World Journal of Gastrointestinal Endoscopy

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World J Gastrointest Endosc 2024 October 16; 16(10): 566-580

DOI: 10.4253/wjge.v16.i10.566

ISSN 1948-5190 (online)

META-ANALYSIS

Safety and efficacy of peroral endoscopic myotomy for treating achalasia in pediatric and geriatric patients: A meta-analysis

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade D, Grade D, Grade D

Novelty: Grade B, Grade C, Grade D, Grade D

Creativity or Innovation: Grade B, Grade C, Grade D, Grade D

Scientific Significance: Grade A, Grade C, Grade C, Grade D

P-Reviewer: Jankovic J; Tawheed A; Wang Y

Received: May 24, 2024

Revised: August 17, 2024

Accepted: September 14, 2024

Published online: October 16, 2024

Processing time: 144 Days and 1.9 Hours

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Abstract

BACKGROUND

As a less invasive technique, peroral endoscopic myotomy (POEM) has recently been widely accepted for treating achalasia with an excellent safety profile, durability, and efficacy in adults. In pediatric and geriatric patients, the treatment is more difficult.

AIM

To discuss the clinical outcomes of POEM in pediatric and geriatric patients with achalasia.

METHODS

We conducted a comprehensive search of PubMed, Embase and Cochrane Library databases from inception to July 2024. The primary outcomes were technical and clinical success. Secondary outcomes of interest included adverse events and gastroesophageal reflux disease (GERD). The pooled event rates were calculated by comprehensive meta-analysis software.

RESULTS

A total of 32 studies with 547 pediatric patients and 810 geriatric patients were included in this study. The pooled event rates of technical success, clinical success, GERD and adverse events of POEM for treating achalasia in pediatric patients were 97.1% [95% confidence interval (CI): 95.0%-98.3%; I^2 = 0%; P < 0.000], 93.2% (95%CI: 90.5%-95.2%; I^2 = 0%; P < 0.000), 22.3% (95%CI: 18.4%-26.7%; I^2 = 43.874%; P < 0.000) and 20.4% (95%CI: 16.6%-24.8%; I^2 = 67.217%; P < 0.000), respectively. Furthermore, in geriatric patients, the pooled event rates were 97.7% (95%CI: 95.8%-98.7%; I^2 = 15.200%; P < 0.000), 93.2% (95%CI: 90.3%-95.2%; I^2 = 0%; P < 0.000), 23.9% (95%CI: 19.4%-29.1%; I^2 = 75.697%; P < 0.000) and 10.8% (95%CI: 8.3%-14.0%; I^2 = 62.938%; P < 0.000], respectively.

CONCLUSION

Our findings demonstrated that POEM was an effective and safe technique for pediatric and geriatric patients with achalasia.

Key Words: Achalasia; Peroral endoscopic myotomy; Pediatric; Geriatric; Meta-analysis

Core Tip: Peroral endoscopic myotomy (POEM), a minimally invasive procedure, has gained substantial acceptance as a treatment for achalasia due to its excellent safety profile, durability, and efficacy in adults. We conducted this systematic review and meta-analysis to summarize the durability, safety, and efficacy of POEM for treating achalasia in pediatric and geriatric patients. Our results indicated that POEM was an effective and safe technique for pediatric and geriatric patients with achalasia.

Citation: Pu XX, Huang S, Zhong CY, Wang X, Fu SF, Lv YQ, Zou K, Lü MH, Peng Y, Tang XW. Safety and efficacy of peroral endoscopic myotomy for treating achalasia in pediatric and geriatric patients: A meta-analysis. *World J Gastrointest Endosc* 2024; 16(10): 566-580

URL: https://www.wjgnet.com/1948-5190/full/v16/i10/566.htm

DOI: https://dx.doi.org/10.4253/wjge.v16.i10.566

INTRODUCTION

Achalasia is a moderately uncommon esophageal smooth muscle motility disorder characterized by the absence or spastic contractions of the esophageal body and the loss of deglutition-induced relaxation of the lower esophageal sphincter (LES)[1]. Typically, dysphagia is experienced by the patient. Regurgitation of undigested food, heartburn, respiratory symptoms, chest pain, and weight loss are other clinical symptoms of achalasia[2]. The estimated annual incidence rate of achalasia is between 0.03 and 1.63 *per* 100000 people, and the annual prevalence of achalasia is reported to range from 1.8 to 12.6 *per* 100000 people[3]. Achalasia can occur at all ages and equally in men and women, with no racial predilection [3], but it is an exceedingly rare illness in the pediatric population, with an estimated prevalence between 0.02 and 0.31 *per* 100000 children, approximately 10 times lower than that in adults[4-6]. The prevalence increases with age, with a peak in the seventh decade of life[7].

Botulinum toxin injection, laparoscopic Heller myotomy (LHM) and pneumatic dilation (PD) are available therapeutic approaches for achalasia[8-11]. In the past decade, a novel technique called peroral endoscopic myotomy (POEM) was created to combine an endoscopic approach with the principles of natural orifice transluminal endoscopic surgery to perform myotomy for achalasia. The American College of Gastroenterology clinical guidelines indicate that POEM and LHM result in comparable symptomatic improvements in patients with achalasia[3]. A systematic review and meta-analysis compared the results between 1958 patients after POEM and 5834 patients after LHM, and reported that the predicted probability of improvement in dysphagia was 93.5% for POEM and 91.0% for LHM at 12 months, and 92.7% for POEM and 90.0% for LHM at 24 months[12].

Briefly, the POEM procedure requires submucosal injection with indigo carmine dye, mucosal incision, submucosal dissection, myotomy and closure of the mucosal incision[3]. The POEM procedure in special populations is similar to that in general patients, with only minor modifications. However, the length of the pediatric esophagus is short, and the esophageal wall in children is relatively thin, which undoubtedly increases the difficulty of the operation[13]. In addition, geriatric patients tend to have more comorbidities, and thus have a higher risk during surgery and anesthesia[14,15].

Therefore, we aimed to conduct this systematic review and meta-analysis to summarize the durability, safety and efficacy of POEM in pediatric and geriatric patients with achalasia.

MATERIALS AND METHODS

This systematic review and meta-analysis strictly conformed to the preferred reporting items for systematic reviews and meta-analyses statement[16]. Our study did not require ethical approval or written consent.

Search strategy

A systematic literature search was conducted *via* the PubMed, Embase and Cochrane Library databases from inception to July 2024, with studies limited to those written in the English language. The key words included "peroral endoscopic myotomy", "per-oral endoscopic myotomy", "POEM", "achalasia" and all possible combinations (Supplementary Table 1). To ensure a thorough search of the literature, the words "pediatric" and "geriatric" were not used. In addition to searching the literature using keywords, the inclusion of articles following a meticulous review of references was pursued to identify those that satisfied the specified criteria for inclusion.

Study selection

Two authors screened the titles and abstracts of all articles separately, in accordance with the exclusion and inclusion criteria. Next, the full texts of relevant articles were reviewed after screening. Any disagreements between reviewers in the search process were resolved by discussion with a third reviewer. The inclusion criteria were as follows: (1) Population: Patients diagnosed with achalasia and aged ≤ 18 years (pediatric) or ≥ 60 years (geriatric); (2) Treatment: POEM; and (3) Outcomes: Technical and clinical success, adverse events and gastroesophageal reflux disease (GERD). Exclusion criteria were as follows: (1) Case reports with < 5 patients, reviews, and animal experiments; (2) Studies that did not provide enough data; and (3) Studies not published in the English language.

Data extraction and definition

Data regarding the characteristics of the selected studies (first author, year of publication, country, study type, study interval, number of patients, gender and age), pre- and postoperative data of the patients (duration of symptoms, myotomy length, operation time, length of hospital stay and follow-up time), and clinical outcomes (technical success and clinical success rates, adverse events and GERD rates) were independently extracted by two authors using a prepared standardized form. The definition of technical success was completion of the entire POEM procedure. Clinical success was regarded as an Eckardt score ≤ 3 during the follow-up period after POEM. The severity of adverse events was graded on the basis of the American Society for Gastrointestinal Endoscopy (ASGE) lexicon[17]. GERD included symptomatic reflux and reflux esophagitis.

Quality assessment of the studies

Two reviewers independently conducted a quality assessment using the National Institutes of Health (NIH) quality assessment tool, which is applicable for pre-post studies with no control group[18].

Statistical analysis

Statistical analysis was performed using comprehensive meta-analysis software version 3.0 (Biostat, Englewood, NJ, United States). The outcomes are presented as pooled event rates and 95% confidence interval (CI), and the significance degree P was set at < 0.05. Heterogeneity among the studies was assessed using the I^2 statistic. Significant heterogeneity was considered, if the I^2 value was ≥ 50%, and a random-effect model was used. A funnel plot was used to evaluate publication bias.

RESULTS

Eligible studies

A total of 4620 articles was identified in the initial search, and 3206 studies remained after the removal of duplicates. On the basis of the inclusion and exclusion criteria, 41 articles were eligible after the titles and abstracts were reviewed. Nine studies were excluded as the cohorts included fewer than five patients or due to overlapping publications. Ultimately, 32 articles were included in this review (pediatric patients, n = 20[19-38]; geriatric patients, n = 12[13,39-49]) (Figure 1).

According to the NIH quality assessment tool, 13 studies were of good quality, eight studies showed fair quality, and one study exhibited poor quality (Supplementary Table 2 and Supplementary Table 3). The reasons why the study was rated as poor quality were as follows: The eligibility criteria and study population were not clearly described; Only five pediatric patients who underwent POEM were enrolled in this study; The definition of outcomes was not clearly described; Blinding or masking means were used for the outcome evaluations; P values were not reported. Due to the lack of information in articles published in conference abstracts, no quality assessment was conducted.

Role of POEM for achalasia in pediatric patients

Baseline characteristics: Table 1 shows the baseline characteristics of the original studies of POEM for treating achalasia in pediatric patients[19-38]. Twenty articles involving 547 pediatric patients investigated the efficacy and safety of POEM, including 5 prospective studies and 15 retrospective studies. Among these articles, seven studies were conducted in China, four in the United States, two in Japan, two in Italy, two in India, one in France, one in Israel and one in Chile. These studies were performed between 2007 and 2021. The age of the patients in these studies ranged from 0.9 to 18 years,

Table 1 Baseline characteristics of the studies on peroral endoscopic myotomy for achalasia in pediatric patients

Ref.	Country	Study type	Study interval	Patients (*n*)	Gender (M:F)	Age (yr)	Duration of symptoms (month)	Myotomy length (cm)	Operation time (min)	Hospital stay (day)	Follow-up (month)	Method of GERD diagnosis
Li *et al*[19], 2015	China	Prospective	October 2011 to March 2014	9	4:5	14.1 (10-17)	26.4 (6-60)	8.3	56.7	-	16.3 (3-30)	Esophageal manometry, barium esophagram and EGD
Chen *et al*[20], 2015	China	Prospective	August 2010 to July 2012	27	11:16	13.8 (6-17)	20.4 (6-36)	9.6 (7-11)	39.4 (21-90)	3.2 (1-7)	24.6 (15-38)	EGD
Caldaro *et al*[21], 2015	Italy	Retrospective	2009 to 2014	9	3:6	12.2 ± 3.8	-	11 ± 2	62 ± 12.7	4.1 (2-7)	12.7 (5-28)	pH-monitoring and EGD
Tang *et al*[22], 2015	China	Retrospective	July 2012 to August 2014	5	3:2	15	12 (3-15)	8 (6-11)	50 (40-90)	7 (5-13)	18 (12-23)	EGD, mano-metry
Tan *et al*[23], 2016	China	Retrospective	January 2007 to June 2015	12	6:6	13.7 ± 2.6	23.6 ± 16.8	-	-	-	36	EGD, esophageal manometry
Stavropoulos *et al*[24], 2017	United States	Retrospective[1]	2013 to 2016	10	7:3	14.7 (10-17)	21 (3-84)	11.4 ± 5.98	55 (33-111)	1.2 (1-2)	15 (1-30)	-
Zangen *et al*[25], 2017	Israel	Retrospective[1]	-	5	2:3	15.4 (10- 18)	-	11.2 (10-14)	62 (43-73)	-	6	HRM
Kethman *et al*[26], 2018	United States	Prospective	2014 to 2016	10	8:2	13.4 ± 3.3	-	7 (4-9)	142 (60-259)	-	-	-
Miao *et al*[27], 2018	China	Prospective	October 2014 to October 2016	21	9:12	5.5 (0.9-18)	18 (3.6-30)	9 (6-11)	40 (30-55)	9 (7-12)	13.2 (3-24)	99mTc DTPA scintigraphic examinations, gastroscopy and esophageal manometry
Korrapati *et al*[28], 2018	India	Retrospective[1]	-	15	10:5	15 (3-18)	21.9 (6-54)	8 (6-11)	85.3 ± 31	4.4 ± 2.5	19.8 (1.5-51)	EGD
Nishimoto *et al*[29], 2018	Japan	Retrospective[1]	May 2015 to November 2017	13	-	15 (10-18)	-	-	-	-	18.3 (0-30)	-
Mangiola *et al*[30], 2018	Italy	Retrospective[1]	January 2012 to June 2017	26	12:14	10.9 (2-17)	18.2 ± 14.9	10 ± 2.6	56.2 ± 12.6	3.7 ± 1.7	30.2 ± 15.4	Manometry, 24 h pH-monitoring, and EGD
Yamashita *et al*[31], 2018	Japan	Retrospective[1]	September 2011 to June 2017	7	-	15.0 (9-18)	30.7 (1-84)	14 (7-24)	-	-	39.6 (18-54)	-
Choné *et al*[32], 2019	France	Retrospective	January 2012 to August 2018	117	69:48	14.2 (3.7)	21.3 (21.2)	8.3 (3-21)	72.5 (16-240)	3.9 (1-14)	18 (3.3-53.7)	-
Nabi *et al*[33], 2019	India	Retrospective	September 2013 to Jan 2018	44	22:21	14.58 ± 3.41	24 (2-96)	10.09 (5-15)	65.46 (18-240)	3 (2-4)	18 (1-53.1)	Symptoms, EGD and 24-h pH-impedance
Liu *et al*[34], 2019	China	Retrospective	August 2010 to	130	82:48	-	12 (0-13)	7.2 ± 1.4	30 (15-255)	3 (1-21)	40 (4-88)	Barium swallow, EGD and HRM

			August 2017									
Saez *et al*[35], 2020	Chile	Retrospective	March 2017 to November 2019	5	4:1	11 (5-15)	-	9.8 (9-11)	70 (50-120)	2 (1-3)	20.5 (4 -37)	EGD and HRM
Wood *et al*[36], 2020	United States	Prospective	2014 to 2019.	21	14:7	13 (2-17)	-	7 ± 1.1	92 ± 52	1 ± 0.5	12	-
Peng *et al*[37], 2022	China	Retrospective	October 2011 to November 2016	24	14:10	14.42 ± 2.65	14.5 (3-84)	9 (5-10)	58.67 ± 19.10	6.42 ± 2.15	85.75 ± 25.91	Gerd Q score and EGD
Petrosyan *et al* [38], 2022	United States	Retrospective	July 2015 to September 2021	37	23:14	11.6 ± 4.5	-	6.5 ± 0.93	138.1 ± 62.2	2.4 ± 0.9	22.6 ± 20	-

[1]Published conference abstracts.

M: Male; F: Female; POEM: Peroral endoscopic myotomy; pH: Potential of hydrogen; EGD: Esophagogastroduodenoscopy; HRM: High resolution esophageal manometry; 99mTc DTPA: Diethylenetriaminepentaacetic acid.

and 55.4% of the patients were male. The duration of symptoms ranged from 12 to 26.4 months. The mean myotomy length and operation time was mentioned in 18 and 17 studies, which ranged from 6.5 to 14 cm and 30 to 142 minutes, respectively. Furthermore, the length of hospital stay and follow-up time ranged from 1 to 9 days and from 6 to 85.75 months, respectively.

Clinical outcomes: In total, 20 studies (Table 2) reported the technical success and clinical success rates of POEM for achalasia in pediatric patients; The pooled rates were 97.1% (95%CI: 95.0%-98.3%; I^2 = 0%; P < 0.000) and 93.2% (95%CI: 90.5%-95.2%, I^2 = 0%; P < 0.000], respectively (Figure 2A and B). On the other hand, the pooled rates of GERD and adverse events were 22.3% (95%CI: 18.4%-26.7%; I^2 = 43.874%; P < 0.000) and 20.4% (95%CI: 16.6%-24.8%; I^2 = 67.217%; P < 0.000), respectively (Figure 2C and D). It must be noted that the definition of adverse events in each study was inconsistent, with some authors defining adverse events as those requiring intervention or major adverse events[33,34], whereas others defined gas-related complications without clinical symptoms as adverse events[19,23,27].

Role of POEM for achalasia in geriatric patients

Baseline characteristics: There were eight original studies and four conference abstracts on the efficacy and safety of POEM in geriatric patients, and the results are shown in Table 3[13,39-49]. Among these articles, four studies were conducted in Japan, three in the United States, three in China, one in Italy, and one in the Netherlands. All studies were retrospective cohort studies, and were conducted from September 2008 to May 2021. A total of 810 geriatric patients aged 67.9 to 84 years (aged ≥ 80 years in one study) were included in this study, and 50% of the patients were male. The duration of symptoms, reported in nine studies, ranged from 4.4 to 30 years. Myotomy length was mentioned in 10 studies, which ranged from 10 to 14.5 cm. In addition, the operation duration of POEM, reported in 8 studies, ranged from 46.87 to 138.3 minutes. Moreover, the duration of hospital stay and the follow-up time ranged from 1 to 9.8 years and from 2 to 41 months, respectively.

Clinical outcomes: Overall, the 12 studies (Table 4) had pooled rates of technical success, clinical success, GERD and adverse events of 97.7% (95%CI: 95.8%-98.7%; I^2 = 15.200%; P < 0.000), 93.2% (95%CI: 90.3%-95.2%; I^2 = 0%, P < 0.000), 23.9% (95%CI: 19.4%-29.1%; I^2 = 75.697%; P < 0.000), and 10.8% (95%CI: 8.3%-14.0%; I^2 = 62.938%; P < 0.000), respectively (Figure 3).

Table 2 Clinical outcomes of the studies on peroral endoscopic myotomy for achalasia in pediatric patients, *n* (%)

Ref.	Technical success	Clinical success	GERD	Adverse events
Li *et al*[19], 2015	9/9 (100)	9/9 (100)	1/9 (11.1)	2/9 (11.1)
Chen *et al*[20], 2015	26/27 (96.3)	26/26 (100)	5/26 (19.2)	9/26 (34.6) (Cumulative adverse events on CT scan: 53)
Caldaro *et al*[21], 2015	9/9 (100)	9/9 (100)	1/9 (11.1)	1/9 (11.1)
Tang *et al*[22], 2015	5/5 (100)	4/4 (100)	0 (0)	0 (0)
Tan *et al*[23], 2016	12/12 (100)	12/12 (100)	2/12 (16.7)	3/12 (8.3)
Stavropoulos *et al*[24], 2017	10/10 (100)	10/10 (100)	2/5 (40)	4/10 (40)
Zangen *et al*[25], 2017	5/5 (100)	5/5 (100)	0 (0)	0 (0)
Kethman *et al*[26], 2018	10/10 (100)	8/10 (80)	0 (0)	3/10 (30)
Miao *et al*[27], 2018	21/21 (100)	21/21 (100)	6/21 (28.6)	12/21 (57.1)
Korrapati *et al*[28], 2018	15/15 (100)	15/15 (100)	0 (0)	2/15 (13.3)
Nishimoto *et al*[29], 2018	13/13 (100)	12/13 (92.3)	-	2/13 (15.4)
Mangiola *et al*[30], 2018	25/26 (96.2)	26/26 (100)	4/17 (23.5)	6/26 (23.1)
Yamashita *et al*[31], 2018	7/7 (100)	7/7 (100)	-	0 (0)
Choné *et al*[32], 2019	116/117 (99.1)	106/117 (90.6)	17/117 (21.4)	7/117 (8.5)
Nabi *et al*[33], 2019	43/44 (97.7)	40/44 (90.9)	11/20 (55)	11/43 (25.6)
Liu *et al*[34], 2019	129/130 (99.2)	108/113 (95.6)	30/111 (27.0)	5/130 (3.8)
Saez *et al*[35], 2020	5/5 (100)	5/5 (100)	2/5 (40)	0 (0)
Wood *et al*[36], 2020	21/21 (100)	21/21 (100)	-	6/21 (28.6)
Peng *et al*[37], 2022	24/24 (100)	23/24 (95.8)	5/21 (23.8)	0 (0)
Petrosyan *et al*[38], 2022	37/37 (100)	37/37 (100)	3/37 (8.1)	9/37 (24.3)

GERD: Gastroesophageal reflux disease; CT: Computed tomography.

Publication Bias: Most of the funnel plots were relatively symmetric, suggesting that publication bias was not significant (Figure 4, Figure 5A and B). However, funnel plots regarding GERD and adverse events in geriatric patients displayed substantial asymmetry (Figure 5C and D).

DISCUSSION

Achalasia is a relatively uncommon disorder of the esophageal smooth muscle, and the annual incidence and prevalence increases with age, but it can affect all ages[1]. Due to the short length and weak wall of the esophagus in pediatric patients, and esophagus modifications contributing to a corkscrew esophagus, increased comorbidities and poor treatment tolerance in geriatric patients[43,49-52], the difficulty of surgery and the incidence of postoperative adverse events in these populations are increased.

Currently, the purpose of all treatment methods for achalasia is to reduce the hypertonicity of the LES to attain the goals of reducing symptoms, improving esophageal emptying, and avoiding further dilation of the esophagus[3]. Pharmacologic, botulinum toxin injection, PD, POEM, and LHM are currently available therapeutic approaches. Specifically, pharmacologic therapy is the least effective treatment for achalasia, resulting in a short-term reduction in LES pressure in 13%-65% of patients and symptom relief in 0%-87% of patients[8]. The effect of botulinum toxin is limited as it is not long-lasting and requires repeated therapy[9]. PD is an effective choice for patients with achalasia, and reports suggest that 50%-93% of patients might achieve symptom relief[1]. However, a recent meta-analysis demonstrated that the long-term efficacy of PD was inferior to that of POEM[10]. LHM is generally regarded as the gold standard because it can provide long-lasting symptom relief; however, for geriatric patients and patients with multiple comorbidities, it is not appropriate as it is an invasive procedure and can result in operative complications[11-13].

The minimally invasive technique POEM was first described by Inoue *et al*[15]. This technique is used for treating achalasia in adults, and is becoming increasingly available in pediatric and geriatric patients. The clinical guidelines established by the ASGE in the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) paper[3] showed that POEM for achalasia treatment is considered a viable therapeutic modality and should fulfil the following criteria: (1) ≥ 80% efficacy at 12 months after the procedure (Eckardt score ≤ 3 with a dysphagia component of ≤ 2); and (2)

Table 3 Baseline characteristics of the studies on peroral endoscopic myotomy for achalasia in geriatric patients

Ref.	Country	Study type	Study interval	Patients (*n*)	Gender (M:F)	Age (yr)	Duration of symptoms (month)	Myotomy length (cm)	Operation time (min)	Hospital stay (day)	Follow-up (month)	Method of GERD diagnosis
Wang *et al*[39], 2016	China	Retrospective	January 2010 to December 2015	21	12:9	67.9 ± 4.3	13.9 ± 11.7	-	-	-	21.8	EGD, esophageal manometry and barium esophagram
Chen *et al*[13], 2018	United States	Retrospective	January 2010 to January 2016	76	40:36	84 ± 3.2	24.0 (17.8-30.3)	10.0 ± 4.0	103.7 ± 47.9	3	8.5 (IQR: 2.2-18.2)	-
Landi *et al*[40], 2018	Italy	Retrospective[1]	May 2011 to April 2017	88	39:49	72.2 ± 4.7	-	12.3 ± 3	-	-	24	-
Liu *et al*[41], 2019	China	Retrospective	August 2010 to December 2017	139	65:74	70.22 ± 5.68	8 (IQR: 2-20)	10.57 ± 1.81	50 (IQR: 36-76)	3 (IQR: 2-4)	41 (IQR: 26-60)	Barium swallow, EGD and HRM
Klair *et al*[42], 2019	United States	Retrospective[1]	December 2014 to October 2018	62	36:26	72.3 ± 5.7	-	13.8	-	1.9	-	-
Abe *et al*[43], 2020	Japan	Retrospective	April 2015 to March 2019	28	12:16	≥ 80	5.5 (0.25-59)	14.5 (4-26)	60.5 (36-124)	9.8 (4-51)	-	EGD and HRM
Sanaka *et al*[44], 2020	United States	Retrospective	April 2014 to May 2019	55	31:24	74 (70-79)	30 (12-60)	10 (IQR: 8-10)	90 (IQR: 7.5-110)	1 (IQR: 1-2)	2.4 (IQR: 2.2-2.7)	HRM, timed barium esophagram and 24-h esophageal pH study
Angeli Abad *et al*[45], 2020	Netherlands	Retrospective[1]	September 2008 to June 2019	66	28:38	83 (80-92)	10.5 (0.2-62.4)	-	-	7 ± 4.1	12	-
Okada *et al*[46], 2021	Japan	Retrospective	September 2011 to March 2020	100	40:60	74.2 (65-93)	10.3 ± 13.6	12.5 (3-25)	138.3 (50-460)	-	36	-
Nakamura *et al* [47], 2021	Japan	Retrospective	August 2014 to May 2021	11	7:4	81 (75-87)	5 (2-40)	13 (8-19)	109 (62-144)	-	36	EGD, esophagography and HRM
Ujiie *et al*[48], 2021	Japan	Retrospective	January 2015 to December 2019	18	12:6	78 (75-86)	4.4 (0.05-50.2)	10 (5-16)	104 (45-165)	-	2	IRP, HRM and EGD
Zhao *et al*[49], 2022	China	Retrospective[1]	November 2010 to September 2019	146	-	-	-	7.09 ± 2.49	46.87 ± 19.29	-	-	GerdQ score

[1]Published conference abstracts.

M: Male; F: Female; EGD: Esophagogastroduodenoscopy; HRM: High resolution esophageal manometry; IRP: Integrated relaxation pressure; IQR: Interquartile range; pH: Potential of hydrogen.

Serious adverse event rate ≤ 6% and mortality rate ≤ 0.1% within 30 days after the procedure.

Previous investigations have demonstrated that POEM can provide short-term benefits in pediatric patients, with a median follow-up period of approximately 13.2 to 40 months. Given that children have a longer life expectancy, the long-term therapeutic outcomes for this patient group are especially significant[37]. The largest series of POEM for children with achalasia was conducted in China by Liu *et al*[34] published in 2019. The authors retrospectively evaluated a total of 130 pediatric patients. The technical success rate for POEM in these patients was 99.2%, and the clinical success rates at 1,

Table 4 Results of the studies on peroral endoscopic myotomy for achalasia in geriatric patients, *n* (%)

Ref.	Technical success	Clinical success	GERD	Adverse events
Wang *et al*[39], 2016	21/21 (100)	20/21 (95.2)	2/21 (9.5)	1/21 (4.8)
Chen *et al*[13], 2018	71/76 (93.4)	59/65 (90.8)	13/76 (16.1)	11/76 (14.5)
Landi *et al*[40], 2018	88/88 (100)	84/88 (95.4)	-	-
Liu *et al*[41], 2019	138/139 (99.3)	79/85 (92.9)	20/85 (23.53)	4/139 (2.88)
Klair *et al*[42], 2019	62/62 (100)	55/62 (88.7)	-	5/62 (8.1)
Abe *et al*[43], 2020	28/28 (100)	17/17 (100)	3/23 (13.0)	8/28 (28.6)
Sanaka *et al*[44], 2020	55/55 (100)	36/38 (94.7)	6/51(11.8)	3/55 (5.5)
Angeli Abad *et al*[45], 2020	66/66 (100)	19/20 (95.0)	-	5/66 (7.6)
Okada *et al*[46], 2021	100/100 (100)	92/92 (100)	-	11/100 (11)
Nakamura *et al*[47], 2021	11/11 (100)	11/11 (100)	1/11 (9)	3/11 (27.3)
Ujiie *et al*[48], 2021	18/18 (100)	18/18 (100)	1/18 (5.6)	0 (0)
Zhao *et al*[49], 2022	146/146 (100)	(96.33)	(15.60)	-

GERD: Gastroesophageal reflux disease.

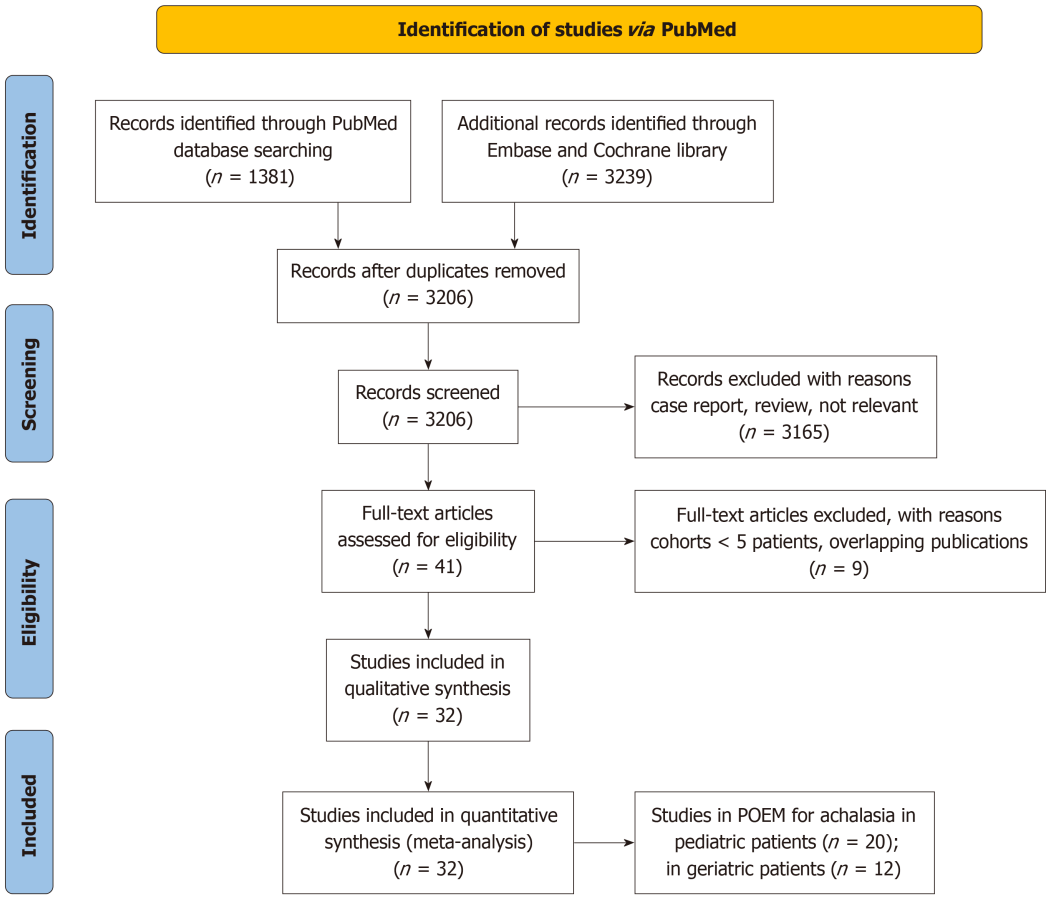


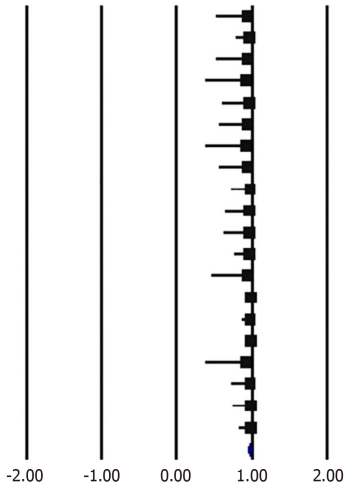
Figure 1 Flow diagram showing study selection. POEM: Peroral endoscopic myotomy.

3, and 5 years were 98.2%, 96.5%, and 95.6%, respectively. In our study, the pooled technical and clinical success rates for pediatric patients were 97.1% (95%CI: 95.0%-98.3%; I^2 = 0%; P < 0.000) and 93.2% (95%CI: 90.5%-95.2%; I^2 = 0%, P < 0.000), and the follow-up time ranged from 6 to 85.75 months. These findings build on the outcomes of earlier research and offer further support that POEM is a highly effective therapeutic approach for childhood achalasia.

A

Technical success

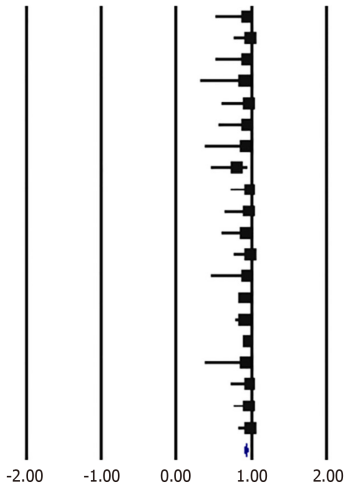
Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Li et al, 2015	0.950	0.525	0.997	2.029	0.042
Chen et al, 2015	0.963	0.779	0.995	3.197	0.001
Caldaro et al, 2015	0.950	0.525	0.997	2.029	0.042
Tang et al, 2015	0.917	0.378	0.995	1.623	0.105
Tan et al, 2016	0.962	0.597	0.998	2.232	0.026
Stavropoulos et al, 2017	0.955	0.552	0.997	2.103	0.035
Zangen et al, 2017	0.917	0.378	0.995	1.623	0.105
Kethman et al, 2018	0.955	0.552	0.997	2.103	0.035
Miao et al, 2018	0.977	0.723	0.999	2.629	0.009
Korrapati et al, 2018	0.969	0.650	0.998	2.390	0.017
Nishimoto et al, 2018	0.964	0.616	0.998	2.289	0.022
Mangiola et al, 2018	0.962	0.772	0.995	3.156	0.002
Yamashita et al, 2018	0.938	0.461	0.996	1.854	0.064
Choné et al, 2019	0.991	0.942	0.999	4.733	0.000
Nabi et al, 2019	0.977	0.856	0.997	3.718	0.000
Liu et al, 2019	0.992	0.947	0.999	4.841	0.000
Saez et al, 2020	0.917	0.378	0.995	1.623	0.105
Wood et al, 2020	0.977	0.723	0.999	2.629	0.009
Peng et al, 2022	0.980	0.749	0.999	2.724	0.006
Petrosyan et al, 2022	0.987	0.822	0.999	3.033	0.002
	0.971	0.950	0.983	12.169	0.000



B

Clinical success

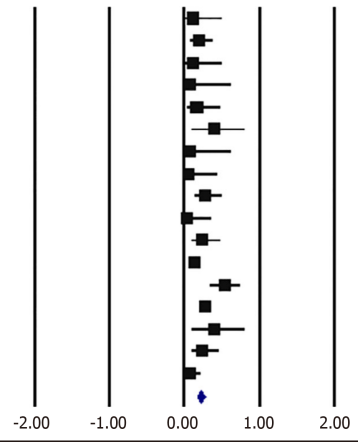
Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Li et al, 2015	0.950	0.525	0.997	2.029	0.042
Chen et al, 2015	0.981	0.764	0.999	2.781	0.005
Caldaro et al, 2015	0.950	0.525	0.997	2.029	0.042
Tang et al, 2015	0.900	0.326	0.994	1.474	0.140
Tan et al, 2016	0.962	0.597	0.998	2.232	0.026
Stavropoulos et al, 2017	0.955	0.552	0.997	2.103	0.035
Zangen et al, 2017	0.917	0.378	0.995	1.623	0.105
Kethman et al, 2018	0.800	0.459	0.950	1.754	0.080
Miao et al, 2018	0.977	0.723	0.999	2.629	0.009
Korrapati et al, 2018	0.969	0.650	0.998	2.390	0.017
Nishimoto et al, 2018	0.923	0.609	0.989	2.387	0.017
Mangiola et al, 2018	0.981	0.764	0.999	2.781	0.005
Yamashita et al, 2018	0.938	0.461	0.996	1.854	0.064
Choné et al, 2019	0.906	0.838	0.947	7.152	0.000
Nabi et al, 2019	0.909	0.782	0.965	4.391	0.000
Liu et al, 2019	0.956	0.898	0.981	6.717	0.000
Saez et al, 2020	0.917	0.378	0.995	1.623	0.105
Wood et al, 2020	0.977	0.723	0.999	2.629	0.009
Peng et al, 2022	0.958	0.756	0.994	3.069	0.002
Petrosyan et al, 2022	0.987	0.822	0.999	3.033	0.002
	0.932	0.905	0.952	13.996	0.000



C

GERD

Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Li et al, 2015	0.111	0.015	0.500	-1.961	0.050
Chen et al, 2015	0.192	0.082	0.387	-2.884	0.004
Caldaro et al, 2015	0.111	0.015	0.500	-1.961	0.050
Tang et al, 2015	0.083	0.005	0.622	-1.623	0.105
Tan et al, 2016	0.167	0.042	0.477	-2.078	0.038
Stavropoulos et al, 2017	0.400	0.100	0.800	-0.444	0.657
Zangen et al, 2017	0.083	0.005	0.622	-1.623	0.105
Kethman et al, 2018	0.045	0.003	0.448	-2.103	0.035
Miao et al, 2018	0.286	0.134	0.508	-1.897	0.058
Korrapati et al, 2018	0.031	0.002	0.350	-2.390	0.017
Mangiola et al, 2018	0.235	0.091	0.486	-2.061	0.039
Choné et al, 2019	0.145	0.092	0.221	-6.754	0.000
Nabi et al, 2019	0.550	0.336	0.747	0.446	0.655
Liu et al, 2019	0.270	0.196	0.360	-4.647	0.000
Saez et al, 2020	0.400	0.100	0.800	-0.444	0.657
Peng et al, 2022	0.238	0.103	0.460	-2.270	0.023
Petrosyan et al, 2022	0.081	0.026	0.223	-4.031	0.000
	0.223	0.184	0.267	-10.212	0.000



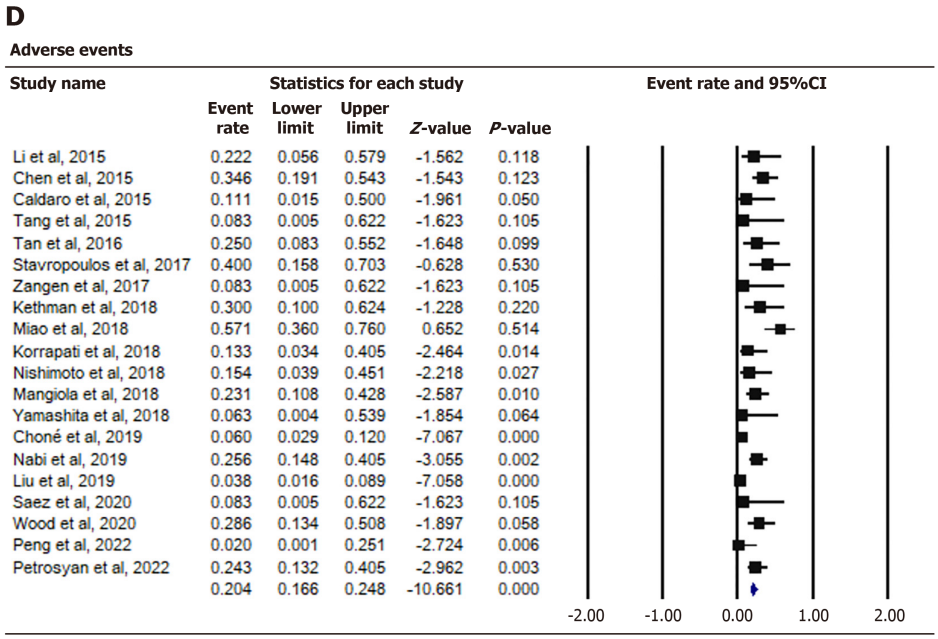


Figure 2 Forest plot of peroral endoscopic myotomy for achalasia in pediatric patients. A: Technical success; B: Clinical success; C: Gastroesophageal reflux disease; D: Adverse events. GERD: Gastroesophageal reflux disease.

Most cases of achalasia occur in individuals between the ages of 30 and 50 years, although it is not uncommon for older adults to be diagnosed with the condition. The risk of aspiration pneumonia, a potentially lethal complication of regurgitation in achalasia, is particularly high in the elderly, highlighting the significance of exploring effective clinical interventions for this patient population[46]. To date, many studies have reported the results of POEM in elderly patients [39-49]. Zhong *et al*[52] published a meta-analysis that included seven studies involving 469 geriatric patients. They reported that the pooled technical success rate was 98.1%, and the pooled clinical success rate was 92.5%. We conducted a more comprehensive study and found that the pooled technical and clinical success rates for geriatric patients were 97.7% (95%CI: 95.8%-98.7%; I^2 = 15.200%; P < 0.000) and 93.2% (95%CI: 90.3%-95.2%; I^2 = 0%, P < 0.000), respectively.

POEM can potentially enhance the quality of life in pediatric patients as they mature. Nevertheless, it is important to be aware of the potential adverse events following POEM, which may include GERD, pneumoperitoneum, pneumothorax, pneumonitis, mucosal injury, subcutaneous emphysema and mediastinal emphysema[53]. Our study revealed that the pooled adverse event rate following POEM in pediatric achalasia was 20.4% (95%CI: 16.6%-24.8%; I^2 = 67.217%; P < 0.000), and the pooled GERD rate was 22.3% (95%CI: 18.4%-26.7%; I^2 = 43.874%; P < 0.000). Chen *et al*[20] reported cumulative adverse events of 53 on the basis of computed tomography scans, which were related to gas. They revealed that this high incidence was due to air for insufflation in 20 patients (76.9%). They also demonstrated that air insufflation had a higher rate of postoperative gas-related adverse events than carbon dioxide insufflation [84.6% (11/13) *vs* 16.7% (1/6)][22]. In addition, Lee *et al*[54] included 12 studies involving 146 pediatric patients who underwent POEM. The authors found that at least 93% of the children experienced an improvement in achalasia symptoms after POEM, with a limited number of patients reporting minor adverse effects that could be controlled conservatively. Recently, Zhong *et al*[55] published an updated meta-analysis involving a total of 11 studies with 389 children. The pooled major adverse event rate was reported to be 12.8%, while the pooled GERD rate was 17.8%. Two meta-analyses suggested that POEM was effective and safe for treating achalasia in pediatric patients[54,55].

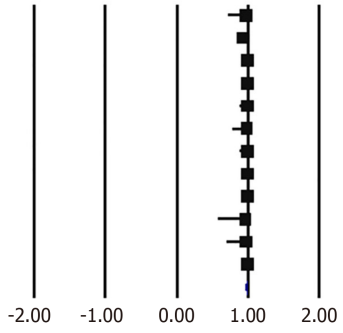
In geriatric patients, the pooled adverse events and GERD rates following POEM for achalasia were 10.8% (95%CI: 8.3%-14.0%; I^2 = 62.938%; P < 0.000) and 23.9% (95%CI: 19.4%-29.1%; I^2 = 75.697%; P < 0.000], respectively. Furthermore, Zhong *et al*[55] published a meta-analysis including 7 studies involving 469 geriatric patients, and the major adverse event rate was 9.0%, and the clinical reflux rate was 17.4%. In total, almost all these studies indicated that POEM is a safe and effective treatment for geriatric patients with esophageal achalasia[56].

There were several limitations in our analyses. First, the results of the NIH quality assessment revealed that one of our included studies was of poor quality, which may have reduced the evidence quality in our article. In addition, our study lacked several characteristic indicators, including achalasia type, American Society of Anesthesiology physical status classification system score, type of myotomy, pre- and postoperative Eckardt score, and LES pressure; thus, the analysis was not comprehensive. In addition, the study examining GERD and adverse events in geriatric patients exhibited publication bias; therefore, future investigations should include subgroup analyses to determine the underlying reasons for this. Furthermore, as the symptoms of GERD are very similar to those of achalasia, possible confusion could have occurred during interpretation of the results. A large proportion of cases with long-term follow-up could not be objectively evaluated for GERD, and the possibility of selection bias could not be completely ruled out. Both may have led to a higher pooled rate of GERD. Lastly, almost all of the studies were small sample, nonrandomized and observational studies, which may have been subject to a range of biases.

A

Technical success

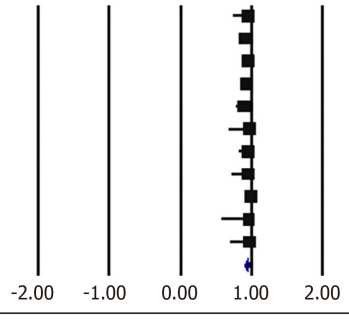
Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Wang et al, 2016	0.977	0.723	0.999	2.629	0.009
Chen et al, 2018	0.934	0.851	0.972	5.734	0.000
Landi et al, 2018	0.994	0.917	1.000	3.650	0.000
Liu et al, 2019	0.993	0.951	0.999	4.909	0.000
Klair et al, 2019	0.992	0.885	1.000	3.401	0.001
Abe et al, 2020	0.983	0.777	0.999	2.834	0.005
Sanaka et al, 2020	0.991	0.873	0.999	3.315	0.001
Abad et al, 2020	0.993	0.892	1.000	3.445	0.001
Okada et al, 2021	0.995	0.926	1.000	3.741	0.000
Nakamura et al, 2021	0.958	0.575	0.997	2.170	0.030
Ujiie et al, 2021	0.974	0.690	0.998	2.519	0.012
Zhao et al, 2022	0.997	0.948	1.000	4.010	0.000
	0.977	0.958	0.987	12.159	0.000



B

Clinical success

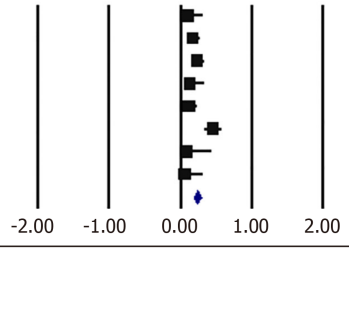
Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Wang et al, 2016	0.952	0.729	0.993	2.924	0.003
Chen et al, 2018	0.908	0.809	0.958	5.334	0.000
Landi et al, 2018	0.955	0.885	0.983	5.949	0.000
Liu et al, 2019	0.929	0.852	0.968	6.087	0.000
Klair et al, 2019	0.887	0.782	0.945	5.137	0.000
Abe et al, 2020	0.972	0.678	0.998	2.479	0.013
Sanaka et al, 2020	0.947	0.813	0.987	3.979	0.000
Abad et al, 2020	0.950	0.718	0.993	2.870	0.004
Okada et al, 2021	0.995	0.920	1.000	3.681	0.000
Nakamura et al, 2021	0.958	0.575	0.997	2.170	0.030
Ujiie et al, 2021	0.974	0.690	0.998	2.519	0.012
	0.932	0.903	0.952	13.515	0.000



C

GERD

Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Wang et al, 2016	0.095	0.024	0.311	-3.028	0.002
Chen et al, 2018	0.171	0.102	0.273	-5.181	0.000
Liu et al, 2019	0.235	0.157	0.337	-4.609	0.000
Abe et al, 2020	0.130	0.043	0.335	-3.064	0.002
Sanaka et al, 2020	0.118	0.054	0.238	-4.636	0.000
Abad et al, 2020	0.455	0.339	0.575	-0.738	0.461
Nakamura et al, 2021	0.091	0.013	0.439	-2.195	0.028
Ujiie et al, 2021	0.056	0.008	0.307	-2.753	0.006
	0.239	0.194	0.291	-8.502	0.000



D

Adverse events

Study name	Event rate	Lower limit	Upper limit	*Z*-value	*P*-value
Wang et al, 2016	0.048	0.007	0.271	-2.924	0.003
Chen et al, 2018	0.145	0.082	0.243	-5.449	0.000
Liu et al, 2019	0.029	0.011	0.074	-6.936	0.000
Klair et al, 2019	0.081	0.034	0.180	-5.218	0.000
Abe et al, 2020	0.286	0.150	0.476	-2.190	0.028
Sanaka et al, 2020	0.055	0.018	0.156	-4.804	0.000
Abad et al, 2020	0.076	0.032	0.169	-5.377	0.000
Okada et al, 2021	0.110	0.062	0.188	-6.542	0.000
Nakamura et al, 2021	0.273	0.090	0.586	-1.449	0.147
Ujiie et al, 2021	0.026	0.002	0.310	-2.519	0.012
	0.108	0.083	0.140	-14.047	0.000

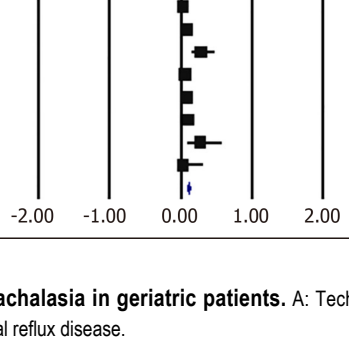


Figure 3 Forest plot of peroral endoscopic myotomy for achalasia in geriatric patients. A: Technical success; B: Clinical success; C: Gastroesophageal reflux disease; D: Adverse events. GERD: Gastroesophageal reflux disease.

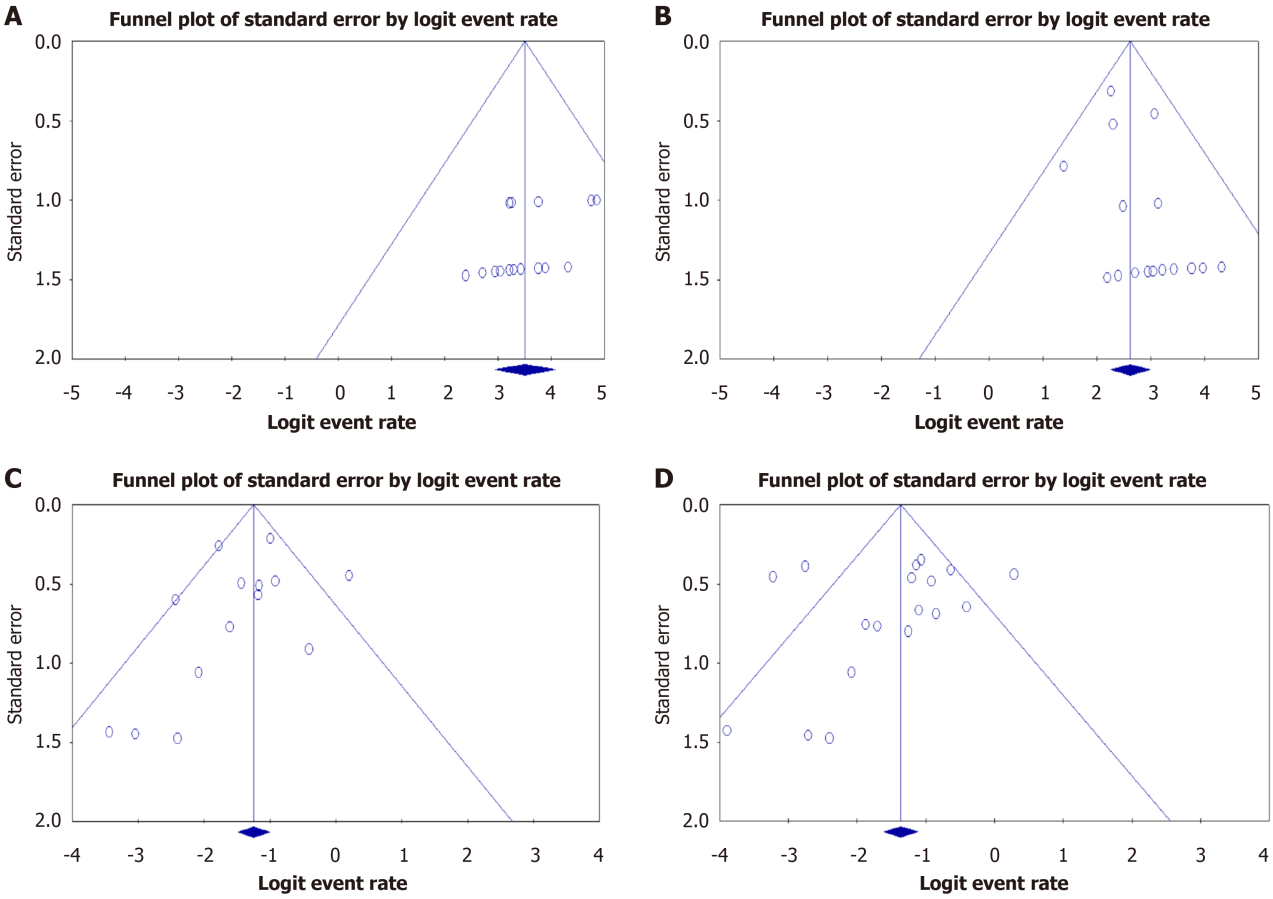


Figure 4 Assessment of publication bias in pediatric patients. A: Technical success; B: Clinical success; C: Gastroesophageal reflux disease; D: Adverse events.

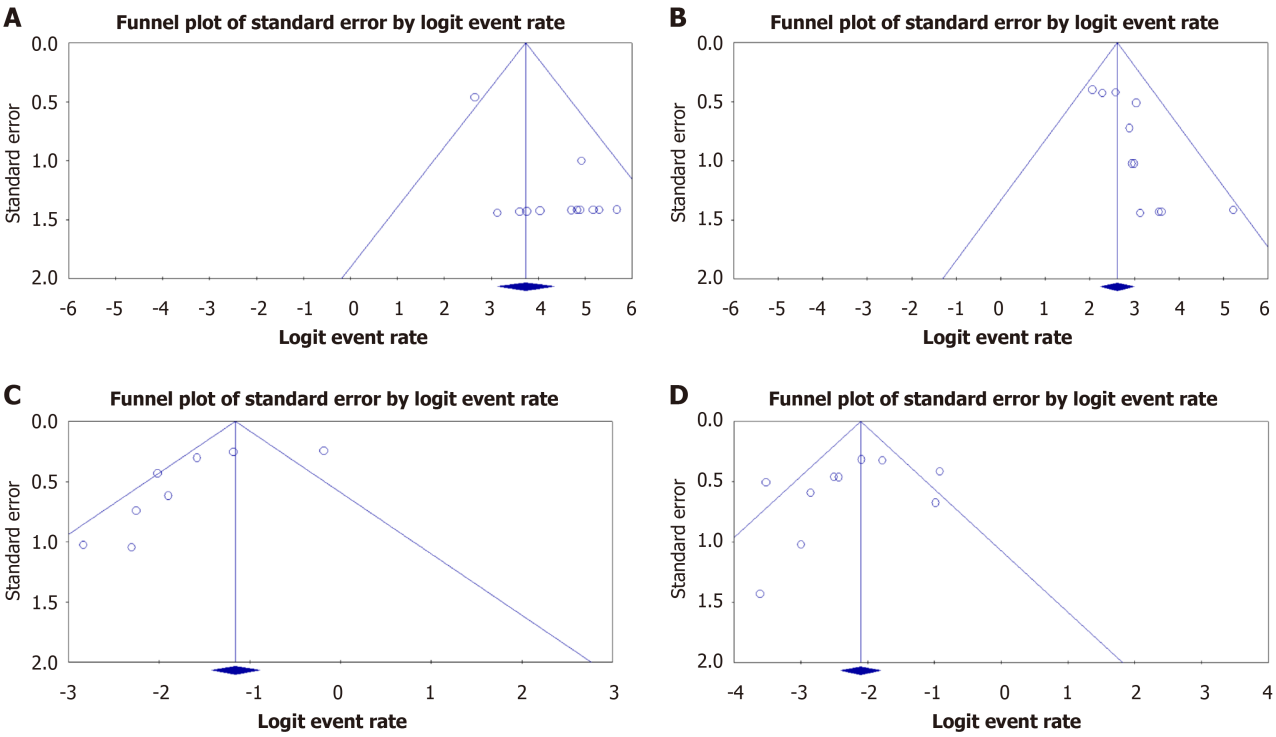


Figure 5 Assessment of publication bias in geriatric patients. A: Technical success; B: Clinical success; C: Gastroesophageal reflux disease; D: Adverse events.

CONCLUSION

Currently, on the basis of the available published evidence, POEM has been shown to be an effective and safe therapy for achalasia in both pediatric and geriatric patients. Nevertheless, there is a need for additional high-quality randomized controlled trials to establish the optimal treatment approach for achalasia within these specific populations.

FOOTNOTES

Author contributions: Tang XW and Pu XX contributed to study conception and design; Pu XX, Huang S and Zhong CY contributed to drafting of the manuscript; Wang X, Fu SF, Lv YQ, Zou K, Lü MH contributed to acquisition of data and critical revision; Tang XW and Peng Y contributed to revision of the manuscript, and final approval of the manuscript; All authors have read and approved the final manuscript.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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S-Editor: Fan M
L-Editor: Webster JR
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