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REVIEW ARTICLE

# Peroral endoscopic myotomy (POEM) for the treatment of pediatric achalasia: a systematic review and meta-analysis

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## Abstract

**Background** Achalasia is a rare primary esophageal dysmotility disorder in children. Peroral endoscopic myotomy (POEM) is a novel endoscopic technique which has shown promising results for treating achalasia in adults. However, limited data on efficacy and safety in pediatric patients are available. We performed a systematic review and meta-analysis to evaluate the efficacy and safety of POEM in pediatric achalasia.

**Methods** We searched MEDLINE, Embase, PubMed, and Web of Science databases through July 2018. Studies were eligible for inclusion if they conducted POEM in pediatric patients. Main outcomes were Eckardt score and lower esophageal sphincter (LES) pressure before and after POEM. Secondary outcomes were clinical success rate and adverse events associated with POEM. Two reviewers independently reviewed the studies, collected data, and assessed quality of evidence using Methodological Index for Non-Randomized Studies (MINORS). Pooled estimates were calculated using random effects meta-analyses. Heterogeneity was quantified using the inconsistency statistic, and funnel plot was used to assess publication bias.

**Results** A total of 12 studies with 146 pediatric patients (53.68% female) underwent POEM for the treatment of achalasia (mean duration of disease of 19.48 months). There was a significant reduction in Eckardt score by 6.88 points (Mean Difference (MD) 6.88, 95% confidence interval (CI), 6.28–7.48, $P < .001$) and LES pressure by 20.73 mmHg (MD 20.73, 95% CI, 15.76–25.70, $P < .001$) following POEM. At least 93% of the patients experienced improvement or resolution of achalasia symptoms both short and long terms after POEM, with small proportion of patients experiencing minor adverse effects which could be managed conservatively.

**Conclusions** POEM is efficacious and safe for treating achalasia in pediatric populations. Large comparative or randomized trials are warranted to confirm the efficacy and safety of POEM compared to other surgical procedures for achalasia.

**Keywords** Achalasia · Peroral endoscopic myotomy · POEM · Meta-analysis · Systematic review

## Abbreviations

| | |
|---|---|
| POEM | Peroral endoscopic myotomy |
| LES | lower esophageal sphincter |
| LHM | laparoscopic Heller myotomy |
| GERD | gastroesophageal reflux disease |
| NOTES | natural orifice transluminal endoscopic surgery |
| PRISMA | Preferred Reporting items for Systematic Reviews and Meta-Analyses |
| MINORS | Methodological Index for Non-Randomized Studies |
| CI | Confidence Interval |
| MD | Mean Difference |

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Achalasia is a neurodegenerative motility disorder of the esophagus characterized by a failure of the lower esophageal sphincter (LES) to relax after swallowing, accompanied by a loss of peristalsis in the distal esophagus [1, 2]. It has a prevalence of 10 cases per 100,000 in adults. However,

in children, it is quite rare, with an estimated incidence of 0.02–0.11 cases per 100,000, and is most often seen in the setting of congenital disorders such as Allgrove syndrome and familial glucocorticoid deficiency [1, 3, 4]. Clinically, achalasia manifests as dysphagia to solids and liquids, regurgitation of undigested food or saliva, chest pain, and weight loss or poor weight gain in the majority of patients. Clinical symptoms are further corroborated by upper endoscopy, followed by esophageal manometry with or without a barium swallow test in order to establish a diagnosis [5, 6].

Management of achalasia ranges from medical therapy (e.g., botulinum toxin), pneumatic dilation, and surgical treatment, with the goal of treatment being to reduce LES pressure and improve symptoms [7, 8]. Pneumatic dilation stretches the LES and is successful in the majority of cases, but repeated dilations with bigger balloons subsequently are often required to maintain efficacy of the treatment. This can prove to be inefficient in pediatric patients, who may undergo more frequent recurrences due to longer lifespan [9]. Surgical myotomy, in particular laparoscopic Heller myotomy (LHM), is the mainstay of treatment for patients who do not respond to pneumatic dilation; this procedure involves weakening the LES by cutting its circular muscle fibers [10]. LHM leads to gastric reflux, which is addressed with a concurrent fundoplication procedure. However, despite this, LHM is associated with numerous adverse events including gastroesophageal reflux disease (GERD), perforation, pneumothorax, and bleeding [11]. Recently, peroral endoscopic myotomy (POEM) has emerged as a promising treatment modality for achalasia [12–15]. POEM is a natural orifice transluminal endoscopic surgery (NOTES) that can be used to perform myotomy [14, 16]. POEM is less invasive than LHM, and numerous adult studies have demonstrated excellent patient outcomes at with minimal recovery time and low complication rates [12, 17–20]. POEM is also less expensive than LHM and is associated with faster recovery, making it a potential candidate to replace LHM as the standard therapy for achalasia [21–23].

Due to the success of POEM in adult population, it is increasingly being explored as a treatment option in the pediatric patient population, with several early studies showing promising results at short-term follow-up [13, 16, 24]. Given the growing body of the literature on POEM for pediatric patients and the absence of a review of the literature, this systematic review and meta-analysis aim to establish the efficacy of POEM in treating pediatric patients with achalasia.

## Materials and methods

### Search strategy

We conducted a systematic search of the following databases covering the period from database inception through August 2018: MEDLINE, EMBASE, Web of Science, and PubMed. The search terms were designed and conducted with the help of an expert medical librarian with input from study investigators. The search strategy included keywords such as "peroral endoscopic myotomy", "POEM", and "esophageal achalasia" (Supplementary Table 1). To ensure a comprehensive search, we searched the literature available on POEM without including the term "pediatric" to narrow down the search prior to screening. We also searched the references of published studies and searched grey literature manually to ensure that relevant articles were not missed. We did not discriminate full texts by language. This systematic review and meta-analysis are reported in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) [25]. Ethics approval and written consent were no required for this study.

### Eligibility criteria and data abstraction

Articles were eligible for inclusion if the study studied the effect of POEM on achalasia in pediatric patients (< 18 years old). We included both single-arm (effect of POEM on pediatric achalasia) and double-arm studies (POEM versus other surgical management of achalasia). Studies were excluded if they were (1) non-pediatric studies; (2) no clear diagnostic or clinical evaluation of achalasia (e.g., Eckardt scoring system, esophageal manometry, barium X-ray, upper endoscopy); (3) non-human studies; (4) case-reports, editorials, and review papers.

Screening of searched titles, abstracts, and full texts were done independently by at least two reviewers. Reviewers were not blinded to author name, institution, or where the manuscript was published. Any discrepancies that occurred during the title and abstract screening stages were resolved by automatic inclusion to ensure that all relevant publications were not missed. Two reviewers independently conducted data abstraction onto a standardized spreadsheet designed *a priori*. The following data were abstracted from included studies: study characteristics (author, country, year of publication, study design, funding source, study design), patient demographics (age at time of surgery, number of patients included, % female, duration of disease, number of previous treatment history, type of achalasia, and history of congenital disorders), POEM characteristics (type of POEM knife, mean procedure time, submucosal length, total myotomy length, mean feeding postoperative day, length of stay, and definition of treatment success), adverse events, and outcomes. Discrepancies at the full text and data abstraction stages were resolved by consensus between two reviewers and if disagreement persisted, a third reviewer was consulted.

### Outcomes assessed & risk of bias assessment

Achalasia is characterized by a failed relaxation of the lower esophageal sphincter and absent peristalsis of the distal esophagus. As such, measuring lower esophageal pressure upon esophageal manometry and using the Eckardt score for grading of symptoms can be used to monitor the course of disease pre-and post-treatment (5,6). Articles included in the systematic review and meta-analysis had to report at least one of the primary outcomes of interest before and after the procedure, which included: (1) mean Eckardt score, (2) lower esophageal sphincter (LES) pressure (mmHg), (3) complete resolution or improvement of achalasia (defined by each studies' definition of treatment success). Secondary outcomes included length of stay in the hospital and postoperative pain score and analgesic requirements. Methodological index for non-randomized studies (MINORS) tool was used to assess the risk of bias for individual studies [26].

### Statistical analysis

All statistical analyses and meta-analysis were performed on Cochrane Review Manager 5.3 (London, United Kingdom) and STATA, version 14 (StataCorp, College Station, TX) with a level of significance set at P of $< 0.05$. We performed pairwise meta-analyses using a DerSimonian and Laird random effects model for continuous variables. Pooled effect estimates were obtained by calculating the mean difference (MD) in outcomes along with their respective 95% confidence intervals (CI) to confirm the effect size estimation. In addition, mean and standard deviation were estimated for studies that only reported median and interquartile range using the estimation method proposed by Wan et al. [27]. For studies that only reported the mean without standard deviation, we contacted the authors for missing information or alternatively used the method by Sung et al. to calculate the standard deviation (SD) of the overall effect estimate when necessary [28, 29]. To minimize the bias that could potentially be introduced with this method, we performed a sensitivity analysis excluding these studies that did not report SD to observe the difference in effect estimates. The pooled proportion with patients with complete resolution or improvement in achalasia was calculated using the Freeman–Tukey double arcsine transformation of proportions. DerSimonian and Laird random effects meta-analysis of proportions was used to generate the overall effect size of each outcome. Assessment of heterogeneity was completed using the inconsistency ($I^2$) statistic. We considered $I^2$ higher than 50% to represent considerable heterogeneity [30]. Publication bias was assessed using a funnel plot. In addition, we performed subgroup analyses based on follow-up time points and sensitivity analysis based on study type.

## Results

### Study characteristics

From 2220 potentially relevant citations, 12 studies were eligible for inclusion three prospective cohort [31–33], 4 retrospective cohort [16, 34–36], and five case series [24, 37–40] with three of the studies being published conference abstracts [39–41] with extractable data. Figure 1 depicts a PRISMA flow diagram of study selection process, and study characteristics are reported in detail in Table 1. All studies investigated the efficacy and safety of POEM on pediatric achalasia. Two studies were comparative in nature, one comparing POEM to balloon dilatation and one with LHM. Included studies recruited patients between 2009 and 2017 with a median follow-up of 14 months (1–36 months) across all outcome measurements. A total of 146 patients (53.68% females) were included in this review. The weighted mean age of pediatric patients at time of POEM was 12.08 years with the duration of disease prior to POEM being 19.48 months. Previous interventions before POEM were reported for 30 patients which included: 13 pneumatic balloon dilatations, one botulinum injection, one temporary esophageal stent placement, and 13 unspecified pharmacologic treatment. Type of achalasia that each patient had was reporting using the Chicago Classification of esophageal motility disorders [42] in only five studies, with 13 patients with Type 1, 14 patients with Type 2, and one patient with Type 3 achalasia (Figs. 2, 3).

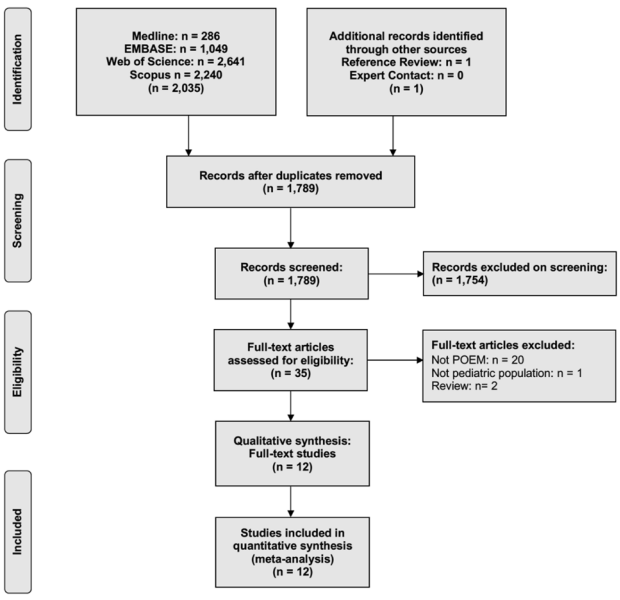


**Fig. 1** PRISMA Diagram—transparent reporting of systematic reviews and meta-analysis flow diagram outlining the search strategy results from initial search to included studies

**Table 1** Study characteristics of included studies

| Study | Study design | Year | N | % female | Age, yr (SD) | Follow-up time points | Duration of disease (SD) | N previous treatment history | Type of achalasia | History of congenital disorders |
|---|---|---|---|---|---|---|---|---|---|---|
| Familiari (2013) [24] | Case series | 2012–2013 | 3 | 100% | 9 (0.29) | 3, 6, 12 months | 17 months (17.06) | None | 100% Type 1 | None |
| Caldaro (2015) [16] | Retrospective cohort | 2009–2014 | 9 | 66.7% | 12.2 (3.8) | 12.7 months | N/R | 1 - Pneumatic balloon dilation | N/R | 1 – Pilocytic Astrocytoma |
| Li (2015) [31] | Prospective cohort | 2011–2014 | 9 | 55% | 14.1 (2.15) | 16.3 months | 26.40 months (18.68) | None | N/R | None |
| Chen (2015) [32] | Prospective cohort | 2010–2012 | 27 | 60% | 13.8 (2.75) | 24.6 months | 20.4 months (8.4) | 8 – Pharmacologic treatment<br>5 – Pneumatic balloon dilation<br>1 – Botulinum injection<br>1 – Temporary stent | N/R | 9– Severe Growth Retardation |
| Tang (2015) [37] | Case series | 2012–2014 | 5 | 40% | 15 (1.45) | 18 months | 6.3 months (5.24) | 2 – Pneumatic balloon dilation | 100% Type 1 | None |
| Tan (2016) [34] | Retrospective cohort | 2007–2015 | 12 | 50% | 13.7 (2.6) | 3, 6, 12, 24, 36 months | 23.6 months (16.8) | None | N/R | None |
| Miao, 2017 | Prospective cohort | 2014–2016 | 21 | 57% | 5.5 (4.28) | 13.2 months | 18 months (6.6) | 5 – Pharmacologic treatment<br>1 – Pneumatic balloon dilation | N/R | 3 – Severe Growth Retardation |
| Nabi, 2017 | Retrospective cohort | 2013–2016 | 10 | 60% | 14.2 (2.74) | 3 months | N/R | 2–Pneumatic balloon dilation | 40% Type 1<br>50% Type 2<br>10% Type 3 | None |
| Stavropoulos (2017) [39] | Case series[a] | 2013–2016 | 10 | N/R | 14.7 (2.02) | 15 months | 21 months (23.4) | 2–Pneumatic balloon dilation | N/R | N/R |
| Zangen (2017) [36] | Retrospective cohort* | NR | 5 | 60% | 15.4 (10.18) | 6 months | N/R | N/R | 100% Type 2 | N/R |
| Kethman (2018) [38] | Case series | 2014–2016 | 10 | 20% | 13.4 (2.89) | 1 month | N/R | None | 90% Type 2<br>10% Type 1 | None |
| Mangiola (2018) [40] | Case series* | 2012–2017 | 25 | 53.8% | 10.9 (4.5) | 30.6 months | 18.2 months (14.9) | 2–Pneumatic balloon dilation | N/R | None |

*N/R* not reported; *SD* standard deviation

[a]Published conference abstracts

## POEM characteristics

POEM technique did not vary significantly between studies, as all studies generally followed the steps consisting of esophageal mucosal incision, entry into submucosa, creating the submucosal tunnel, incising the esophageal muscle fibers, and closing the mucosal incision after myotomy. Moreover, majority of the studies defined "clinical/treatment success" as patients having Eckardt score of less than three after the procedure. Table 2 shows the detailed characteristics of POEM in each included study. POEM knives used in the studies were triangle-tip knife (four studies; Olympus, Tokyo, Japan), hybrid knife (three studies; ERBE, Tubingen, Germany), and hook knife (one study; Olympus, Tokyo, Japan), and rest of the studies did not report the type of equipment that they used for the POEM procedure. The mean procedure time was 56.79 min, mean submucosal tunnel length was 11.14 cm, and mean total myotomy length was 9.01 cm across all studies. After POEM, the mean length of stay in hospital was 4.82 days with mean postoperative feeding after 2.04 days.

## Achalasia outcomes

From the 12 studies included in the review, 11 studies reported Eckardt score (n = 119), 10 studies reported LES pressure (n = 124), and all studies reported number of patients with improvement or resolution of achalasia symptoms (n = 146). The baseline and post-POEM Eckardt scores and LES pressure values of included studies are reported in Supplementary Table 2. After POEM, mean Eckardt score was significantly decreased by 6.88 points (MD 6.88, 95% CI, 6.28–7.48, $P < .001$, $I^2 = 75\%$) and LES pressure was significantly lowered by 20.73 mmHg (MD 20.73; 95% CI, 15.76–25.70, $P < .001$, $I^2 = 93\%$). Similar to these clinical parameters of achalasia, meta-analysis of proportions demonstrated an improvement or resolution of achalasia in 94% of patients (95% CI, 82–100%, $I^2 = 71\%$). Heterogeneity was high across all outcome measurements, ranging from $I^2$ of 71–93%. Symmetry shown in our funnel plots suggests that there is a low possibility of publication bias, which might mean that there are a low number of unpublished negative studies (data not shown) [43] However, this result may be

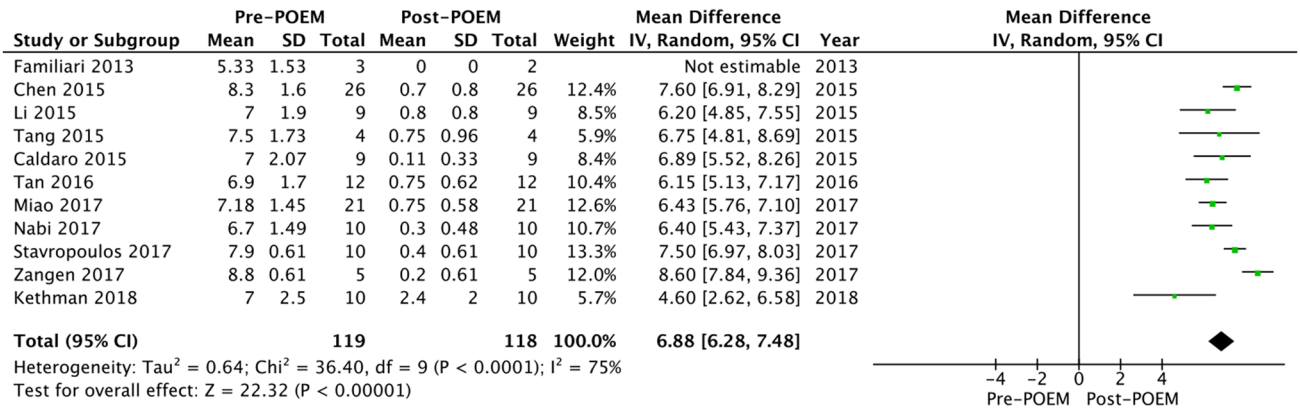


**Fig. 2** Forest plot of random effects meta-analysis assessing the effect of POEM on mean Eckardt score before and after surgery

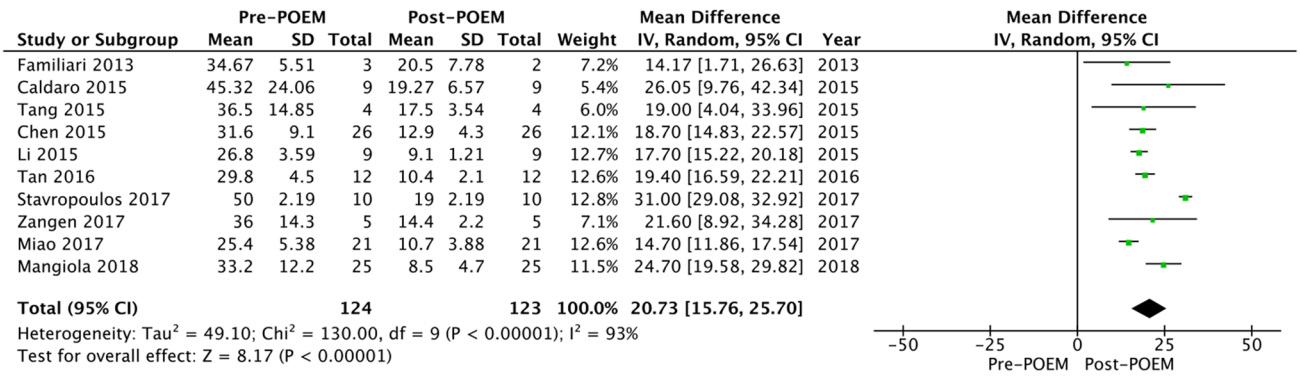


**Fig. 3** Forest plot of random effects meta-analysis assessing the effect of POEM on mean lower esophageal sphincter (LES) pressure (mmHg) before and after surgery

**Table 2** POEM characteristics

| Study | POEM knife type | Mean procedure type (minutes) | Mean submucosal tunnel length (cm) | Total Myotomy length (cm) | Mean length of stay (days) | Mean feeding postoperative day | Definition of treatment success |
|---|---|---|---|---|---|---|---|
| Familiari (2013) [24] | Triangle tip | 60.66 (13.87) | 13.33 (1.53) | 10 (1.73) | 5 days (1.73) | 2.67 days (0.58) | Eckhardt score of 0 |
| Caldaro (2015) [16] | Triangle tip | 62 (12.7) | N/R | 11 (2) | 4.1 (1.4) | 2.3 (1–3) | N/R |
| Li (2015) [31] | Hybrid | 56.7 (19.53) | 11.3 (1.22) | 8.3 (0.87) | N/R | 2 (0) | Eckhardt score < 3 |
| Chen (2015) [32] | Hybrid, triangle tip, and hook knife | 39.4 (17.4) | N/R | 9.6 (1.1) | 3.2 (1–7) | 2 (0) | Eckhardt score < 3 |
| Tang (2015) [37] | Hybrid | 56 (19.81) | 12.6 (3.29) | 2.8 (0.45) | 7.6 (3.13) | 2 (0) | Eckhardt score < 3 |
| Tan (2016) [34] | N/R | N/R | N/R | N/R | N/R | 2 (0) | Eckhardt score < 3 |
| Miao, 2017 | N/R | 40 (30–55) | 10 (8–15) | 9 (6–11) | 10 (7–14) | 2 (0) | Symptom relief |
| Nabi, 2017 | Triangle tip | 47.6 (19.74) | N/R | 10 (6–13) | N/R | 2 (0) | N/R |
| Stavropoulos (2017) [39] | N/R | 55 (33–111) | N/R | N/R | 1 (1–2) | N/R | Eckhardt score < 3 |
| Zangen (2017) [36] | N/R | 62 (43–73) | N/R | 11.2 (10–14) | N/R | N/R | N/R |
| Kethman (2018) [38] | N/R | 142 (60–259) | 12 (10–13) | 7 (4–9) | 1.4 (0.52) | 2 (0) | Eckhardt score < 3 |
| Mangiola (2018) [40] | N/R | N/R | N/R | N/R | N/R | N/R | Eckhardt score < 3 |

*POEM* Peroral endoscopic myotomy; *N/R* not reported

biased due to the low number of studies and participants [44].

## Adverse events

Adverse events were reported by all studies, with two studies involving 15 patients not encountering any adverse events (Table 3). Out of all the studies included, only one patient had recurrence of achalasia [36]. There were no reported cases of surgical conversion, ICU admission, mortality, and other major adverse events. Most of the studies did not report individual patient's adverse events, and as a result, we were unable to discern whether more than one adverse effect occurred in a single patient. As a result, we were unable to calculate the accurate proportion of patients who experienced adverse events. Adverse effects reported across all studies included: mucosal injury (n = 7), esophageal tear (n = 1), esophageal leak (n = 1), focal atelectasis (n = 2), pneumoperitoneum (n = 13), pneumothorax (n = 4), pneumonitis/pneumonia (n = 15), pleural effusion (n = 9), subcutaneous or mediastinal emphysema (n = 25), retroperitoneal CO2 (n = 2), fever (n = 1), and severe-postoperative pain (n = 2). There were also cases of clinical reflux symptoms after POEM such as heartburn (n = 2), regurgitation (n = 11), and reflux esophagitis (n = 5). Despite the wide-range of adverse events that occurred after POEM, most of them were minor and self-limiting adverse events that could be treated conservatively. Pneumoperitoneum was managed with 20-gauge needle [32], pleural effusions were treated with thoracic drainage [32], and perforations and bleeding could be controlled by endoscopic clipping or hemostasis. Moreover, clinical reflux symptoms were managed conservatively with proton pump inhibitors [45, 46].

## Subgroup analysis

To assess the difference in POEM outcomes between short-term and long-term follow-ups, we conducted a subgroup analysis separating studies with follow-up time point of greater than 12 months and less than 12 months. In short-term follow-up studies, POEM resulted in a significantly decrease in Eckardt score by 6.36 points (MD 6.36, 95% 4.93–7.78, $P < .001$), and a significant lowering of LES pressure by 19.26 mmHg (MD 19.26, 95% 16.58–21.94, $P < .001$). In long-term follow-up studies, Eckardt score was significantly decreased by 7.03 points (MD 7.03, 95% 6.50–7.55, $P < .001$) and LES pressure was lowered by 21.53 mmHg (MD 21.53, 95% 15.10–27.96, $P < .001$). Moreover, 96% of the patients experienced improvement or resolution of symptoms short-term (95% CI, 85–100%), and 93% in long-term (73–100%) (Fig. 4). Hence, the efficacy of POEM was not substantially different between follow-up time points. In addition, conducting a sensitivity analysis removing the conference abstracts or the studies that did

**Table 3** Adverse events related to POEM in pediatric population

| Study | | Adverse events description | Number of cumulative adverse events | Studies reported individual patient adverse events |
|---|---|---|---|---|
| Familiari (2013) [24] | 3 | Mucosal injury: 1 | 1 | Yes |
| Caldaro (2015) [16] | 9 | Minor esophageal tear: 1<br>Pneumoperitoneum: 1 | 2 | |
| Li (2015) [31] | 9 | Reflux esophagitis: 1<br>Subcutaneous emphysema:1 | 2 | |
| Chen (2015) [32] | 27 | Mucosal injury: 1<br>Fever: 1<br>Severe postoperative pain: 2<br>Subcutaneous emphysema: 7<br>Mediastinal emphysema: 10<br>Pneumothorax: 4<br>Pneumoperitoneum: 9<br>Pleural effusion: 9<br>Pneumonitis: 13<br>Clinical reflux events: 5<br>Focal atelectasis:2 | 63 | No |
| Tang (2015) [37] | 5 | None | 0 | Yes |
| Tan (2016) [34] | 12 | Heartburn: 1<br>Subcutaneous emphysema:1 | 2 | |
| Miao, 2017 | 21 | Heartburn and regurgitation: 6<br>Subcutaneous emphysema and/or mediastinal emphysema: 6<br>Pneumonia: 1 | 13 | Yes |
| Nabi, 2017 | 10 | Pneumoperitoneum: 2<br>Retroperitoneal $CO_2$:2<br>Subcutaneous emphysema:1 | 5 | |
| Stavropoulos (2017) [39] | 10 | None | 0 | Yes |
| Zangen (2017) [36] | 5 | Recurrence: 1 | 1 | Yes |
| Kethman (2018) [38] | 10 | Pneumoperitoneum:1<br>Mucosal injury:1<br>Pneumothorax: 1 | 3 | |
| Mangiola (2018) [40] | 25 | Esophageal leak: 1<br>Aspiration pneumonia: 1<br>Ulceration at EGJ: 4<br>Reflux esophagitis: 4 | 10 | |

*EGJ* esophagogastric junction; *CO2* carbon dioxide

not report SD in our pooled random effects meta-analysis did not result in any substantial differences in results (data not shown).

### Quality assessment of studies

The mean MINORS score of included studies was $11.42 \pm 1.55$, which indicates a fair quality of evidence for non-randomized studies [26]. A comprehensive list of MINORS for included studies are available in Supplementary Table 3. In brief, all 12 studies had a clearly stated objective, endpoints appropriate to the aims of the study, and unbiased assessment of study endpoint. Majority of the studies had a follow-up time point greater than 12 months (9/12 studies), had less than 5% of loss to follow-up (10/12 studies). Only 5 out of 12 studies included consecutive patients and half of the studies collected their data prospectively. Lastly, all studies lacked a prospective calculation of study size.

## Discussion

POEM is a promising new treatment for achalasia that is purportedly more efficient and less invasive than current standards of treatment, with multiple studies demonstrating positive outcomes with few adverse effects in adults [47–49]. In this systematic review and meta-analysis of POEM for the treatment of pediatric achalasia, we found that POEM is both efficacious and safe in pediatric patients, with the

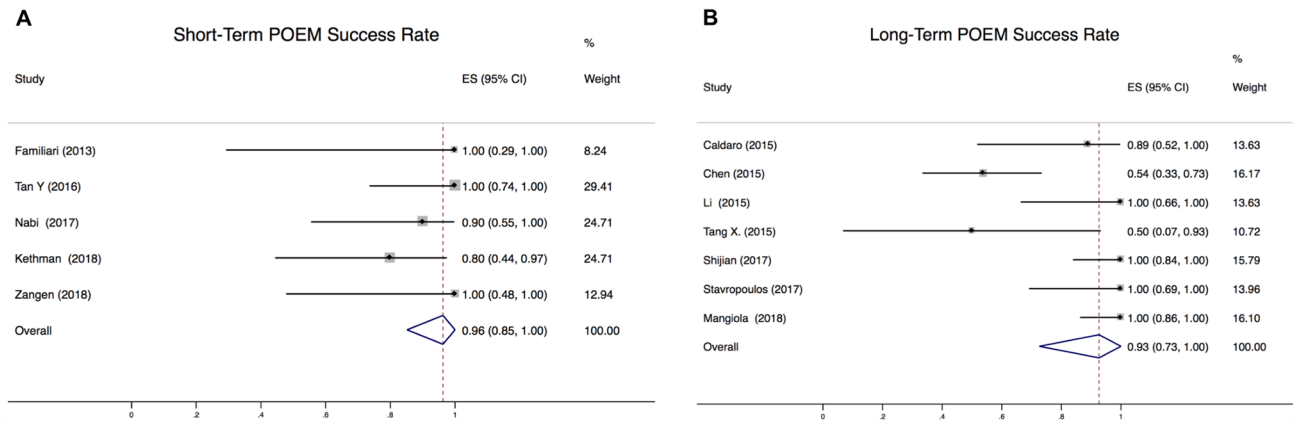


**Fig. 4** Meta-analysis of proportions forest plot of success rate (complete resolution or improvement) of achalasia in pediatric patients. **A** Short-term outcomes (less than 12 months follow-up). **B** Long-term outcomes (greater 12 months follow-up)

vast majority of patients seeing complete resolution of achalasia symptoms. We found that POEM is efficacious in significantly decreasing mean Eckardt score by 6.88 points (95% CI, 6.28–7.48, $P < .001$) and LES sphincter pressure by 20.73 mmHg (95% CI, 15.76–25.70, $P < .001$) following treatment, with an overall success rate for improvement/resolution of symptoms of 94% of patients (95% CI, 82–100%). Subgroup analysis of follow-up time showed that greater than 93% of patients with both short and long-term follow-up saw resolution of symptoms, indicating that POEM retains its efficacy over time.

To our knowledge, this is the first systematic review and meta-analysis addressing the utility of POEM in the pediatric population. As a minimally invasive endoscopic procedure, the shorter recovery times, reductions in pain, and lack of surgery-related adverse events associated with POEM may be especially desirable in children [11, 50, 51]. In our analysis, a study by Tan et al. revealed better intermediate and long-term efficacy in POEM than endoscopic balloon dilatation, and a study by Caldaro et al. showed LHM and POEM are comparable in efficacy. In adults, certain studies have shown superiority or, at least, non-inferiority of POEM compared to alternative treatments such as LHM. However, these studies were much larger than those included in our analysis, with a systematic review by Schlottman et al. reviewing data on 5834 patients who underwent LHM against 1958 patients who underwent POEM [22, 52]. Therefore, larger studies including randomized trials are necessary to establish the utility of POEM in pediatric patients in relation to other treatments achalasia, as has been done for adults [12, 23, 48, 53]. In our studies, adverse events were mostly limited to minor events that were managed during surgery or conservatively after surgery, such as mucosal injuries or clinical reflux symptoms, which is similar to what was reported in adult patients [23, 54]. The majority of serious adverse events that occurred were from a few select studies [32, 33] instead of being spread across all studies, indicating skill level of the operator and the endoscopic team may be important in determining outcomes. Indeed, POEM is a relatively technically challenging procedure that may require an experienced operator to achieve optimal outcomes, in both pediatric and adult patients [20, 35]. Furthermore, postoperative GERD is an important issue following POEM or any other achalasia treatment critically, the majority of studies did not provide data on ambulatory 24-h pH monitoring, which is the gold standard in the diagnosis of GERD [55]. Additional outcomes that are commonly reported in adult studies of POEM, such as postoperative pain score and postoperative analgesic requirements, among others, were not included in any of the studies we identified [23]. This may be because outcomes such as pain level are difficult to ascertain in pediatric patients [56]. Regardless, future trials should collect these data in order to better establish comparison of pediatric POEM outcomes to outcomes in adults.

Overall, our review supports the claim that the age of patients is not a contraindication to POEM technique, but further work is necessary to establish its utility in comparison to other achalasia treatment modalities in pediatric patients before POEM can be recommended as a first-line treatment [16]. In adults, POEM has been shown to be superior to LHM, providing similar outcomes and safety profile with shorter hospitalization, lower cost, and less scarring and discomfort [21, 57, 58]. Though Caldaro et al. came to similar conclusions, the limited size of this single study makes it difficult to definitively recommend POEM over LHM as first-line treatment of pediatric achalasia. Pediatric surgeons and interventional gastroenterologists should understand that POEM is a safe and effective procedure in young patients, but clinical judgment must be used in deciding between treatment modalities in these

patient populations, as the current level of evidence as identified by our review is insufficient to make any definitive recommendations on altering standard of care.

Our findings should be interpreted in light of a number of limitations. MINORS assessment of the included studies indicates that there was an overall fair quality of evidence for non-randomized studies in our review [26]. However, it is important to consider that several of our included studies were case series with no control groups or comparators, which is a very low level of evidence [59]. Despite the total number of patients being 142, all of the included studies had a small sample size of under 30 patients. In addition, most of the studies included did not report a follow up time greater than 2 years, which is necessary to establish efficacy and safety of the procedure past 2 years. In this study, we have included all the pediatric POEM studies in the literature. However, there may be a few pediatric patients in non-pediatric study cohorts, which we could not capture in our analysis. There were no randomized trials included, and only two of the included studies reported a comparison of POEM to another treatment modality. As a result, it is difficult to draw conclusions on the efficacy of POEM relative to the standard of care (LHM) or to endoscopic balloon dilatation, limiting the applicability of our findings to the general pediatric population. Several studies also had missing data on POEM characteristics, with some studies not reporting the mean submucosal tunnel length, total myotomy length, and type of knife used, making it difficult to compare the practice variation that exists when conducting POEM in pediatric patients. Any unknown potential heterogeneity in the execution of the procedure could also be a confounding factor in our results.

## Conclusion

Our review demonstrates that POEM is effective and safe for pediatric patients. It demonstrates a significant decrease in both Eckardt score and LES pressure after surgery, with a substantial proportion of patients experiencing improved or complete resolution symptoms after surgery. However, future high-quality studies, preferably randomized controlled trials comparing POEM to another modality such as LHM or balloon dilatation, are warranted in order to recommend POEM as a first-line procedure for pediatric patients with achalasia.

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## Compliance with ethical standards

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