	<1 year, 12; 1-5 years, 28; and >5 years, 6	9.4 (0.1-40.0)	9.4 (0.3-30.0)	0.7 (0.2-2.1)	0.7 (0.3-2.5)	5.0 (0.3-34.0)	4.1 (0.3-31.0)	3 (1.5-4.7)	3 (1.0-5.0)
Previous treatments (*n*)	POEM, 1; PD, 7	BTI or PD or HM, 23	BTI or PD or HM, 18	BTI, 2; PD, 7	BTI, 3; PD, 9	None	None	PD, 12	PD, 9
Chicago classification, type I/type II/type III	26/19/1	16/45/2	9/52/2	12/24/0	26/48/0	0/46/0	0/48/0	12/22/0	13/24/0
Follow-up (months)	3	20.1 (6-48)	23.6 (6-48)	26.8 (8-54.3)	29.5 (6-58.8)	12	12	12	12

Continuous variables presented as mean (SD) or Median (IQR). SM: short myotomy; LM: long myotomy; POEM: peroral endoscopic myotomy; PD: pneumatic dilatation; BTI: botulinum toxin injection; SD: standard deviation; IQR: interquartile range.

Table 2: Details of the POEM procedures.

Study	Wang et al., 2015	Li et al., 2018		Huang et al., 2020		Gu et al., 2020		Nabi et al., 2020	
Group	SM	SM	LM	SM	LM	SM	LM	SM	LM
Total patients (n)	46	63	63	36	74	46	48	34	37
Procedure time (minutes)	52 (30-120)	39.5 (21-74)	49.2 (23-120)	46.6 ± 18.5	62.1 ± 25.2	31.2 ± 15.3	45.6 ± 16.2	44.03 ± 13.78	72.43 ± 27.28
Myotomy direction, A/P	NR	NR	NR	NR	NR	0/46	0/48	34/0	37/0
Tunnel length (cm)	6.8 (4.0-10.0)	7.6 (6-8)	11.8 (10-14)	8.6 ± 1.3	15.1 ± 2.9	NR	NR	NR	NR
Myotomy length (cm)	E: 4.3 (3.0-5.5); G: 1.1 (1.0-2.0); and T: 5.4 (3.5-7.5)	E: 2.9 (2-4); G: 2.0 (1-3); and T: 4.8 (3-6)	E: 6.9 (5-9); G: 2.3 (2-4); and T: 9.2 (8-11)	E: 4.0 ± 0.7; G: 2.1 ± 0.3; and T: 6.0 ± 0.6	E: 8.2 ± 2.7; G: 3.2 ± 1.2; and T: 11.5 ± 3.1	T: 5.66 ± 0.14	T: 10.1 ± 0.54	E: 2.76 ± 0.41; G: 2.70 ± 0.73	E: 7.97 ± 2.40; G: 2.84 ± 0.63
Myotomy extent	SCM, 15; FTM, 31	PFTM, 56; SCM, 1; and FTM, 6	PFTM, 50; SCM, 5; and FTM, 8	NR	NR	SCM, 46	SCM, 48	FTM, 34	SCM and FTM, 37
Hospitalization (days)	2.9 (2-6)	NR	NR	9.9 ± 2.4	9.3 ± 2.9	7.0 ± 0.9	6.5 ± 1.6	2.82 ± 0.67	2.81 ± 0.70

Continuous variables presented as mean ± SD or median (IQR). SM: short myotomy; LM: long myotomy; NR: not reported; E: esophageal; G: gastric; T: total; A/P: anterior/posterior; SCM: selective circular myotomy; FTM: full thickness myotomy; PFTM: progressive full thickness myotomy; SD: standard deviation; IQR: interquartile range.

Table 3: Outcomes reported in the included studies.

Study	Wang et al., 2015	Li et al., 2018		Huang et al., 2020		Gu et al., 2020		Nabi et al., 2020	
Group	SM	SM	LM	SM	LM	SM	LM	SM	LM
Total patients (*n*)	46	63	63	36	74	46	48	34	37
Technical success, *n* (%)	46 (100)	63 (100)	63 (100)	36 (100)	74 (100)	46 (100)	48 (100)	34 (100)	37 (100)
Clinical success, *n*/*N* (%)	46/46 (100)	56/57 (98.2)	55/56 (98.2)	34/36 (94.4)	68/74 (91.9)	44/46 (95.7)	45/48 (93.8)	32/33 (97.0)	29/31 (93.5)
Pre-Eckardt score	8.4 ± 3.2	7.9 (5-11)	7.3 (4-11)	7.1 ± 1.6	7.5 ± 1.9	7.56 ± 1.56	7.12 ± 1.68	6.02 ± 1.33	6.75 ± 1.32
Post-Eckardt score	2.7 ± 1.9	1.1 (0-4)	1.0 (0-4)	1.3 ± 1.2	1.6 ± 1.3	0.76 ± 0.51	0.72 ± 0.42	0.935 ± 0.929	0.818 ± 0.983
Pre-LESP (mm Hg)	39.4 ± 10.1	27.8 (0.7-57.7)	29.6 (9.6-50.4)	41.8 ± 14.3	39.7 ± 13.9	33.5 ± 5.0	32.4 ± 5.3	NR	NR
Post-LESP (mm Hg)	24.4 ± 9.1	15.6 (1.5 -35.7)	17.7 (3.0-38.8)	15.9 ± 3.2	13.3 ± 5.7	11.8 ± 4.4	12.1 ± 3.9	NR	NR
Pre-IRP (mm Hg)	38.6 ± 10.4	NR	NR	NR	NR	23.2 ± 4.8	21.5 ± 4.6	26.40 ± 13.93	28.50 ± 11.01
Post-IRP (mm Hg)	25.7 ± 9.6	NR	NR	NR	NR	10.1 ± 2.4	9.7 ± 2.6	8.60 ± 1.30	7.44 ± 4.30
Pre-DBC (cm)	4.9 ± 2.2	NR	NR	7.91 ± 2.64	8.16 ± 4.37	5.9 ± 1.0	5.6 ± 0.8	NR	NR
Post-DBC (cm)	4.1 ± 2.3	NR	NR	NR	NR	3.7 ± 0.5	3.5 ± 0.5	NR	NR
Pre-HBC (cm)	5.4 ± 2.1	NR	NR	NR	NR	NR	NR	12.99 ± 5.40	11.21 ± 5.36
Post-HBC (cm)	2.6 ± 1.8	NR	NR	NR	NR	NR	NR	1.90 ± 2.39	2.31 ± 1.71

Continuous variables presented as mean ± SD or median (IQR). SM: short myotomy; LM: long myotomy; LESP: lower esophageal sphincter pressure; IRP: integrated relax pressure; DBC: diameter of barium column; HBC: height of barium column; SD: standard deviation; IQR: interquartile range.

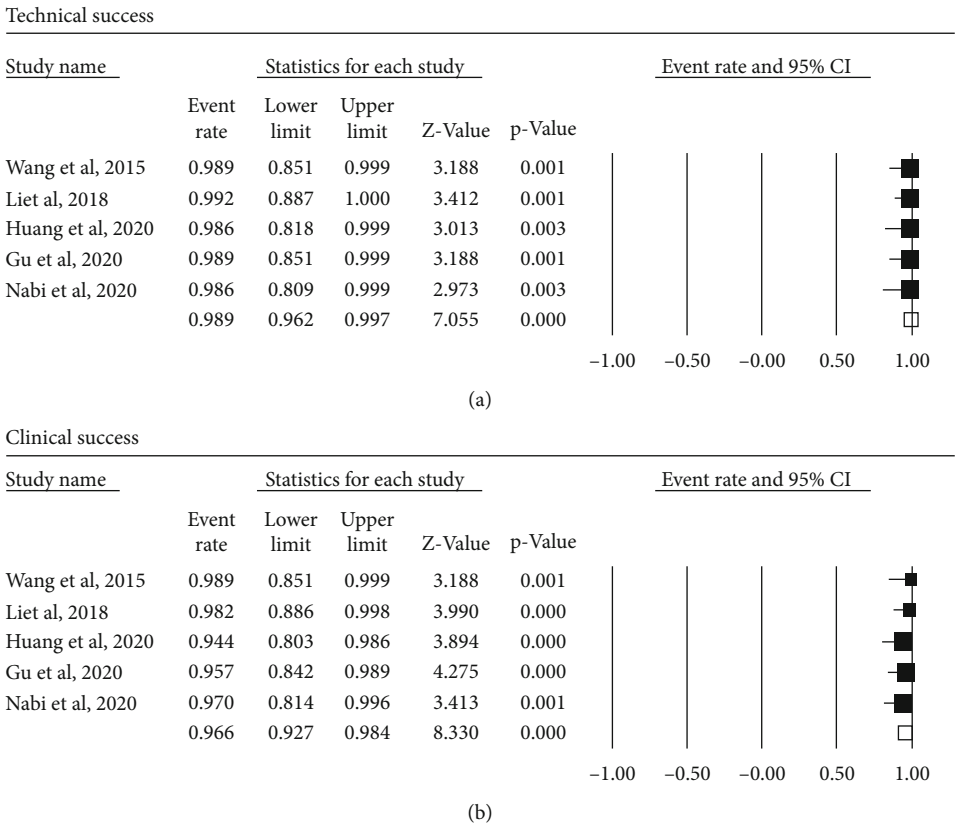

Figure 2: Forest plot presenting the pool event rate for technical success (a) and clinical success (b) of the modified peroral endoscopic myotomy with shorter myotomy in achalasia.

arm and $n = 127$ in the post-POEM arm, MD 18.82, 95% CI 13.58 to 24.05, Figure 3(b)). With respect to the IRP, achalasia patients treated with SM showed significant response as compared to pre-POEM (3 studies, $n = 126$ in the pre-POEM arm and $n = 126$ in the post-POEM arm, MD 13.49, 95% CI 12.10 to 14.87, Figure 3(c)). For the DBC, achalasia patients treated with SM showed significant improvement as compared to pre-POEM (2 studies, $n = 92$ in the pre-POEM arm and $n = 92$ in the post-POEM arm, MD 1.57, 95% CI 0.20 to 2.93, Figure 3(d)).

3.6. SM versus LM in Terms of Efficacy. Four studies compared clinical outcomes of SM with LM involving 179 patients in SM and 222 patients in LM. In terms of clinical success, as the heterogeneity among studies was low ($I^2 = 0\%$, $P = 0.89$), we used fixed-effect model for the analysis. Achalasia patients treated with SM showed noninferior response as compared to LM (4 studies, $n = 172$ in the SM arm and $n = 209$ in the LM arm, RR 1.02, 95% CI 0.98 to 1.06, $P = 0.41$, Figure 4). With respect to the procedure-related parameters, as the heterogeneity among studies with regard to the total procedure time was significant ($I^2 = 68\%$, $P = 0.03$), we used random-effect model for the analysis. Meanwhile, as the heterogeneity among studies with regard to the length of hospital stay was low ($I^2 = 37\%$, $P = 0.20$), we used fixed-effect model for the analysis. The total procedure time of SM was significantly shorter than that of LM (4 studies, $n = 179$ in the SM arm and $n = 222$ in the LM arm, MD -16.30, 95% CI -23.10 to -9.49, $P < 0.001$, Figure 5(a)). However, the length of hospital stay did not differ significantly between the groups (3 studies, $n = 116$ in the SM arm and $n = 159$ in the LM arm, MD 0.17, 95% CI -0.09 to 0.44, $P = 0.20$, Figure 5(b)). For Eckardt score, LESP, and IRP, the LM seemed to show more improvement compared with SM; however, the difference between the two groups were not found to be statistically significant (Figure 6).

3.7. SM versus LM in Terms of Reflux-Related Events. Postoperative reflux-related events including symptomatic reflux, reflux esophagitis on endoscopy, and abnormal acid reflux based on pH monitoring were evaluated, respectively. As for the symptomatic reflux, SM showed no significant difference compared with LM (3 studies, $n = 145$ in the SM arm and $n = 185$ in the LM arm, RR 0.66, 95% CI 0.37 to 1.18, $P = 0.16$, Figure 7(a)). Regarding the endoscopic findings, SM showed a lower trend of GERD with borderline significance compared with LM (4 studies, $n = 179$ in the SM arm and $n = 222$ in the LM arm, RR 0.64, 95% CI 0.40 to 1.01, $P = 0.06$, Figure 7(b)). With regard to the abnormal acid reflux based on pH monitoring, SM significantly decreased post-POEM GERD incidence compared with LM (2 studies, $n = 73$ in the SM arm and $n = 78$ in the LM arm, RR 0.58, 95% CI 0.36 to 0.94, $P = 0.03$, Figure 7(c)). As the heterogeneity among studies was low in the above

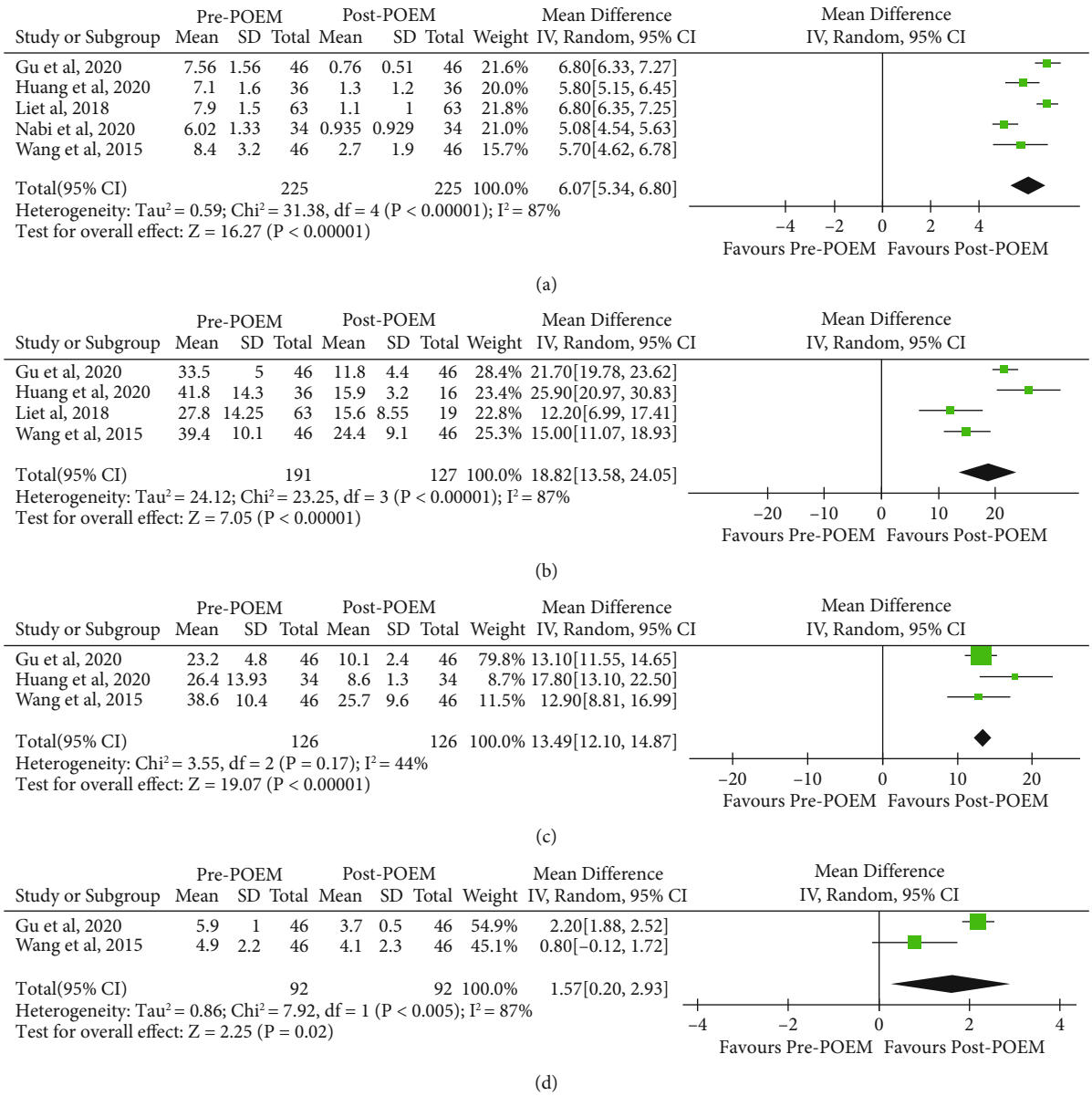

Figure 3: Forest plot presenting the mean difference of Eckardt score (a), lower esophageal sphincter pressure (b), integrated relax pressure (c), and diameter of barium column (d) between before and after peroral endoscopic myotomy with shorter myotomy in achalasia.

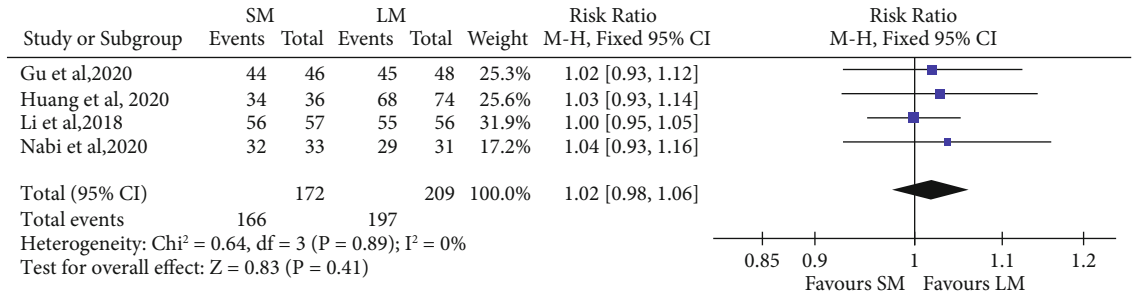

Figure 4: Forest plot presenting the risk ratio of clinical success between shorter myotomy and longer myotomy of peroral endoscopic myotomy in achalasia.

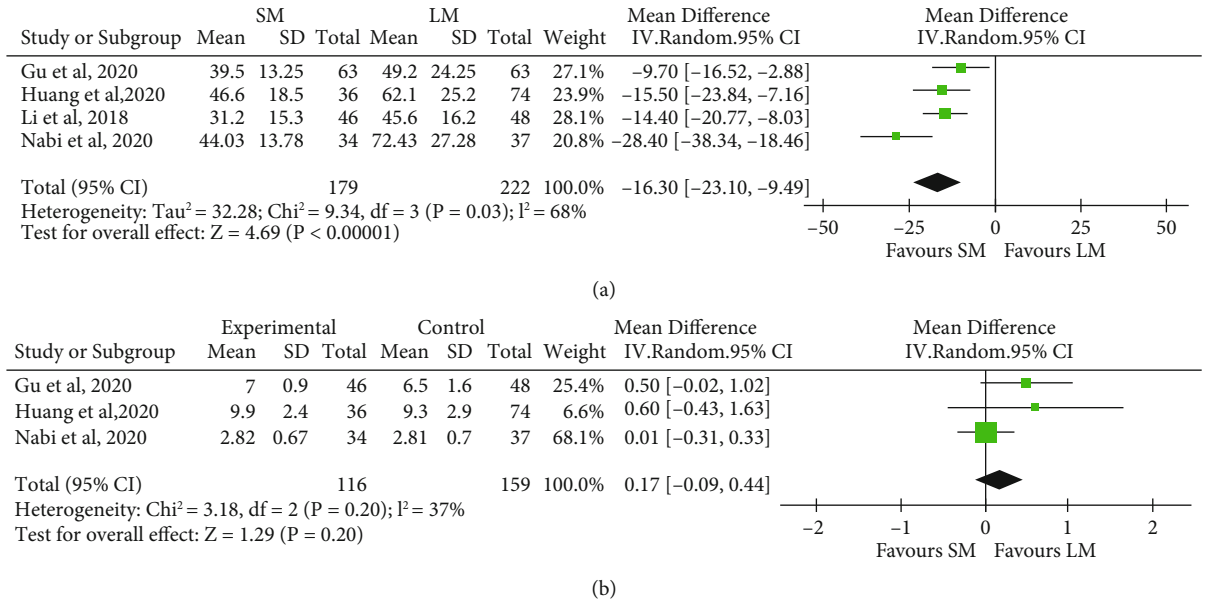

Figure 5: Forest plot presenting the mean difference of total procedure time (a) and length of hospital stay (b) between shorter myotomy and longer myotomy of peroral endoscopic myotomy in achalasia.

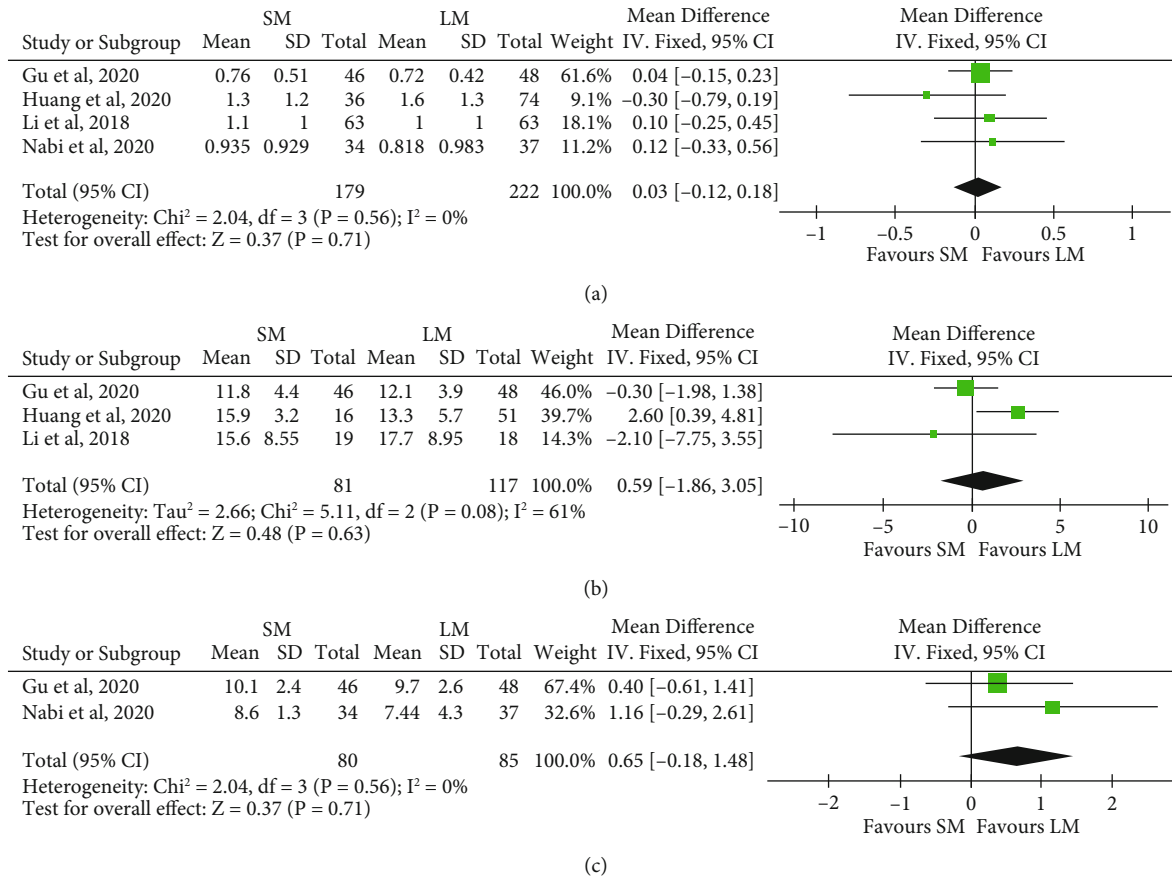

Figure 6: Forest plot presenting the mean difference of post-POEM Eckardt score (a), lower esophageal sphincter pressure (b), and integrated relax pressure (c) between shorter myotomy and longer myotomy of peroral endoscopic myotomy in achalasia.

analysis ($I^2 = 0\%$, $P = 0.94$; $I^2 = 0\%$, $P = 0.92$; $I^2 = 0\%$, $P = 0.73$, respectively), we used fixed-effect model for the analysis.

3.8. Procedure-Related Adverse Events. We did not carry out meta-analysis in procedure-related adverse events due to insufficient data publication. But we performed a detailed

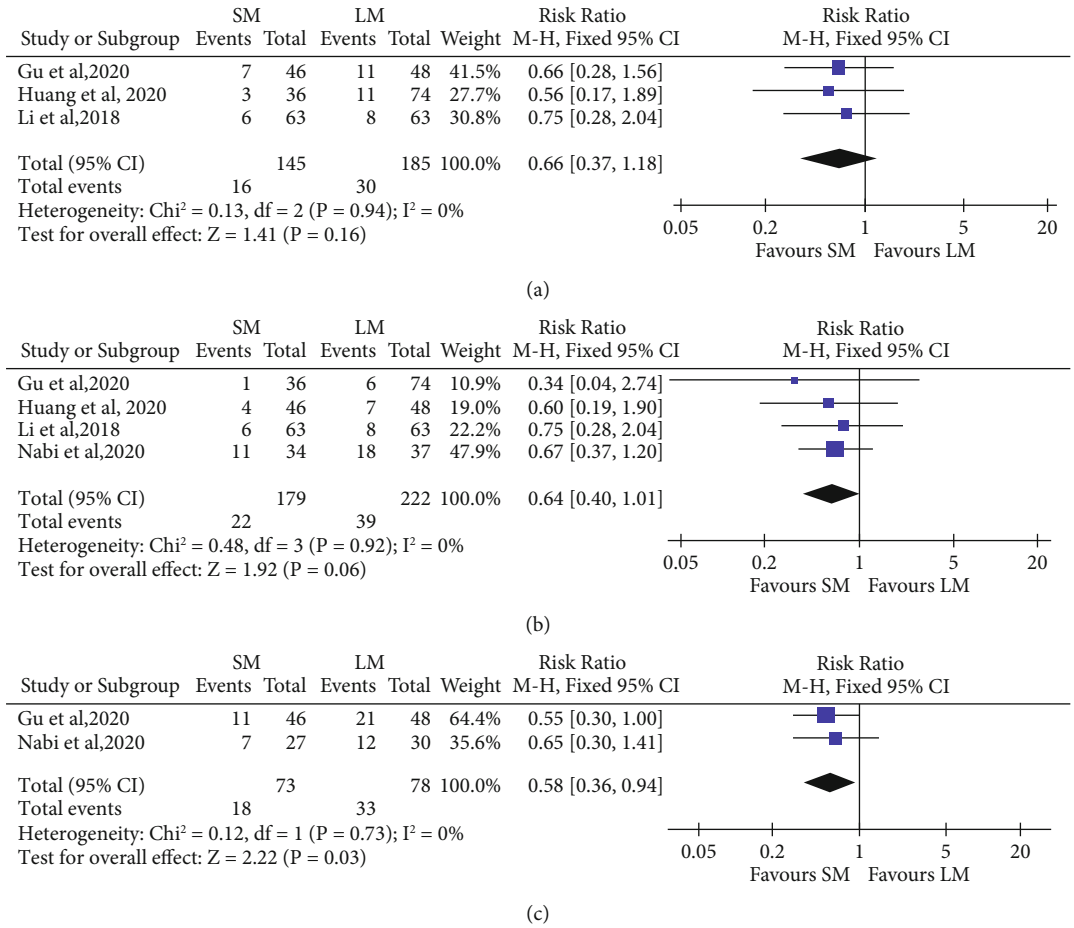

Figure 7: Forest plot presenting the risk ratio of postprocedure GERD measured by symptoms assessment (a), endoscopy (b), and pH monitoring (c) between shorter myotomy and longer myotomy of peroral endoscopic myotomy in achalasia.

summary of all adverse events, which are available in Table 4. The most common adverse events were insufflation-related events ($n = 25.3\%$), such as subcutaneous emphysema, pneumothorax, and pneumoperitoneum. Other common adverse events include bleeding ($n = 9.3\%$) and mucosal injury/perforation ($n = 4.9\%$). All adverse events were resolved with conservative or endoscopic treatment. No surgery intervention was required and no death was reported.

3.9. Reporting Biases and Sensitivity Analysis. Comparing the trial protocols with reported outcomes in the corresponding trial publications and comparing the outcomes reported in the methods and results sections of the trial publications, no reporting bias was found. The sensitivity analysis demonstrated the robustness of all the results by using the leave-one-out method.

3.10. Certainty of Evidence. Based on GRADE, the certainty of evidence that the clinical success of SM was noninferior to LM was low due to the limitation of observational studies, which signified that further research was very likely to have an important impact on our confidence in the estimate of effect and was likely to change the estimate. The certainty of evidence that the SM decreased post-POEM GERD incidence compared with LM was moderate due to the nature of RCT and inconsistency of the results, which signified that further research was likely to have an important impact on our confidence in the estimate of effect and may change the estimate. The certainty of evidence that the SM decreased the total procedure time compared with LM was very low due to the limitation of observational studies and significant heterogeneity, which signified that any estimate of effect was very uncertain.

4. Discussion

To our knowledge, this is a systematic review and meta-analysis to evaluate the efficacy and safety of SM and compare the clinical outcomes between SM and LM for achalasia. Based on our analysis, we demonstrated that the SM was noninferior to LM in terms of providing clinical success, and it could even lower the incidence of post-POEM GERD regarding to abnormal acid reflux and shorten the total procedure time.

POEM is a novel, minimally invasive, and natural orifice endoscopic technology, involving the process of distal esophagus myotomy via a submucosal tunneling approach [21]. Over the last decade, POEM has prompted a revolutionary shift in achalasia management and has triggered a worldwide dissemination of this new technique [22]. Since

Table 4: Detailed procedure-related adverse events and reflux adverse events.

Study	Group	Total patients (n)	Perioperative adverse events, n (%)	Postprocedure GERD, n (%)
Wang et al., 2015	SM	46	Bleeding, 7 (15.2); perforation, 6 (13.0); pneumothorax, 14 (30.4); pneumoperitoneum, 12 (26.1); and emphysema, 17 (37.0)	Symptoms or endoscopy, 7 (15.2)
Li et al., 2018	SM	63	Mucosal injury, 4 (6.3); pneumoperitoneum, 2 (3.2); and fever (temperature > 38.0°C), 6 (9.5)	Symptoms, 6 (9.5); endoscopy, 6 (9.5)
	LM	63	Mucosal injury, 5 (7.9); pneumothorax, 1 (1.6); pneumoperitoneum, 3 (4.8); pneumomediastinum, 1 (1.6); subcutaneous emphysema, 24 (38.1); and fever (temperature > 38.0°C), 7 (11.1)	Symptoms, 8 (12.7); endoscopy, 8 (12.7)
Huang et al., 2020	SM	36	Major bleeding, 2 (5.6); pneumothorax, 1 (2.8)	Symptoms, 3 (8.3); endoscopy, 1 (2.8)
	LM	74	Major bleeding, 3 (4.1); pneumothorax, 2 (2.7); and mucosal perforation, 1 (1.4)	Symptoms, 11 (14.9); endoscopy, 6 (8.1)
Gu et al., 2020	SM	46	None	Symptoms, 7 (15.2); endoscopy, 4 (8.7); and pH, 11 (23.9)
	LM	48	Mucosal injuries, 1 (2.08)	Symptoms, 11 (22.9); endoscopy, 7 (14.6); and pH, 21 (43.8)
Nabi et al., 2020	SM	34	Subcutaneous emphysema, 4 (11.76); capnoperitoneum requiring decompression, 3 (8.82); retroperitoneal CO2, 4 (11.76); minor bleeding episodes, 12 (35.29); and mucosal injuries requiring clipping, 1 (2.94)	Endoscopy, 11 (32.4); pH, 7 (25.92)
	LM	37	Subcutaneous emphysema, 4 (11.76); capnoperitoneum requiring decompression, 3 (8.10); retroperitoneal CO 2, 2 (5.40); minor bleeding episodes, 17 (45.94); mucosal injuries requiring clipping, 1 (2.70)	Endoscopy, 18 (48.6); pH, 12 (40.00)

SM: short myotomy; LM: long myotomy.

its introduction by Inoue et al. [4], LM (approximately 10 cm) has been developed into a common practice on a global scale [13]. But the technological elements of POEM have been continuing to be improved in an attempt to make the procedure safer, more effective, and reproducible [23]. Major technical variations in POEM procedure include myotomy length, anterior versus posterior myotomy approach, and full-thickness versus partial-thickness myotomy [24]. These techniques generally vary with operator expertise and preferences in clinical practice [23]. However, these technical aspects are sometimes affected by patient characteristics. In recent years, studies investigating clinical outcomes in connection with these factors have been increasingly published [8, 11–14]. Although these modifications have technically facilitated the procedure, the effect of esophageal myotomy length on POEM outcomes is still controversial. Therefore, we conduct this systematic review and meta-analysis to evaluate the efficacy and safety of the modified POEM with SM and compare the clinical success rate and incidence of reflux-relative AEs between SM and LM in idiopathic achalasia patients.

At this time, the research has proven that POEM is both effective and safe, with a reported overall clinical success rate more than 90% [25, 26]. Consistent with earlier studies, our results show that POEM treatment produces great symptom alleviation and manometric parameter improvement. Meanwhile, there were no severe AEs in all of the individuals. This study revealed and reaffirmed the fact that the POEM is an effective and safe treatment for those with achalasia.

However, POEM has been especially challenging and time-consuming in complex achalasia such as sigmoid-type esophagus, prior treatments, and presence of submucosal fibrosis. Our current study found that the SM significantly shortened the total procedure time compared with LM. Shorter operating time can potentially reduce the overall expense of the procedure by avoiding the need for additional endoscopic tools. In addition, perioperative AEs, especially gas-related events, have been shown to be fewer in cases with shorter procedure duration [11, 27]. Because SM can make POEM easier than the standard myotomy, it is likely to be a better option for these cases. However, we did not find a significant difference in procedure-related adverse events between SM and LM due to the insufficient data. In addition, the length of hospital stay did not differ significantly between the two groups. Therefore, more studies are needed to demonstrate the benefits of SM in POEM procedure.

As is well known, acquired GERD is a notable deficiency in the development of POEM. Based on the objective measurements, the incidence of post-POEM GERD is reported between 10% and 57%, and it appears to be the main challenge of the operation [28, 29]. Identifying intraprocedural factors that increase the likelihood of the development of post-POEM GERD is conceivably valuable to decrease its incidence. Several studies have confirmed that increased length of gastric myotomy lead to increased incidence of post-POEM GERD [9, 30]. However, a recent meta-analysis found that variations in the myotomy technique do not differ in the incidence of post-POEM GERD and

could not recommend modifications to the POEM technique to reduce its rate [31]. In this study, we found that the SM decreased post-POEM GERD incidence compared with LM regarding abnormal acid reflux. It has been proven that the circular muscle may contribute to esophageal shortening due to the spiral-shaped structure and the role that it plays in axial movements [13, 23, 32]. Hence, circular muscle keeps reflux of stomach contents from entering the esophagus and thus pushes refluxate downward and back into the stomach again theoretically. When POEM was conducted with SM, it means that longer circular muscles were remained. As a result, we concluded that this may be the reason why SM can lower the incidence of post-POEM abnormal esophageal acid exposure.

By making use of functional lumen imaging and endoscopic esophageal topography, adjustments and customization to the POEM technique have been made much easier. The increased use of this technology is allowing patients to gain more accurate assessments of the sufficiency of a myotomy by having access to real-time measurements of pressure and compliance of the esophagus. At the present time, there are no set optimal distensibility targets; however, this adjuvant technology will play a significant role in the procedure's future [22].

In this study, there are several limitations. Firstly, it was conducted with only five studies, of which four studies were performed in China, meaning that our results may not applicable universally. Meanwhile, the types of studies included in the meta-analysis were heterogenous with only 2 RCTs and others were observational studies. Secondly, most enrolled individuals are adult type I and type II achalasia meaning that our results may not apply to the type III achalasia. Thirdly, we are unable to compare the long-term efficacy and safety between SM and LM due to the short-term and various follow-up. Therefore, there are several suggestions in future studies. Firstly, large prospective multicenter RCTs with long-term follow-up are needed. Secondly, we recommend that an additional analysis to determine whether there is a difference in the above results between different countries or Asian and Western populations. Thirdly, double scope technique can be utilized to detect the length of esophageal and gastric myotomy to avoid underestimated or overestimated the outcomes [33].

In conclusion, based on our analysis, SM and LM of POEM are comparable in terms of providing treatment efficacy for achalasia patients, whereas less operation time and lower incidence of post-POEM abnormal esophageal acid exposure are observed in SM.

Data Availability

The data that support the results of this study are available from Dr. Han Zhang (443191590@qq.com) upon reasonable request.

Conflicts of Interest

Han Zhang, Xinyi Zeng, Shu Huang, Huifan Xia, Lei Shi, Jiao Jiang, Wensen Ren, Yan Peng, Muhan Lü, and Xiaowei Tang have no conflicts of interest or financial ties to disclose.

Authors' Contributions

Xiaowei Tang and Muhan Lü conceived and designed the study. Jiao Jiang, Wensen Ren, and Lei Shi were responsible for data acquisition. Shu Huang and Huifang Xia critically revised the manuscript. Xinyi Zeng and Yan Peng interpreted the data. Han Zhang drafted the manuscript. Xiaowei Tang revised the manuscript. Xiaowei Tang approved the final manuscript. Han Zhang, Xinyi Zeng, and Shu Huang contributed equally to this work.

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Supplementary Materials

Supplementary tables including electronic database search strategy, reasons for the excluded articles, and quality assessment of included studies are available online. *(Supplementary Materials)*

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Research Article

Modified Peroral Endoscopic Myotomy Technique for Type II Achalasia: A Multicenter Retrospective Study

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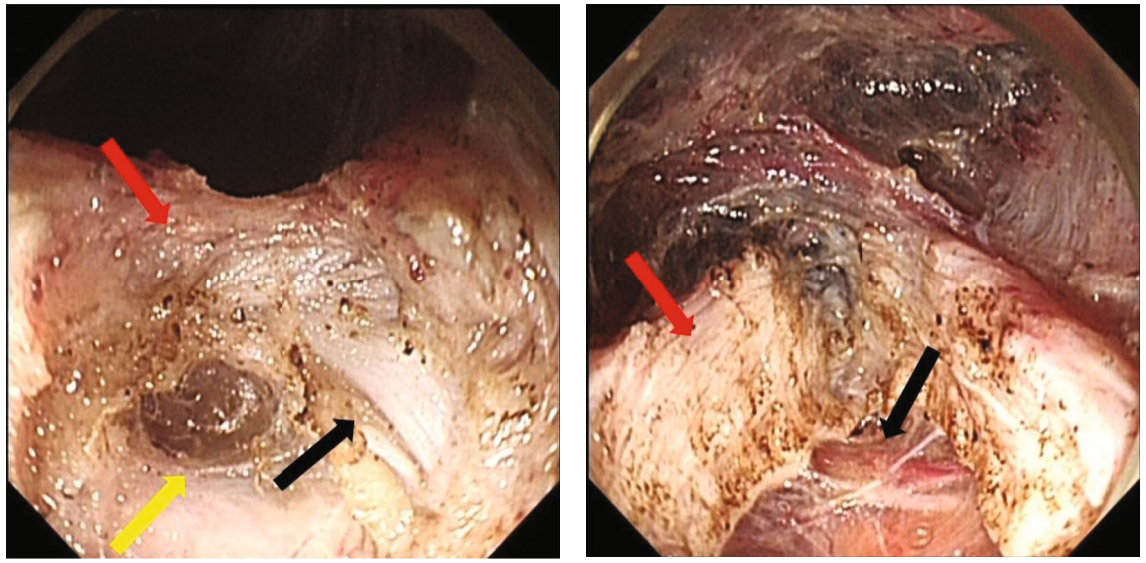
Aim. This retrospective study is aimed at evaluating the outcomes of a modified peroral endoscopic myotomy (POEM) technique in patients with type II achalasia. *Methods*. We performed a modified POEM procedure, which involved a shorter (total myotomy length = 4 cm), full-thickness myotomy, on 31 patients with type II achalasia. Clinical success rates, technical success rates, pre- and postoperative esophageal manometry results, complications, and reflux-related adverse events were evaluated. *Results*. The clinical success (Eckardt score ≤ 3) rates were 100% and 88.9% within 2 years and beyond 2 years postoperatively, respectively. The median lower esophageal sphincter pressures (LESP) decreased from 31.6 (26.7-49.7) mmHg preoperatively to 13.4 (10.5-21.6) and 11.8 (7.4-16.7) mmHg ($P < 0.001$) at 6 and 12 months postoperatively, respectively. The median integrated relaxation pressure (IRP) decreased from 27.8 (20.6-37.5) mmHg preoperatively to 12.9 (11.3-23.4) and 11.6 (9.6-16.8) mmHg ($P < 0.001$) at 6 and 12 months after POEM, respectively. Only one case (3.2%) of mucosal injury, four (12.9%) cases of reflux esophagitis, and two (6.5%) cases of gastroesophageal reflux symptoms were reported. *Conclusions*. The modified POEM technique showed excellent outcomes in patients with type II achalasia.

1. Introduction

Achalasia is an esophageal motility disorder characterized by incomplete relaxation of the lower esophageal sphincter (LES) and disordered peristalsis in the esophageal body, which induce changes in the esophageal function of bolus transport and food stasis [1]. According to the Chicago classification version 4, achalasia is defined as an abnormal median IRP with 100% failed peristalsis, with three characteristic phenotypes: type I, peristalsis absent; type II, ≥20% swallows with panesophageal pressurization; and type III, ≥20% of swallows with premature contraction [2]. The treatment of achalasia requires lowering the LESP through medications, endoscopic injection of botulinum toxin, pneumatic dilation (PD), or laparoscopic Heller myotomy (LHM). POEM is a minimally invasive endoscopic treatment for achalasia first described by Inoue et al. in 2008 [3]. Since its introduction, thousands of POEM procedures have been performed; POEM has been reported to be safe and effective. Existing uncontrolled reports suggest efficacy equal to or superior to LHM, and emerging randomized controlled trial data suggest that POEM is more effective than PD [4].

There is no consensus regarding the dissection of the sphincter muscles and the overall technique, and even the periprocedural management varies across centers and endoscopists. Most endoscopists selectively dissect only the circular muscle; however, others prefer dissecting both circular and longitudinal muscle layers, but there are no criteria for dissection of the muscle layers.

At our centers, we developed a strategy for treating type II achalasia using high-resolution manometry (HRM) data, in which a shorter tunnel was created and full-thickness



(a) (b)

Figure 1: (a) The red arrow indicates the circular muscle layer, the black arrow indicates the longitudinal muscle layer, and the yellow arrow indicates the external coat of the esophagus. (b) The red arrow indicates the circular and longitudinal muscle layers, and the black arrow indicates the external coat of the esophagus.

dissection of the LES and cardiac sphincter was performed. This study presents an introduction to our procedure, its clinical success, and the rate of adverse events.

2. Methods

2.1. Patients. Patients with type II achalasia who underwent modified POEM at the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University and the People's Hospital of Ma'anshan from January 2015 to August 2020 were enrolled in our study. The inclusion criteria for our study were as follows: (1) patients diagnosed with type II achalasia by clinical symptoms, barium meal, HRM, and esophagogastroduodenoscopy (EGD); (2) age ≥ 18 years; and (3) Eckardt score > 3. The following exclusion criteria were applied: (1) history of gastrointestinal tumors, (2) history of treatment by POEM, (3) history of esophageal or mediastinal surgery, and (4) length of the LES > 4 cm. Finally, 31 consecutive patients were included in this study. All patients had no contraindications for POEM and provided written informed consent before POEM. This study was approved by the Ethics Committee of the Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University.

2.2. Preoperative Evaluation. The patients were examined for symptoms and analyzed using the Eckardt score. They next underwent barium esophagography for esophageal dynamics analysis. HRM was used to characterize the esophageal disorders and measure the length of the LES, IRP, and LESP.

2.3. POEM Technique. The patients were instructed to fast for ≥24 hours and undergo EGD one or two days before the procedure to cleanse the esophagus of any residual material. The length of the LES was measured on HRM. Myotomy measuring 4 cm was used to ensure complete dissection of the LES. POEM was performed under general anesthesia with airway intubation. A forward-viewing endoscope with CO_2 insufflation was used. A transparent plastic cap was attached to the endoscope tip. Before beginning the procedure, the gastroesophageal junction (GEJ) was identified, and its distance from the incisors was determined. The site of submucosal tunnel entry was selected as 6 cm proximal to the GEJ. The submucosal tunnel was terminated 2 cm distal to the GEJ. The GEJ was confirmed based on the distance to the incisors through the esophageal lumen (esophageal tunnel) and the identification of increased vascularity with spindle-shaped veins in the tunnel. We performed a full-thickness dissection of both the circular and longitudinal muscle layers of the LES and the cardiac sphincter (Figure 1). The full-thickness dissection length was 4 cm, each being 2 cm proximal and distal to the GEJ (equivalent to the length of the LES and the cardiac sphincter extending 1 cm on both sides). Finally, the entry was closed with hemostatic clips to avoid potential leakage of luminal fluid into the tunnel and mediastinum. All procedures were performed by expert endoscopists with 10 years of experience in endoscopic procedures at two medical centers.

2.4. Post-POEM. Patients were hospitalized after the procedure and administered intravenous antibiotics. After computed tomography confirmed the absence of perforation, a 24-hour fasting period was ensured before commencing clear water intake on day 1 postoperatively. On day 2, a soft diet was started and maintained for several days, followed by a regular diet.

2.5. Outcomes and Follow-Up. The primary outcomes of the study were the technical and clinical success rates. Technical success was defined as the successful completion of POEM.

Clinical success was defined as an Eckardt score of ≤3 after POEM. The secondary outcomes included POEM-related adverse events, IRP and LESP on HRM before and after POEM, reflux-related adverse events, and procedure time. Mucosal injury, perforation, bleeding, and pneumothorax were recorded as POEM-related adverse events. Reflux-related adverse events included reflux esophagitis, esophageal acid exposure, and gastroesophageal reflux disease (GERD) symptoms. Reflux esophagitis was confirmed by EGD and classified by the Los Angeles classification [5]. A percentage of acid exposure time (%AET, esophageal pH < 4) of >4.2% was defined as abnormal acid exposure [6]. GERD symptoms were evaluated using the GERD-*Q* score, and a GERD − *Q* score > 7 was considered to indicate significant GERD symptoms [7].

The EGD, HRM, and Eckardt score evaluations for all patients were scheduled at 6 and 12 months after POEM. Twenty-four-hour pH measurements and GERD-Q questionnaire scores were evaluated at 12 months after POEM. The Eckardt score was retrieved telephonically by interviewing patients every 6 months after POEM.

2.6. Statistical Analysis. Continuous variables are presented as the mean ± standard deviation (SD) or median with range and were tested using paired nonparametric testing. Statistical significance was set at $P < 0.05$. The data were analyzed with IBM SPSS 19.0 software.

3. Results

3.1. Patient Information. Overall, 31 patients (median age: 45 years, range: 31-64 years; eighteen women, thirteen men) were included. The symptoms lasted for a median of 4 (range: 2.6–8.7) years. Eight patients (25.8%) received treatment for achalasia before POEM, 5 (16.1%) received botox injections, 2 (6.5%) underwent PD, and one patient (3.2%) underwent bougie dilation. Table 1 summarizes the data of the measured outcomes.

3.2. POEM Details. All patients successfully underwent POEM procedures, with durations lasting 28–80 (median: 38) minutes. One patient (3.2%) experienced mucosal injury and required perioperative endoscopic clipping of the wound. No patient had perforation, severe bleeding, or pneumothorax (Table 2).

3.3. Efficacy of POEM. The Eckardt score, LESP, and IRP data at 6 months and 12 months after POEM procedures were obtained from 31 patients. The LESP and IRP showed a significant reduction at 6 and 12 months postoperatively. The median LESP decreased from 31.6 to 13.4 mmHg at 6 months after POEM ($P < 0.001$) and to 11.8 mmHg at 12 months after POEM ($P < 0.001$). The median IRP decreased from 27.8 to 12.9 mmHg at 6 months after POEM ($P < 0.001$) and to 11.6 mmHg at 12 months after POEM ($P < 0.001$). At the 6- and 12-month follow-up, the median Eckardt score decreased from 7 (5-10) to 0 (0-2) and 1 (0-2), respectively (Table 3). No patient had an Eckardt score > 3 at 12 months after POEM. The overall clinical success rate was 100% (31/31) within 1 year post-POEM. After 2 years, the available Eckardt scores of 23 patients (74.2%) were still ≤3. The clinical success rate was 100% (23/23). The Eckardt data collected by interview of 9 patients (29.0%) were obtained beyond 2 years post-POEM; only one patient (11.1%, 1/9) required PD because of worsening symptoms (Eckardt score = 5). The overall clinical success rate was 88.9% (8/9).

Table 1: Patient characteristics.

	N = 31
Age, median (range), year	45 (31-64)
Female/male	18/13
Duration of symptoms, median (range), years	4 (2.6-8.7)
The length of LES, mean ± SD, mm	3.1 ± 0.5
Eckardt score, median (range)	7 (5-10)
LESP, median (range), mmHg	31.6 (26.7-49.7)
IRP, median (range), mmHg	27.8 (20.6-47.5)
Previous treatment, *n* (%)	
Botox injection	5 (16.1)
Pneumatic dilation	2 (6.5)
Bougie dilation	1 (3.2)
No treatment	23 (74.2)

Table 2: POEM outcomes.

	N = 31
Technology success rates, *n* (%)	31 (100)
Procedures time, median (range), min	38 (28-80)
POEM-related adverse events, *n* (%)	
Mucosal injury	1 (3.2)
Perforation	0 (0)
Severe bleeding	0 (0)
Pneumothorax	0 (0)
Reflux-related adverse events, *n* (%)	
Abnormal acid exposure, *n* (%)	6 (19.4)
Endoscopic esophagitis, *n* (%)	4 (12.9)
GERD symptom, *n* (%)	2 (6.5)
GERD-*Q* score	4.39 ± 2.45

3.4. Reflux-Related Adverse Events. At the 12-month follow-up, a 24 h pH monitoring test and EGD were performed in all patients. Abnormal esophageal acid exposure was observed in 6 cases (19.4%). Four cases (12.9%) of esophagitis (Los Angeles classification A, 3; B, 1) were confirmed by EGD. The patients received a double dose of proton pump inhibitors (PPI) for 6 weeks, followed by repeat EGD, and their esophagitis was found to be completely resolved. Two patients (6.5%) had GERD symptoms and experienced complete symptom remission after standard-dose PPI treatment for 6 weeks (Table 2).

4. Discussion

Achalasia is a rare, primary motility disorder caused by decreased or lost myenteric neurons [8–10]. Patients with achalasia achieve remission due to the reduction in LES

Table 3: Eckardt score, LESP, and IRP data pre- and postoperative POEM.

	Pre-POEM	6 months after POEM	12 months after POEM	*P* value
Eckardt score	7 (5-10)	0 (0-2)	1 (0-2)	<0.001
LESP, mmHg	31.6 (26.7-49.7)	13.4 (10.5-21.6)	11.8 (7.4-16.7)	<0.001
IRP, mmHg	27.8 (20.6-37.5)	12.9 (11.3-23.4)	11.6 (9.6-16.8)	<0.001

and GEJ pressure after treatment with PD, LHM, and endoscopic injection of botulinum toxin [11, 12]. However, these therapies have limitations: PD requires multiple-grade dilations to establish symptom remission, and esophageal perforation occurs frequently during the large dilatations performed initially [13]. Endoscopic injection of botulinum toxin has shown good safety; however, its effects last for only a few months [14]. LHM has traditionally been preferred for achalasia; however, physicians always additionally perform partial fundoplication to reduce the postoperative risk of GERD [15].

POEM was first performed in 2008 and reported in 2010 [3], with various reports on its safety and effectiveness [16–19]. The standard POEM involves a 7 cm myotomy and incision of the muscle layer of the circular muscle bundles [3]. However, in clinical practice, a shorter or full-thickness myotomy has been performed, which shows comparable outcomes to the standard POEM [20, 21]. However, the safety and efficacy of a combined shorter and full-thickness myotomy have not been reported. Thus, we performed this study to evaluate the safety and effectiveness of this modified myotomy technique.

In this study, shorter and full-thickness POEM was successfully performed in all patients with type II achalasia. In our study, the clinical success rates were 100%, 100%, 100%, and 88.9% within six months, 1 year, 2 years, and beyond 2 years after the procedure, respectively. Based on data from recently published literature, the clinical success rates of POEM procedures ranged from 87.9% to 100% at 1 year after POEM [21–25]. The treatment efficacy within 1 year post-POEM in the current study was comparable to that of these studies. A long-term follow-up reported that the clinical success rate was 90.3% at two years after standard POEM [26], which was lower than our results. In our study, the clinical success rate was 100%, which was maintained for 2 years. The findings demonstrated that shorter and full-thickness POEM was more effective than standard POEM. The reason may be the type II achalasia in our study, which is associated with an excellent outcome for POEM [27]. Furthermore, POEM was performed by experienced endoscopists in our study, which may be attributable to the excellent outcome of POEM.

The key point of successful POEM for achalasia was the complete incision of the LES. The mean length of the LES was 3.1 cm in this study. The myotomy length in the esophagus was set at 4 cm to ensure that the LES incision was completely performed. Furthermore, the length of the LES was measured using HRM. The maximum length of the LES was 3.8 cm in our study; thus, a 4 cm myotomy length in the esophagus was sufficient to dissect the LES completely. Recently, a study reported that a shorter POEM (the length of esophageal myotomy was ~3–4 cm) for type II achalasia showed excellent outcomes during the follow-up period [22]. Shorter POEM can avoid unnecessary esophageal muscle excision and may reduce the risk of procedure-related adverse events. Furthermore, shorter myotomy is a better option for complex achalasia, for example, in cases involving a sigmoid-type esophagus. Most endoscopists perform selective dissection of the circular muscle layer alone under the guidance of a standard POEM. However, some medical centers dissect both the circular and longitudinal muscle layers. In the POEM procedure, it is difficult to ensure the dissection of the circular muscle only. Previously, endoscopists required excessive time to protect the fragile longitudinal muscle layer if only the circular muscles were dissected during the POEM procedures. In the current study, the median procedure time was 38 min, which was less than that of a standard and shorter POEM [20, 28]. This may be because our technique involved both a shorter and full-thickness POEM, which could reduce the procedure time [20, 21].

Concerning procedure-related adverse events, only one patient (3.2%) experienced mucosal injury in our study. According to recent reports, procedure-related adverse event rates vary between 3.2% and 13.8%, which is consistent with our results [16, 21, 29]. There is a consensus that GERD is a common complication after POEM. According to recent reports, the incidence of GERD after POEM ranges from 16.8% to 57.8% [16, 30–32]. A shorter POEM may decrease the risk of subsequent GERD because the antireflux barrier in the esophagus is well preserved. A randomized controlled trial that compared standard and shorter POEM treatment for type II achalasia reported abnormal esophageal acid exposure rates in the shorter myotomy group, which were significantly lower than those in the standard group (23.9% vs. 43.8%) [22]. The incidences of GERD symptoms and reflux esophagitis were 15.2% and 8.7% in this study, respectively. Our study reported an incidence of abnormal esophageal acid exposure (19.4%), GERD symptoms (12.9%), and reflux esophagitis (6.5%), which was similar to the corresponding results from a previous study [22]. The findings demonstrated that shorter and full-thickness POEM may reduce the incidence of acid reflux-related adverse events. Full-thickness myotomy may increase the incidence of acid reflux-related adverse events after POEM. Interestingly, the incidence of acid reflux-related adverse events was not different between full-thickness myotomy and circular muscle myotomy in some reports [20, 23, 33]. Our results suggest that shorter and full-thickness myotomy did not increase the postoperative incidence of acid reflux-related adverse events. Thus, there is no need to deliberately protect the longitudinal muscles. The findings of our study demonstrated that shorter and full-thickness myotomy could decrease the

procedure time and was potentially more effective than standard POEM.

There are some limitations to our study. First, this study had a small sample size; it was a retrospective and nonrandomized study, although patients from two centers were enrolled. Moreover, only type II achalasia patients were enrolled in our study, suggesting that our results may not be suitable for other types of achalasia. Hence, future research should involve a large-scale prospective randomized controlled study design, which can confirm our findings effectively.

5. Conclusions

In summary, a shorter and full-thickness POEM is safe and feasible for the treatment of patients with type II achalasia. Our findings suggest that this shorter and full-thickness POEM can improve the quality of life of such patients.

Data Availability

The datasets used or analyzed during the current study are available from the corresponding authors on reasonable request.

Conflicts of Interest

All authors have no conflict of interest.

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Research Article

A New Preparation Method for Peroral Endoscopic Myotomy in Patients with Achalasia Can Effectively Reduce the Esophageal Residual Contents: A Comparative Retrospective Study

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Background and Aim. After routine fasting for patients with achalasia before POEM (peroral endoscopic myotomy) procedure, solid contents may still remain in the esophagus. We aimed to compare the efficacy and patient satisfaction in patients with and without drinking large amounts of carbonated beverages preoperatively. *Methods*. This retrospective study enrolled 65 achalasia patients who underwent POEM from June 2017 to October 2021. Based on the preoperative diet strategies, patients were divided into carbonated beverage group ($n = 48$) and control group ($n = 17$). Demographic and clinical data, duration of preoperative endoscopy, quality of esophagus cleansing, and patient satisfaction on preoperative procedure were collected and compared. In the current study, we established the quality of esophagus cleansing: Grade A, no remnants or only liquid or frothy discharge; Grade B, a little amount of solid content remained; and Grade C, a large amount of solid content remained. *Results*. There were 41 Grade A, 6 Grade B, and 1 Grade C patients in the carbonated beverage group, while there were 8 Grade A, 6 Grade B, and 3 Grade C patients in the control group (p value = 0.001). The esophagus cleansing degrees were significantly ameliorated after drinking carbonated beverages in all the three subtypes of achalasia according to the degree of dilatation. The mean duration of preoperative endoscopy was 6.54 ± 2.250 minutes in the carbonated beverage group and 10.27 ± 4.788 minutes in the control group (p value = 0.010). The score of patient satisfaction concerning the procedure before the POEM in the carbonated beverage group was 4.5 ± 0.652, while the score in the control group was 4.35 ± 0.702 (p value = 0.436). In the multivariate analysis, patient satisfaction was significantly associated with male (odds ratio 0.296, 95% CI: 0.097-0.905, p value = 0.033). *Conclusions*. Drinking carbonated beverages reduce the duration of preoperative endoscopy and ameliorate the esophagus cleansing degrees without impairing patient satisfaction.

1. Introduction

Achalasia is an esophageal motor disorder characterized by a failure of the relaxation of the lower esophageal sphincter (LES) and disturbed esophageal peristalsis, with an estimated prevalence of 0.5–1.0 per 100 000 population per year [1, 2]. The clinical symptoms include dysphagia, regurgitation, chest pain, weight loss, and even pulmonary complications [2].

Current treatment options include peroral endoscopic myotomy (POEM), endoscopic pneumatic dilation, endoscopic botulinum toxin injection, and surgical laparoscopic Heller's myotomy (LHM) [3]. The current treatments are usually effective in alleviating symptoms, with different advantages and drawbacks [4, 5]. These treatments are aimed at eliminating the barrier to the passage of food through reducing the LES pressure and improving the relaxation of LES [6]. POEM, initially described in pig model in 2007 [7], is an endoscopic (scarless) method of myotomy that was first reported in clinical trial in 2010 [8]. POEM enables endoscopists to carry out a myotomy of esophageal circular muscle fibers around the GEJ and into the stomach

by a submucosal tunnel. On the basis of multitude clinical trials, POEM has been proved to be effective and safe [6, 9–13], supporting the consideration of it as an initial treatment option for patients with achalasia [14, 15].

After routine fasting for upper endoscopy in achalasia patients, large amounts of retained food frequently remain in the esophagus. Evacuation of the retained contents before anesthesia induction is indispensable in order to prevent regurgitation from flowing into the trachea, even the contamination of the esophageal remnants from flowing into the mediastinum or thoracic or abdominal cavity [16]. To ensure the safety of POEM, preoperative endoscopy with a large channel should be performed to ensure the clearance of the esophageal contents [17]. However, the preoperative endoscopy without anesthesia is always time-consuming and painful, especially for the patients with solid food remained in esophagus. Thus, we aimed to develop an effective and less painful preparation method. We found that drinking large amounts of carbonated beverages in a short time leads to the emesis of the remained esophageal contents due to the high carbon dioxide pressure accumulated in the bottom of the esophagus. Therefore, the major purpose of this study was to compare the efficacy and patients' satisfaction of this newly developed method and previous preparation method in a retrospective design.

2. Methods

2.1. Study Design. This was a retrospective research conducted in Shanghai East Hospital, a tertiary referral center in China between June 2017 and October 2021. The diagnosis of achalasia is based on Eckardt score, esophagogastroduodenoscopy (EGD), barium esophagography, and high-resolution manometry (HRM). Demographic and clinical data were collected, including patient's age, gender, body mass index (BMI), symptom duration, previous POEM, Eckardt score, Chicago classification (according to high-resolution manometry), degree of esophageal dilatation, and duration of preoperative endoscopy.

A total of 65 achalasia patients who underwent POEM were retrospectively enrolled and were divided into 2 groups according to different preparation methods before POEM. All these patients took proton pump inhibitor (PPI) during around 10 days before POEM. 17 patients took only clear liquid diet (around 3000 ml without carbonated beverage) within 48 hours before the POEM, water (around 2500 ml) within 24 hours before it and fasting within 6 hours before it [18], which was regarded as the control group. 48 patients were required to take only carbonated beverage within 48 hours before the POEM and to fasting within 6 hours before it as well, which was regarded as the carbonated beverage group. These patients were requested to prepare 3 liters of carbonated beverage per day and drink 1 liter at a time in a short period of time to cause emesis to evacuate residual contents.

All the enrolled patients completed a questionnaire concerning the score of satisfactory and tolerance about the preparation before POEM (excellent = 5; very good = 4; good = 3; fair = 2; poor = 1).

Written informed consent was obtained from all patients before enrollment. The study protocol was approved by the institutional ethics committee of Shanghai East Hospital and was performed in accordance with the Declaration of Helsinki.

2.2. Definitions. In the Chicago classification system, achalasia consists of three distinct subtypes (types I, II, and III) according to the pattern of esophageal contractility shown by HRM [19]. Dilatation of esophagus is divided into three grades: grade I (diameter of esophageal lumen < 4 cm), grade II (diameter: 4-6 cm), and grade III (diameter > 6 cm or sigmoid type) [20].

In this study, we defined the quality of esophagus cleansing as Grade A (only liquid or frothy discharge or no remnants), Grade B (a little amount of solid food remained), and Grade C (a large amount of solid food remained), as shown in Figure 1.

2.3. Outcomes. The primary outcome was quality of esophagus cleansing. Different subtypes of the two groups were also compared. The second outcome included duration of preoperative endoscopy and patient satisfaction.

2.4. Statistical Analysis. Continuous variables were presented as mean ± standard deviation (SD), and their statistical differences were conducted by Student's t-test. Categorical variables were presented as percentages and 95% confidence intervals (CIs), and their statistical differences were analyzed with Chi-square test or rank sum test. Predictors of patient satisfaction were assessed by logistic regression analysis. The results were considered statistically significant at a two-sided p value of < 0.05. Data were analyzed using commercially available statistical software packages SPSS version 18.0 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Patient Characteristics. A total of 65 consecutive patients were included in this retrospective study. Of these patients, there were 48 patients in the carbonated beverage group and 17 patients in the control group. There were no significant differences between the two groups in terms of age, gender, body mass index (BMI), symptom duration, and previous history of POEM (Table 1). Three patients in the carbonated beverage group and 2 patients in the control group experienced endoscopic pneumatic dilation previously. None of the patients experienced endoscopic botulinum toxin injection previously. All the patients in the carbonated beverage group had vomiting symptoms before POEM, while none of the patients in the control group vomited.

3.2. Primary Outcome. There were 41 Grade A, 6 Grade B, and 1 Grade C in the carbonated beverage group, while there were 8 Grade A, 6 Grade B, and 3 Grade C in the control group (p value = 0.001) (Table 2). The esophagus cleansing degrees were significantly improved after taking carbonated beverages to cause emesis. In any of the subtypes of achalasia according to the degree of dilatation, the esophagus

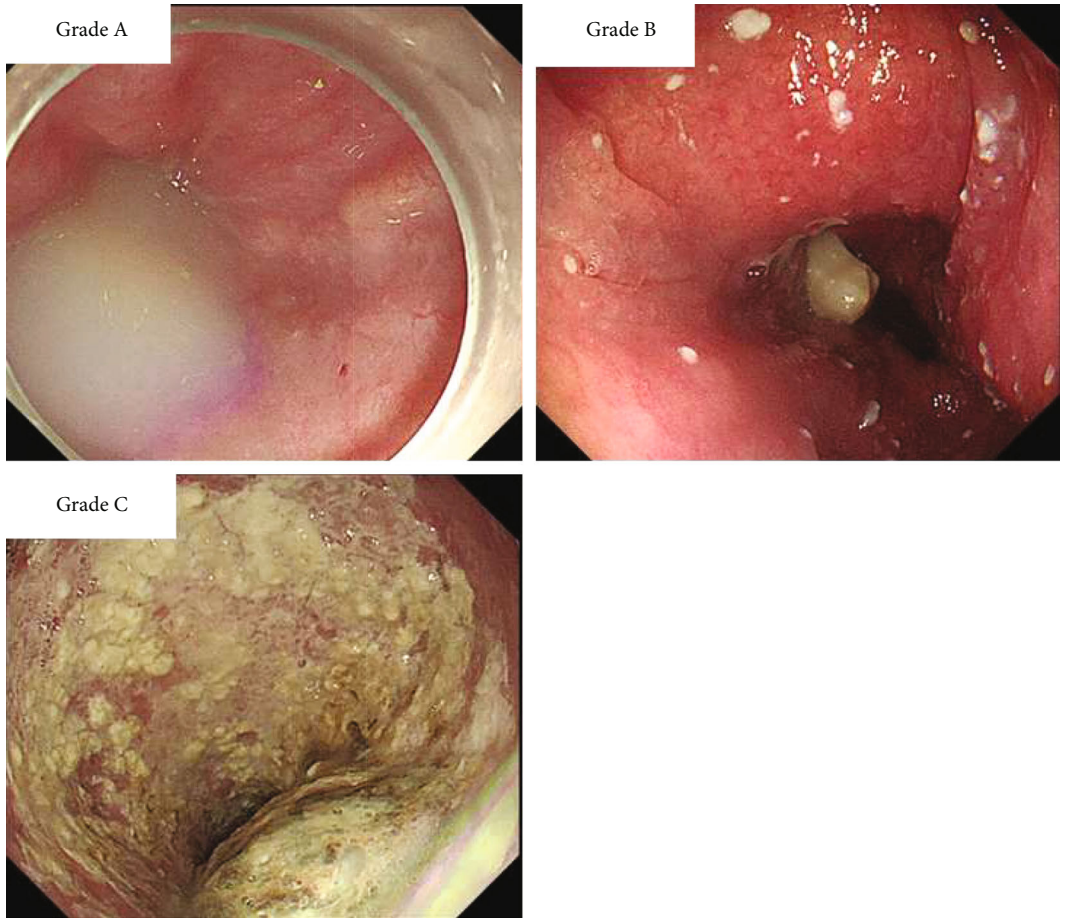

Figure 1: Quality of esophagus cleansing. In the current study, the quality of esophagus cleansing was defined as follows: Grade A (only liquid or frothy discharge or no remnants), Grade B (a little amount of solid food remained), and Grade C (a large amount of solid food remained).

Table 1: Baseline patient characteristics of the carbonated beverage group and the control group.

	Carbonated beverage group ($n = 48$)	Control group ($n = 17$)	p value
Age (years)	49.8 ± 17.9	53.5 ± 10.4	0.300
Sex, male	25 (52.1%)	9 (52.9%)	0.951
BMI	19.8 ± 3.1	20.6 ± 3.6	0.214
Symptoms duration (years)	5.8 ± 2.6	6.4 ± 3.1	0.759
Previous POEM	5 (10.4%)	3 (17.6%)	0.436
Eckardt score	8.5 ± 1.8	7.9 ± 1.8	0.238
Sigmoid type	4 (8.3%)	2 (11.8%)	0.648

BMI: body mass index; POEM: peroral endoscopic myotomy.

cleansing degrees were more significantly ameliorated in the carbonated beverage group than the control group (Table 2). In type I and type II of achalasia according to the Chicago classification, the esophagus cleansing degrees in the carbonated beverage group were also significantly ameliorated (Supplementary Table 1). However, in type III of Chicago classification, there were no significant differences between the two groups (p value = 0.48) (Supplementary Table 1).

3.3. Secondary Outcome. The duration of preoperative endoscopy was significantly reduced in the carbonated beverage group, compared with the control group (6.54 ± 2.250 vs. 10.27 ± 4.788, p value = 0.01). There were no significant differences in the patient satisfaction concerning the procedure before the POEM between the carbonated beverage group and the control group (4.5 ± 0.652 vs. 4.35 ± 0.702, p value = 0.436). However, female patients showed lower satisfactory score than male ones by monofactor analysis (4.26 ± 0.682 vs. 4.65 ± 0.102, p value = 0.017).

In a multivariate analysis, patient satisfaction was significantly associated with male (odds ratio 0.296, 95% CI: 0.097-0.905, p value = 0.033), but not with age (p value = 0.461), previous history of POEM (p value = 0.157), sigmoid type (p value = 0.339), or carbonated beverage group (p value = 0.405) (Table 3).

3.4. Other Findings. In total, there were 27 Grade A, 6 Grade B, and 4 Grade C in type I patients; 17 Grade A, 5 Grade B, and 0 Grade C in type II patients; and 5 Grade A, 1 Grade B, and 0 Grade C in type III patients. There were no significant

Table 2: Comparison of the quality of esophagus cleansing between carbonated beverage group and control group in the subtypes according to degree of dilatation.

Degree of dilatation	Carbonated beverage group Quality of esophagus cleansing				Control group Quality of esophagus cleansing				p value
	Grade A	Grade B	Grade C	Total	Grade A	Grade B	Grade C	Total	
Grade I	23	1	0	24	5	3	0	8	0.015
Grade II	16	2	1	19	3	3	1	7	0.044
Grade III	2	3	0	5	0	0	2	2	0.04
Total	41	6	1	48	8	6	3	17	0.001

Table 3: Multivariate analysis of the factors associated with patient satisfaction concerning the preparation before the procedure.

	Odds ratio (95% confidence interval)	p value
Male vs. female	0.296 (0.097-0.905)	0.033
Age	1.013 (0.979-1.048)	0.461
Re-POEM	0.272 (0.045-1.651)	0.157
Sigmoid type vs. others	3.287 (0.286-37.773)	0.339
Carbonated beverage group vs. control group	0.591 (0.171-2.039)	0.405

POEM: peroral endoscopic myotomy.

differences among type I and type II and type III (type I vs. type II, p value = 0.571; type II vs. type III, p value = 0.753; type I vs. type III, p value = 0.535) in quality of esophagus cleansing.

Totally, there were 28 Grade A, 4 Grade B, and 0 Grade C in grade I patients; 19 Grade A, 5 Grade B, and 2 Grade C in grade II patients; and 2 Grade A, 3 Grade B, and 2 Grade C in grade III patients. The quality of esophagus cleansing of grade I patients was better than that of grade III patients (p value = 0.0001). The quality of esophagus cleansing of grade II patients was also better than that of grade III patients (p value = 0.028). There were no significant differences among grade I and grade II patients (p value = 0.142) in quality of esophagus cleansing.

After drinking large amount of carbonated beverages in a short time, none of the patients had upper digestive hemorrhage due to massive vomiting. The incidence of cardiac mucosal laceration syndrome was 0 under the preoperative endoscopy.

4. Discussion

In this retrospective study, we compared the preoperative preparation of POEM in achalasia patients with and without drinking large amounts of carbonated beverages in terms of quality of esophagus cleansing, duration of preoperative endoscopy, and patient satisfaction. Our study demonstrates that the quality of esophagus cleansing was better in the carbonated beverage group than the control group. The duration of preoperative endoscopy was significantly shortened in the carbonated beverage group compared with the control group. However, there were no significant differences in patient satisfaction between the two groups.

Unlike in the field of surgery, there have been few studies concerning diet strategies in the field of therapeutic endoscopy. What is more, most strategies are solely based on clinical experience rather than concrete evidence. To the best of our knowledge, this is the first study concerning the preoperative diet preparation of patients with achalasia, and this is also the first study to evacuate esophageal residues by high pressure caused by carbonated beverages. We believe that our results contribute to the guideline revision and determination of the preparation protocol strategy for patients with achalasia.

Massive vomiting may cause cardiac mucosal laceration and hemorrhage. However, the incidence of these complications was 0, as shown in the current study. Therefore, this new preparation method was safe and of high tolerance, which has a great potential to be popularized.

Furthermore, as we all know, it is hard to evacuate the solid retained contents in patients with achalasia even using a large-channel endoscopy. Especially in patients with Grade C of esophagus cleansing quality, it is almost impossible to evacuate all the retained contents. Consequently, the POEM procedure had to be postponed due to the high risk during anesthesia induction, and additional couples of days of fasting are obligated. In the current study, the POEM procedure of 1 patient in the carbonated beverage group and 3 patients in the control group had to be rescheduled because of insufficient evacuation of esophageal residues. A prospective study demonstrated that an early postendoscopic submucosal dissection (ESD) diet protocol resulted in lower healthcare costs, more comfortable nourishment, shorter hospitalization, and higher patient satisfaction, compared with the conventional fasting protocol [21]. Therefore, it is inferred that rescheduling POEM due to poor quality of esophagus cleansing resulting in longer fasting and hospitalization time tends to be associated with lower patient satisfaction. Carbonated beverages which help improving the quality of esophagus cleansing can potentially ameliorate patient satisfaction. It was not shown statistically in the current study owning to the limited cases of Grade C patients.

There was no statistical significance in patient satisfaction between the 2 groups probably owning to the limited cases of Grade C patients.

A paradigm change is happening in healthcare. Value-based healthcare is embraced, and patient-centered outcomes are also a growing concern [22]. In the current study, concerning the preparation before POEM, the female patients showed less satisfactory than the male ones. Consistent with previous studies on other digestive diseases, a lower level of satisfaction among female patients was also noted [23]. However, there were no significant differences in patient satisfaction between the carbonated beverage group and the control group. That is to say, vomiting caused by large amounts of carbonated beverages which seemed to bring more pains did not inevitably result in lower patient satisfaction. Furthermore, the duration of preoperative endoscopy decreased significantly in the carbonated beverage group, which may potentially reverse the patient-centered outcomes in pains caused by the vomit.

There were also several limitations in the present study. First, this was a single-center study with a small sample size. Second, this was a retrospective study. Third, a few patients could not tolerate 3 liters of carbonated beverage. The amounts of carbonated beverage taken by each patient were a little bit different. Even with these limitations, this was the first evidence to support the adoption of carbonated beverages as preoperative diet protocol for patient with achalasia. The long-term food stasis and intraesophageal pressure may lead to chronic inflammation of the esophageal mucosa [24]. Additionally, the advantages of preoperative preparation of carbonated beverages in achalasia patients underwent POEM can be easily extended to LHM and other therapeutic endoscopy. Another prospective research with a larger and multicenter study scale should be conducted to further confirm our conclusion. This method might be widely used in clinical practice and adopted in future guideline.

In conclusion, carbonated beverages would help to greatly improve the esophagus cleansing degrees in all subtypes of patients with achalasia according to the degree of dilatation and reduce the duration of preoperative endoscopy. No significant differences were found concerning the patient satisfaction between the carbonated beverage group and the control group.

Data Availability

Data are available on request.

Conflicts of Interest

The authors report no conflicts of interest.

Authors' Contributions

Zehua Zhang, Xiaohan Yan, and Bensong Duan contributed equally to this work. The authors alone are responsible for the content and writing of this article. Zehua Zhang, Xiaohan Yan and Bensong Duan are co-first authors

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Supplementary Materials

Supplementary Table 1: comparison of the quality of esophagus cleansing between carbonated beverage group and control group in the subtypes according to Chicago classification. *(Supplementary Materials)*

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