

Review
Article

Quality of Life Following Peroral Endoscopic Myotomy for Esophageal Achalasia: A Systematic Review and Meta-Analysis

Chunyu Zhong, MD,^{1,†} Shali Tan, MD,^{1,†} Yutang Ren, MD, PhD,² Muhan Lü, MD, PhD,¹ Yan Peng, MD,¹ Xiangsheng Fu, MD, PhD,³ and Xiaowei Tang, MD, PhD¹

Background: Peroral endoscopic myotomy (POEM) is a novel minimally invasive intervention for treating esophageal achalasia. Previous publications have proved its excellent efficacy and safety, and even shown it could improve patients' quality of life (QoL). So, we conducted this study to explore the changes of QoL following POEM.

Methods: A comprehensive literature search was conducted on PubMed, EMBASE, and Cochrane Library covering the period from January 2009 to April 2019. The statistical analysis was carried out using Review Manager 5.3.

Results: A total of 12 studies including 549 patients were identified, which assessed the QoL using validated questionnaires administered. After POEM, the SF-36 questionnaire score of each domain (physical function, role physical function, body pain, general health (GH), social function, vitality, emotional role function, mental health) was significantly increased ($p < 0.05$). Meanwhile, mental component scale (MCS) and physical component scale (PCS) scores were all improved in patients after POEM procedure (MCS: 12.11, 95% confidence interval [CI], 4.67–19.55, $p = 0.001$, $I^2 = 88\%$, PCS: 17.01, 95% CI, 2.91–31.11, $p = 0.02$, $I^2 = 97\%$). The gastroesophageal reflux disease health-related quality of life questionnaires (GERD-HRQL) also decreased significantly after POEM (13.01, 95% CI, 9.98–16.03, $p < 0.00001$, $I^2 = 30\%$).

Conclusions: Our current evidence suggests there is significant improvement in QoL after POEM procedure.

Keywords: achalasia, peroral endoscopic myotomy, quality of life, interventional endoscopy, meta-analysis

Introduction

Achalasia is a rare condition, characterized by a functional obstruction of the esophagus that is caused by failed

relaxation of the lower esophageal sphincter (LES). It is estimated that its annual incidence is 0.5–1.5 per 100,000 population.^{1,2} Clinical symptoms of achalasia include dysphagia for both solids and liquids, regurgitation of

¹Department of Gastroenterology, Affiliated Hospital of Southwest Medical University, Luzhou, China

²Department of Gastroenterology, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China

³Department of Gastroenterology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China

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Corresponding authors: Xiaowei Tang, MD, PhD. Department of Gastroenterology, Affiliated Hospital of Southwest Medical University, Street Taiping No.25, Region Jiangyang, Luzhou 646099, Sichuan Province, China

Email: solitude5834@hotmail.com

Xiangsheng Fu, MD, PhD. Department of Gastroenterology, the Affiliated Hospital of North Sichuan Medical College, Road Wenhua 63#, Region Shunqing, Sichuan 637000, China

Email: drfuxs@gmail.com

[†]These authors contributed equally to this study.



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undigested food, respiratory complications, chest pain, weight loss, and patients often have a reduced quality of life (QoL) and workforce participation.³⁾ Treatment of achalasia aims to disrupt or dissect the LES pressure. Medical therapy is often ineffective, and injection of botulinum toxin into LES is suitable for older and multimorbid patients due to its less invasiveness, but with short-term efficacy. Presently, laparoscopic Heller myotomy (LHM), pneumatic dilatation, and peroral endoscopic myotomy (POEM) have been regarded as the most effective methods for achalasia.⁴⁾ LHM is considered the gold standard in achalasia treatment since it provides superior and long-lasting symptom relief for patients.⁵⁾ However, with the development of endoscopic technique, POEM procedure, which is less invasive than LHM, has been becoming the first choice for more doctors and patients. Previous publications have proved the excellent efficacy and safety of POEM, and even shown this novel endoscopic intervention could improve patients' life quality.⁶⁻¹⁸⁾

QoL is a multidimensional construct that is affected by physical health, psychological health, functional status, and social circumstances which may be classified as disease specific or generic.¹⁹⁾ There is a growing number of people who thought that QoL after procedure was as important as overall survival.²⁰⁾ However, there has been no meta-analysis to review the effect of POEM to QoL. Therefore, we conducted this study to explore the pooled results of QoL following POEM procedure.

Methods

Search strategy

The systematic review was carried out in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).²¹⁾ Electronic database searches were performed in Pubmed, EMBASE, and Cochrane library from January 2009 to April 2019 using the following search terms: achalasia, POEM, peroral endoscopic myotomy, and quality of life. There was no limitation on language. Articles were selected for full-text review based on their title and abstract. References of relevant articles were scanned for potential missed studies. Detailed search terms used in each of the databases are listed in **Supplementary Table 1** (All Supplementary Tables and Figures are available online). Our research does not require IRB approval and written consent.

Study selection

Title, abstracts, and full-text publications of all potentially eligible articles were screened by two reviewers independently. Any disagreements were resolved by discussion and re-examination of the paper. The inclusion criteria were as follows: studies using assessment tools to evaluate the QoL after POEM. The exclusion criteria were as follows: case reports with <3 patients, commentaries or general reviews, conference abstracts, and studies did not provide the available data for QoL assessment tools. For overlapping publications from the same center, only the most recent and comprehensive publication was considered for inclusion.

Data extraction

Two authors performed data extraction independently using a predefined data extraction form. Extracted data included characteristics of studies: first author, year of publication, country, study duration, study design, number of patients, age, gender, follow-up time, QoL assessment tools, QoL score pre-procedure, and post-procedure assessment intervals and compliance.

Outcome measures

The main outcome measures of the studies included improvement in the 36-item short-form Health Survey (SF-36) score and decline in the gastroesophageal reflux disease health-related quality of life (GERD-HRQL) score. The SF-36 is divided into eight healthcare domains that include physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH).²²⁾ Among them, the first four parts constitute physical component scale (PCS) and the last four parts constitute mental component scale (MCS). Every part is scored from 0 to 100, with a higher values indicating a greater perceived QoL. The GERD-HRQL questionnaire is a 10-item disease-specific tool focused on heartburn, dysphagia gas bloat symptoms. Each symptom has an assigned score between 0 and 5 and the total score was 50 points. An additional question, not included in the calculated score, concerns patients' satisfaction with their present condition. The lower the score indicated the higher the QoL.²³⁾

Assessment of study quality

Information relating to the methodological quality was recorded for each study. Quality assessment was done by two reviewers independently using the National Institutes

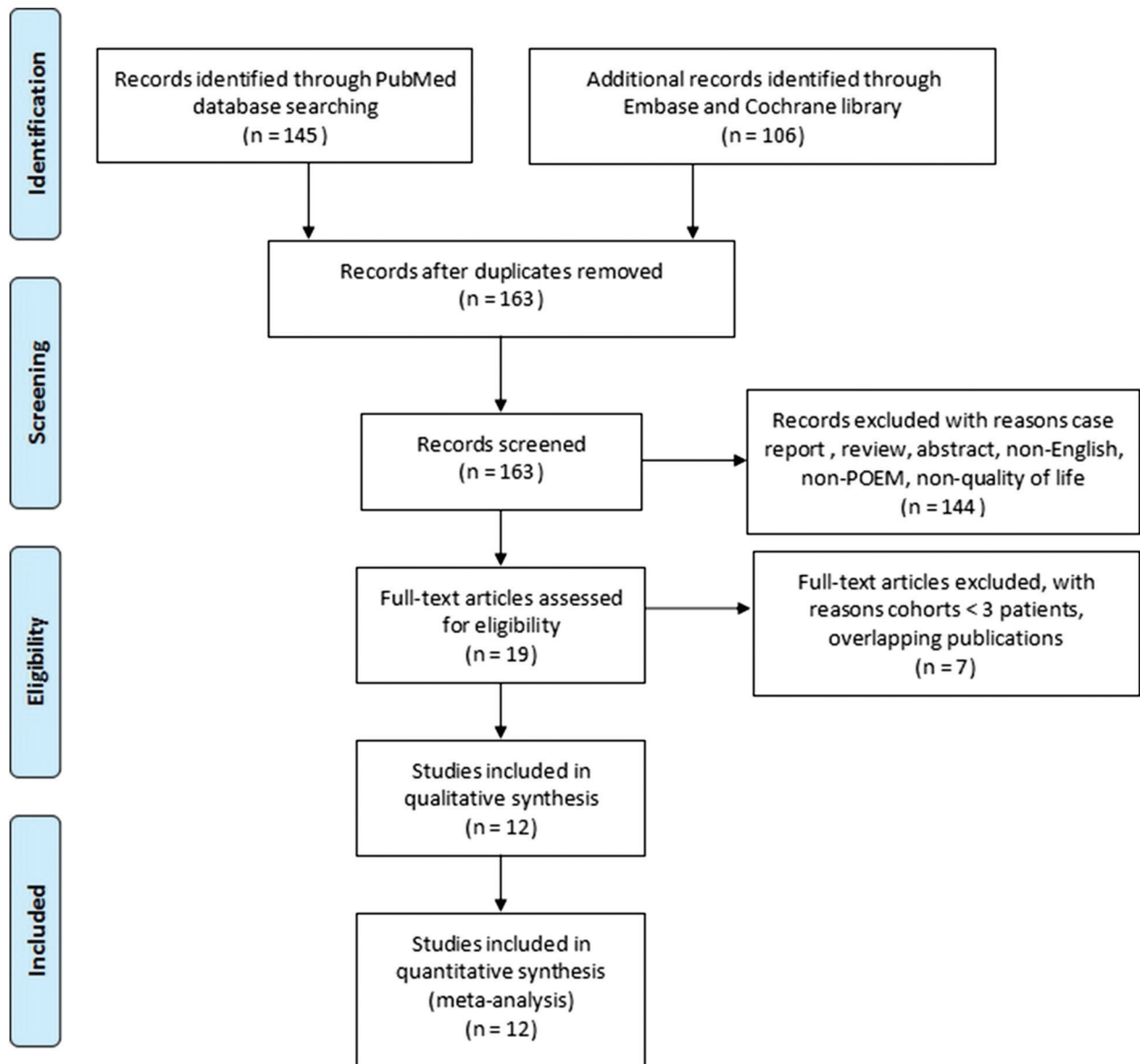


Fig. 1 PRISMA diagram showing the flow of study selection. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

of Health (NIH) quality assessment tool for before–after studies with no control group.²⁴⁾ Studies were rated as “good” when at least 70% out of 12 assessment criteria were fulfilled, “fair” when at least 50%, or poor when less than 50% of the criteria were fulfilled. Any disagreement between reviewers was resolved by consensus.

Statistical analysis

Continuous variables were expressed as the mean, standard deviation (SD), inter-quartile range, and categorical data were displayed as number (n) and percentage. The statistical analysis was carried out using Review Manager 5.3. Statistical heterogeneity among studies

was assessed with the I^2 statistics. I^2 value of greater than 50% was considered to indicate significant heterogeneity. Random-effect model was used when there was heterogeneity, while a fixed effect model was used in the absence of heterogeneity. Publication bias was assessed via visual inspection of the funnel plot.

Results

Characteristics of included studies

As shown in **Fig. 1**, initial search terms identified 251 studies, of which 163 were screened for eligibility criteria after removing duplicates. Of these, 19 studies fulfilled

criteria for eligibility assessment, other 144 studies that were case report, review, abstract, non-English, not related to POEM and not mentioned QoL were excluded. Of the remaining 19 studies, 12 attained the inclusion criteria for quantitative analysis. Among the seven excluded studies, there were cohorts less than three patients or overlapping publications.

Table 1 shows the studies and patient characteristics. All the studies included in our review were published between 2013 and 2018. They were published in the United States (n = 7), China (n = 4), and Mexico (n = 1). Of the included studies, six were retrospective and other six were prospective studies.

Patients’ characteristics

A total of 549 patients were pooled from 12 studies. Only 10 studies included 544 patients reported the patients’ gender and age. Of them, 245 (45.0%) patients were male, and the mean age ranged from 41.6 to 67.0 years. The follow-up duration for the patients was available in 11 studies, which was ranged from 1.2 months to 46.2 months (**Table 1**).

Quality of life

As shown in **Table 2**, in the 12 studies we included, a total of four kinds of scales were used to evaluate the QoL. Among them, seven studies selected SF-36 to evaluate QoL, five selected GERD-HRQL, one selected 12-item short-form Health Survey (SF-12), and one selected a disease-specific questionnaire for achalasia developed and validated in Spanish language with 18 items and four subscales (AE-18).

Each of SF-36 domain scores before and after POEM are shown in **Table 3**. **Figure 2A** revealed the MCS scores were significantly improved in patients after POEM procedure (12.11, 95% confidence interval [CI], 4.67–19.55, p = 0.001, I² = 88%). There were also significantly improved in each domain of MCS scores after POEM, with increasing by 11.91 points for SF (mean difference [MD]: 11.91; 95% CI, 10.56–13.25, p <0.00001, I² = 0%), 8.51 points for VT (MD: 8.51; 95% CI, 4.68–12.44, p <0.0001, I² = 55%), 12.39 points for RE (MD 12.39; 95% CI, 2.06–22.71, p = 0.02, I² = 62%), 7.14 points for MH (MD: 7.18; 95% CI, 6.25–8.11, p <0.00001, I² = 0%) (**Fig. 2B**). Similarly, **Fig. 3A** shows the PCS scores were significantly increased by 17.01 after POEM procedure (MD 17.01, 95% CI, 2.91–31.11, p = 0.02, I² = 97%). There were also significantly improved in each domain of PCS scores

Table 1 The basic characteristics of included studies

Study	Year of publication	Country	Duration	Study design	Patient, n	Age (years)	Gender (M:F)	Follow-up (months)
Meireles et al. ⁽⁷⁾	2013	United States	Jan 2010–Dec 2010	Retrospective	5	42.4	–	–
Ling et al. ⁽⁸⁾	2014	China	Sept 2010–Jun 2012	Prospective	87	41.6 ± 15.6	40:47	1.2 ± 0.3
Orenstein et al. ⁽⁹⁾	2015	United States	May 2011–Sept 2013	Retrospective	40	–	–	10
Li et al. ⁽¹⁰⁾	2015	China	Nov 2011–Aug 2014	Prospective	15	67 (65–84)	6:9	18 (6–39)
Liu et al. ⁽¹¹⁾	2015	China	May 2013–Dec 2013	Retrospective	35	40.2 (15–63)	11:24	11.4 (6–15)
Vigneswaran et al. ⁽¹²⁾	2016	United States	Aug 2011	Prospective	37	64 ± 18	24:13	6.97
Hoppo et al. ⁽¹³⁾	2016	United States	Jan 2013–Oct 2014	Retrospective	25	56.9 (23–86)	–	7 (0.5–17)
Jones et al. ⁽¹⁴⁾	2016	United States	Aug 2012–Jun 2014	Prospective	43	53.5 ± 17.4	27:16	6
Hernández	2017	Mexico	Feb 2012–Nov 2016	Retrospective	65	47 (20–81)	27:38	at least 12
Mondragón et al. ⁽¹⁵⁾	2017	China	2011–2016	Retrospective	13	37.5 ± 13.0	8:5	46.2 ± 4.1
Peng et al. ⁽¹⁶⁾	2017	United States	2011–2016	Prospective	41	63.0 ± 17.9	25:16	at least 12
Perbtani et al. ⁽¹⁸⁾	2018	United States	Mar 2013–Oct 2016	Prospective	143	58 ± 18	77:66	16.4 (12–40)

M:F: male to female; NA: not available

Table 2 Quality-of-life outcomes after POEM procedure

Study	QOL assessment tools	Best score	Preoperative			Postoperative			P value	Assessment intervals (months)	Compliance
			Mean	SD	n	Mean	SD	n			
Meireles et al. ⁷⁾	GERD-HRQL	50	20	-	3	11.3 (7 days) 2 (30 days)	-	3	7 days, 30 days	3/5 (60%)	
Ling et al. ⁸⁾	SF-36 (Sum Physical)	100	32.6	11.2	87	68.5	18.3	87	The last follow-up	-	
Orenstein et al. ⁹⁾	SF-36 (Sum Mental)	100	44.1	12.9	87	67.4	14.6	87	-	40/40 (100%)	
	GERD-HRQL	50	18.28	-	40	5.26	-	40	-	-	
	SF-12 (Sum Physical)	100	41.98	-	40	46.48	-	40	-	-	
	SF-12 (Sum Mental)	100	42.54	-	40	52.02	-	40	-	-	
Li et al. ¹⁰⁾	SF-36 (Sum Physical)	100	76.25	37.52	15	92.25	12.94	15	1, 6	15/15 (100%)	
	SF-36 (Sum Mental)	100	90	25.12	15	92.25	8.23	15	-	-	
Liu et al. ¹¹⁾	SF-36 (Sum Physical)	100	71.47	30.08	35	93.66	14.96	35	1, 6	35/35 (100%)	
	SF-36 (Sum Mental)	100	73.88	26.06	35	90.15	11.83	35	-	-	
Vigneswaran et al. ¹²⁾	SF-36 (Sum Physical)	100	74.25	35.43	37	88.75	35.37	19	3 weeks, 6, 12	19/37 (51%)	
	SF-36 (Sum Mental)	100	71	34.72	37	79.5	23.40	19	-	-	
Hoppo et al. ¹³⁾	GERD-HRQL	50	16.3	11.6	19	6.7	8.1	19	6 weeks, 6, 12	19/25 (76%)	
Jones et al. ¹⁴⁾	GERD-HRQL	50	22	9.15	43	8	6.89	42	6	42/43 (98%)	
Hernández Mondragón et al. ¹⁵⁾	AE-18	90	40 (28-53)	-	65	68	-	50	1, 6, 12, 24, 36, 48	50/65 (77%)	
Peng et al. ¹⁶⁾	SF-36 (Sum Physical)	100	76.73	13.62	13	81.3	11.83	13	36	13/13 (100%)	
	SF-36 (Sum Mental)	100	68.15	16.88	13	72.53	16.88	13	36	-	
Ward et al. ¹⁷⁾	SF-36 (Sum Physical)	100	68.68	-	41	75.05	-	41	3 weeks, 6, 12	25/41 (60%)	
	SF-36 (Sum Mental)	100	64	-	41	73.45	-	41	-	-	
Perbani et al. ¹⁸⁾	GERD-HRQL	50	16.5	-	41	6.79	-	41	<0.05	-	
	SF-36 (Sum Physical)	100	55.8	2.2	143	63.6	3.3	41	1, 6, 12	41/143 (29%)	
	SF-36 (Sum Mental)	100	61.5	2.2	143	71.2	3.6	41	<0.05	<0.05	

*p<0.05 is considered significant. AE-18: A disease-specific questionnaire for achalasia developed and validated in Spanish language with 18 items and four subscales; GERD-HRQL: gastroesophageal reflux disease health-related quality of life; POEM: peroral endoscopic myotomy; QOL: quality of life; SF-36: 36-item Health Survey; SF-12: 12-item Health Survey

Table 3 SF-36 domain scores before and after POEM

Study	Time	Physical function	Role physical	Bodily pain	General health	Social functioning	Vitality	Role emotional	Mental health	Compliance
Li et al. ¹⁰⁾	Preoperative	85 (75–90)	100 (50–100)	68 (52–100)	52 (35–77)	100 (67–100)	80 (50–80)	100 (67–100)	80 (72–88)	–
	Post 1 month	90 (85–90)	100 (81–100)	84 (72–100)	77 (57–77)	100 (78–100)	85 (80–85)	100 (100–100)	84 (80–88)	–
	Post 6 months	90 (85–90)	100 (100–100)	92 (84–100)	87 (72–97)	100 (100–100)	85 (80–85)	100 (100–100)	84 (80–84)	–
Liu et al. ¹¹⁾	Preoperative	93.29 ± 9.54	72.86 ± 40.39	69.45 ± 25.21	50.29 ± 19.56	81.90 ± 23.97	71.14 ± 16.14	67.62 ± 40.00	74.86 ± 15.02	–
	Post 1 month	98.14 ± 5.16	87.14 ± 32.86	86.74 ± 18.04	73.83 ± 15.73	93.33 ± 14.05	83.57 ± 8.88	93.33 ± 23.98	83.20 ± 8.50	–
	Post 6 months	99.16 ± 2.45	92.50 ± 23.6	96.00 ± 8.66	86.97 ± 13.89	98.15 ± 6.08	83.00 ± 3.56	96.76 ± 16.86	82.67 ± 4.15	–
Vigneshwaran et al. ¹²⁾	Preoperative	85 (55–100)	69 (50–100)	73 (45–100)	70 (55–83)	75 (50–100)	56 (44–75)	83 (42–100)	69 (50–88)	37/37 (100%)
	Post 3 weeks	89 (55–100)	88 (63–100)	90 (68–100)	75 (60–85)	88 (50–100)	63 (50–81)	100 (67–100)	78 (69–94)	30/37 (81%)
	Post 6 months	71.4 (50–100)	94 (50–100)	79 (68–100)	75 (65–85)	88 (63–100)	63 (50–75)	100 (58–100)	88 (75–88)	26/37 (70%)
Peng et al. ¹⁶⁾	Preoperative	95 (50–100)	100 (63–100)	85 (45–100)	75 (60–85)	88 (75–100)	63 (56–75)	92 (67–100)	81 (63–88)	19/37 (51%)
	Post 12 months	81.3 ± 12.1	75.0 ± 18.5	76.8 ± 13.7	73.8 ± 8.8	72.0 ± 19.3	63.3 ± 8.6	67 (67–100)	70.3 ± 8.6	13/13 (100%)
	Post Last	83.8 ± 10.7	87.5 ± 13.1	77.7 ± 13.0	76.2 ± 7.0	81.5 ± 14.5	64.6 ± 9.2	67 (67–100)	77.0 ± 8.0	13/13 (100%)
Ward et al. ¹⁷⁾	Follow-up	75.4	65.9	67.3	66.1	64.6	54.9	69.2	67.3	41/41 (100%)
	Preoperative	70.8	81.8	76.9	70.7	83	60.7	78.8	71.3	41/41 (100%)
	Post 12 months	62 ± 2.6	44.5 ± 3.8	59.5 ± 2.3	56.6 ± 2	67 ± 2.5	43.4 ± 2	66.5 ± 3.6	68.3 ± 1.9	143/143 (100%)
Perbtani et al. ¹⁸⁾	Preoperative	69.9 ± 1.8	61.3 ± 4.1	70 ± 2.2	65.3 ± 1.6	76.7 ± 2.6	53.2 ± 1.9	78.5 ± 3.6	76.4 ± 1.7	117/143 (82%)
	Post 1 month	72.2 ± 2.4	69.9 ± 5.4	69.6 ± 2.8	63.2 ± 2.1	82.4 ± 3.3	56.4 ± 2.6	76.5 ± 4.9	75 ± 2.2	65/143 (45%)
	Post 6 months	68 ± 3.2	58.7 ± 7.3	66.5 ± 3.5	61.3 ± 2.5	78.8 ± 4.3	54.4 ± 3.5	76 ± 6.8	75.5 ± 3	41/143 (29%)

POEM: peroral endoscopic myotomy; SF-36: 36-item Health Survey

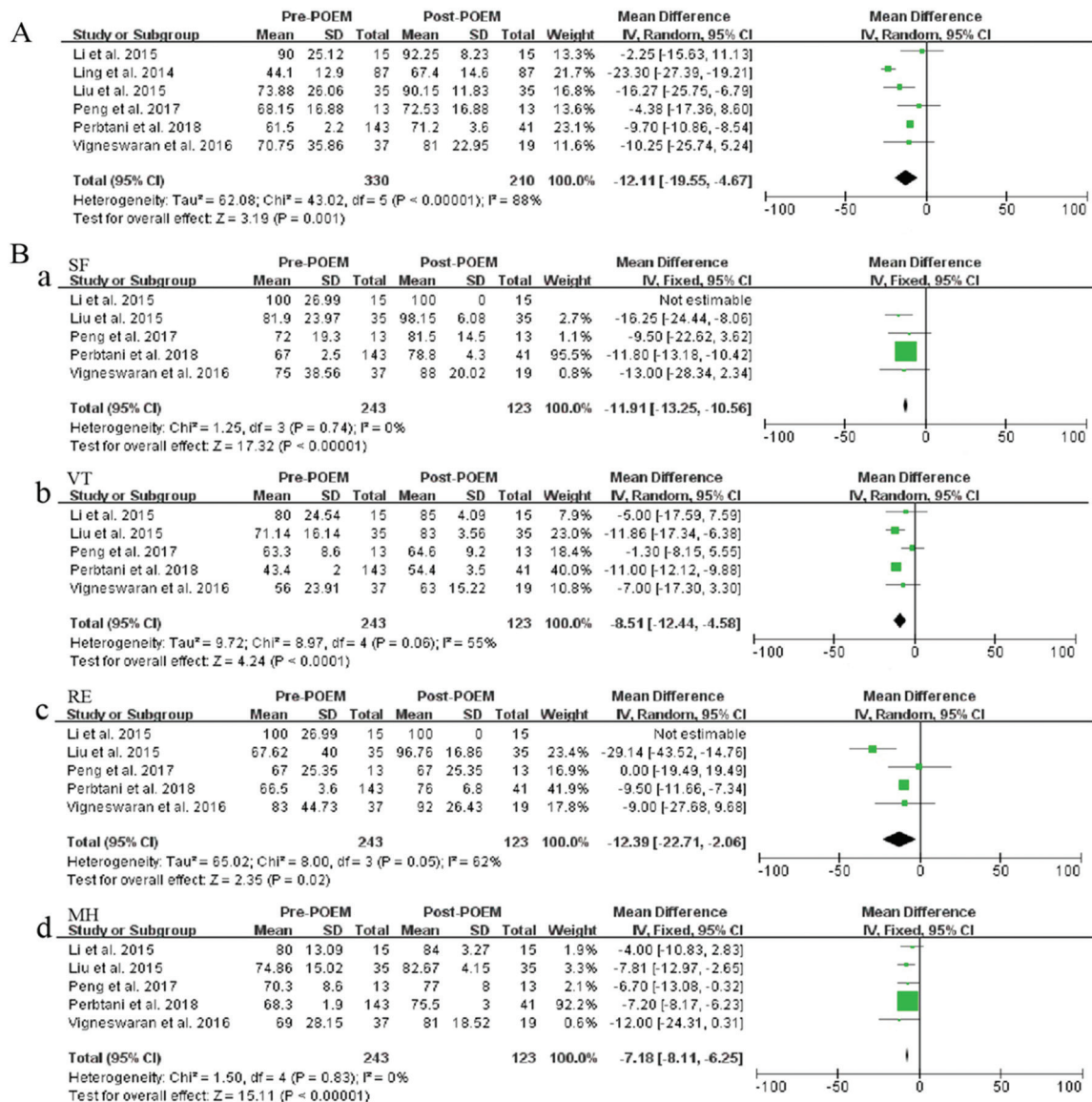


Fig. 2 (A) Forest plot of meta-analysis assessing the QoL of MCS score before and after POEM procedure. (B) Forest plot of each domain for MCS score before and after procedure. MCS: mental component scale; MH: mental health; POEM: peroral endoscopic myotomy; QoL: quality of life; RE: role emotional; SF: social function; VT: vitality

after POEM, with increasing by 5.93 points for PF (MD 5.93; 95% CI, 4.93–6.92, $p < 0.00001$, $I^2 = 0\%$), 14.51 points for RP (MD 14.51; 95% CI, 12.27–16.75, $p < 0.00001$, $I^2 = 20\%$), 13.11 points for BP (MD 13.11; 95% CI, 2.84–23.38, $p = 0.01$, $I^2 = 82\%$), and 15.34 points for GH (MD 15.24; 95% CI, 3.07–27.61, $p < 0.00001$, $I^2 = 94\%$) (**Fig. 3B**). It was also obviously understood the change of the score through visual inspection of the line chart, shown in **Figs 4** and **5**. **Figure 6** shows the mean GERD-HRQL scores were significantly decreased by 13.01 after POEM procedure (MD 13.01, 95% CI, 9.98–16.03, $p < 0.00001$, $I^2 = 30\%$).

During the 6-month follow-up, the MCS and PCS scores were significantly higher in patients at 6 months after POEM procedure (MCS: 11.20, 95% CI, 8.82–13.58, $p < 0.00001$, $I^2 = 0\%$; PCS: 13.01, 95% CI, 11.81–14.21, $p < 0.00001$, $I^2 = 14\%$). There were also significant improvement in each domain of SF-36 scores at 6 months after POEM ($p < 0.05$) (**Supplementary Fig. 1**). Furthermore, the MCS and PCS scores were significantly higher in patients at 12 months after POEM procedure (MCS: 9.70, 95% CI, 8.55–10.86, $p < 0.00001$, $I^2 = 0\%$; PCS: 7.82, 95% CI, 6.75–8.89, $p < 0.00001$, $I^2 = 0\%$). There were also significant improvement in each domain of

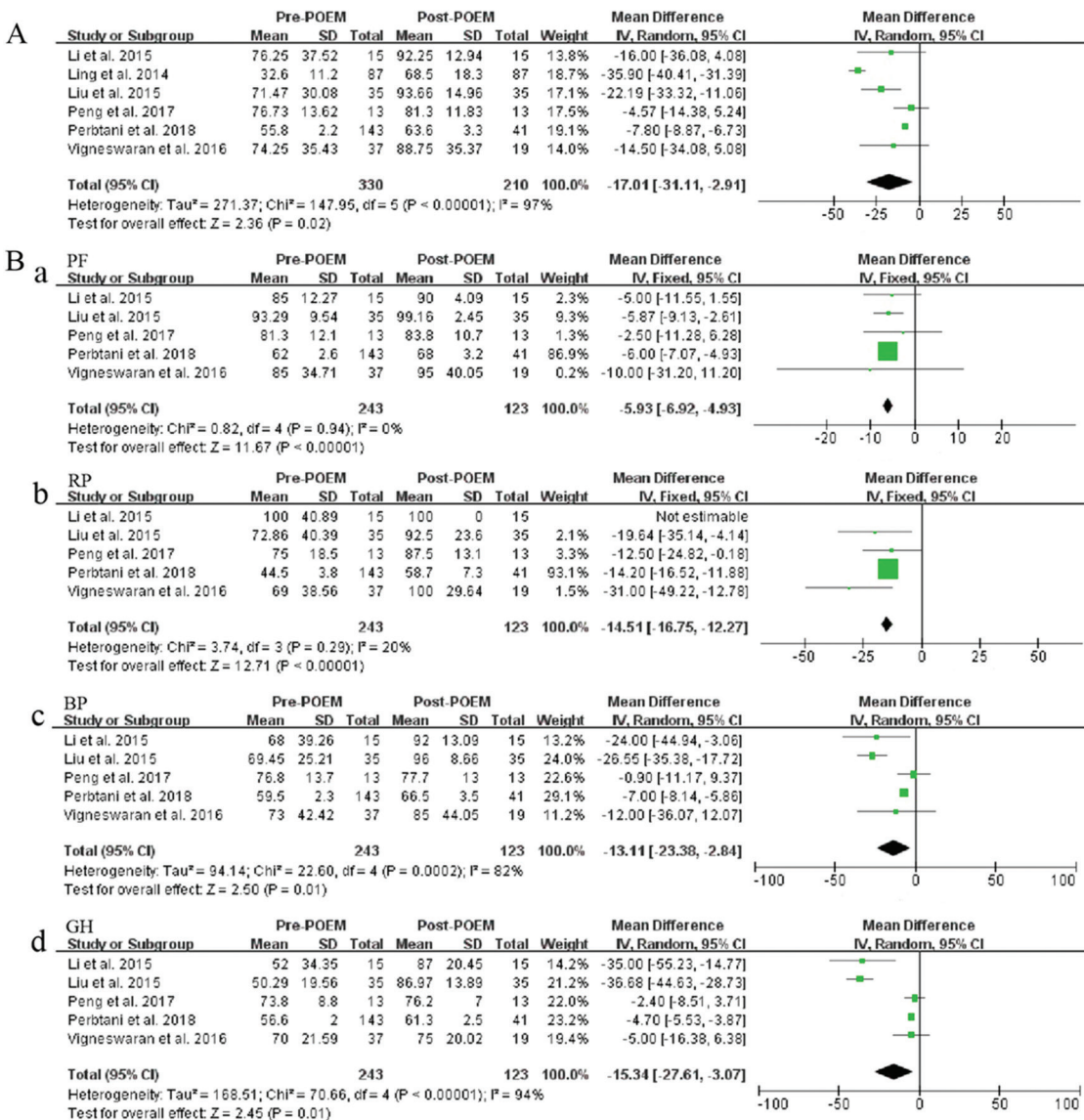


Fig. 3 (A) Forest plot of meta-analysis assessing the QoL of PCS score before and after POEM procedure. (B) Forest plot of each domain for PCS score before and after procedure. BP: bodily pain; GH: general health; MCS: physical component scale; PF: physical function; POEM: peroral endoscopic myotomy; QoL: quality of life; RP: role physical

SF-36 scores at 12 months after POEM (p < 0.05) (Supplementary Fig. 2).

Publication bias and quality of included studies

Through visual inspection of the funnel plot, no publication bias can be generally considered (Supplementary Fig. 3). Supplementary Table 2 shows the quality assessment of each study according to using NIH quality assessment tool. Out of 12 involved studies, seven studies^{11,12,14-18} were of good quality and the remaining five studies^{7-10,13} were of fair quality.

Discussion

The use of endoscopic method for the treatment of achalasia was first reported by Ortega et al in 1980.²⁵ They introduced this technique for using an endoscopic knife to cut the muscular fibers from the luminal side. However, it was not widely accepted for concerning of the high risk of perforation.²⁵ In 2007, Pasricha et al.²⁶ first reported the feasibility of performing endoscopic submucosal esophageal myotomy in four pigs model. Inoue et al.²⁷ successfully performed the first POEM in

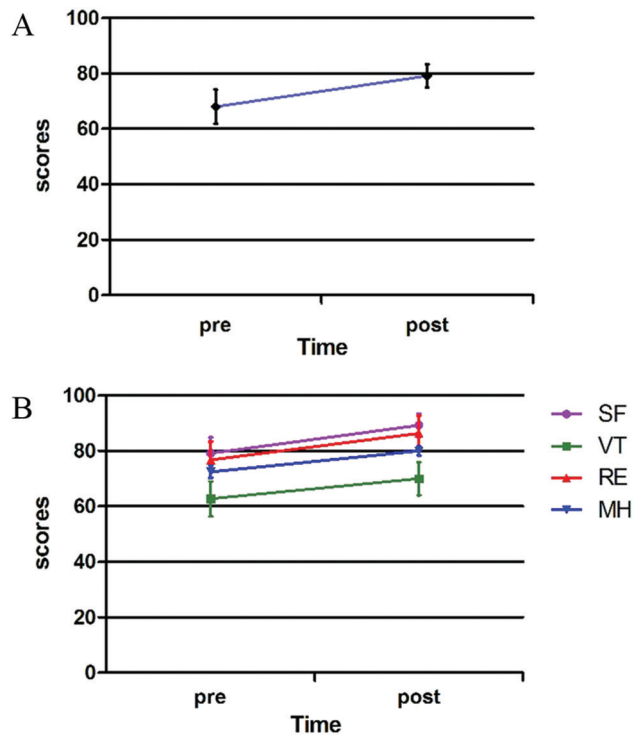


Fig. 4 (A) The changes of MCS score in patients undergoing POEM (The score of MCS increased from 68.06 to 79.09). (B) The changes of each domain for MCS score in patients undergoing POEM (SF from 79.18 to 89.29, VT from 62.77 to 70, RE from 76.82 to 86.35, MH from 72.49 to 80.03). MCS: mental component scale; MH: mental health; POEM: peroral endoscopic myotomy; RE: role emotional; SF: social function; VT: vitality

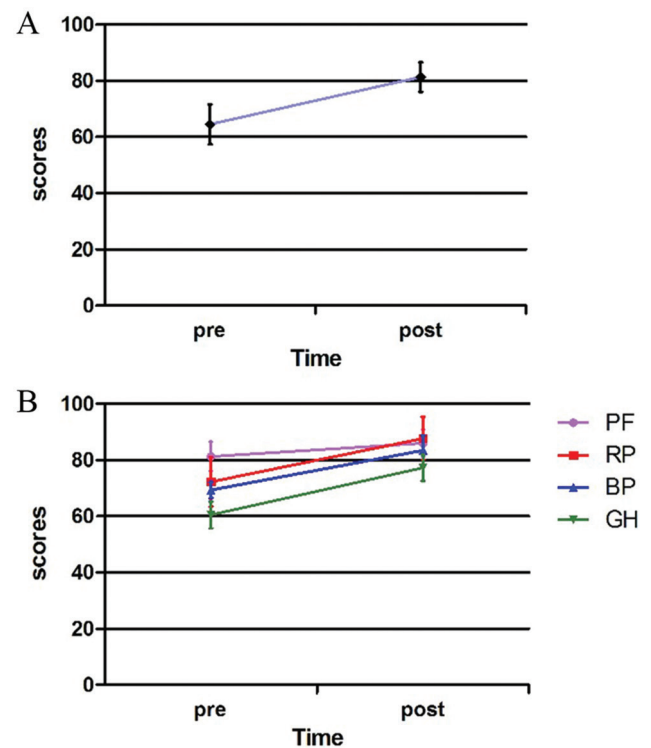


Fig. 5 (A) The changes of PCS score in patients undergoing POEM (The score of PCS increased from 64.52 to 81.34). (B) The changes of each domain for PCS score in patients undergoing POEM. (PF from 81.32 to 86.02, RP from 72.27 to 87.74, BP from 69.35 to 83.44, GH from 60.54 to 77.29). BP: bodily pain; GH: general health; PCS: physical component scale; POEM: peroral endoscopic myotomy; PF: physical function; RP: role physical

humans in 2010. Since then, there have been a number of publications with POEM for achalasia. The meta-analysis of Barbieri et al. and Evensen et al. showed that the pooled technical and clinical success of POEM for treatment achalasia was more than 90%.^{4,28} In addition to the excellent clinical outcomes, this novel endoscopic approach has also been reported to improve the QoL in achalasia patients during follow-up.⁶⁻¹² However, there has been no meta-analysis to review the effect of POEM to QoL for patients. Our study included 12 clinical trials which assessed the impact of POEM interventions for achalasia on QoL. We demonstrated that POEM could significantly improve the QoL for patients, showing the increased of SF-36 scores and decreased of GERD-HRQL scores.

Most of the study we included used the SF-36 to evaluate the improvement of QoL.^{8,11,12,16-18} The SF-36 was a multi-purpose, short-form health survey which contains 36 questions. And it yielded an eight-scale profile (PF, RP, BP, GH, SF, VT, RE, and MH) of scores as well

as PCS and MCS. The SF-36 was regarded as a common measure of health status, and it has been proven useful in comparing general and specific populations, estimating the burden of different diseases and differentiating the health benefits produced by different treatments methods.^{22,29} Our study found that the PCS and MCS, specifically in each eight-scale profile of SF-36 score were significantly increased after POEM procedure. Among the six studies mentioned the SF-36 scale, four articles reported that several domains of the eight domains did not demonstrate any significant differences in scores.^{10,12,16,17} But Liu et al and Perbtani et al reported the each domain of SF-36 was significantly improved.^{11,18} We guess that the reason may be due to the small sample size in these four studies.

The GERD-HRQL scale is a validated 15-item questionnaire describing heartburn and regurgitation to measure the severity of GERD symptoms.²³ Since POEM procedure was aim to disrupt the LES pressure, and no anti-reflux program were added for treatment achalasia,

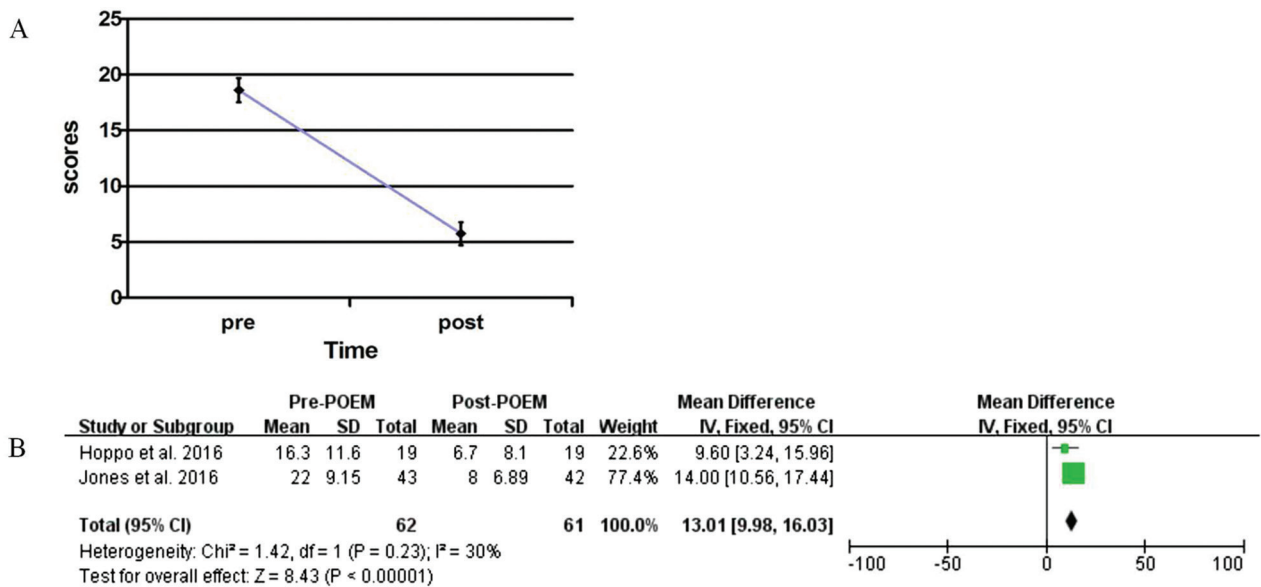


Fig. 6 (A) The changes of GERD-HRQL score in patients undergoing POEM (The score of GERD-HRQL decreased from 18.62 to 5.75). (B) Forest plot of meta-analysis assessing the QoL of POEM on GERD-HRQL score before and after procedure. GERD-HRQL: gastroesophageal reflux disease health-related quality of life; POEM: peroral endoscopic myotomy

the initial focus was post-procedure GERD symptoms. Interestingly, our study found that the POEM procedure could significantly decreased the GERD-HROL scores, which indicated the GERD symptoms were improved. Jones et al. indicated that the majority of patients will have abnormal distal esophageal acid exposure but that does not result in symptoms of reflux. Hoppo et al. deemed that POEM preserved the patients’ anti-flux barrier structure, such as phrenoesophageal membrane and the His angle, which theoretically reduced the risk of post-procedure GERD.¹³⁾ But there were just two studies reported the changes of GERD-HROL scores after POEM, the effect of POEM for GERD-HROL scores still need further researches with long-term follow-up.

In one study by Li et al. we involved, they tried to evaluate the safety and efficacy of POEM for achalasia in patients aged >65 years.¹⁰⁾ They found that the POEM could also significantly improve the QoL of the elderly (PF, RP, VT, SF, BP, and GH scores were all significantly higher after POEM procedure; p <0.05). After we removed this study in our meta-analysis, there was also a significant improvement of QoL after POEM (**Supplementary Fig. 4**).

LHM has been considered to be the gold standard for treating achalasia for a number of years.³⁰⁾ In our involved study, Peng et al. found that there was no difference in QoL between the POEM group and LHM for treating achalasia among the SF-36 scores.¹⁶⁾ LHM

usually added a partial fundoplication to prevent postoperative reflux. But Zurita Macías Valadez et al. showed that even LHM without anti-reflux procedure did not induce significant long-term gastroesophageal reflux.³¹⁾ This phenomenon is similar to our results. POEM also did not add anti-reflux procedure, the score of reflux symptoms of the patients was also improved. Further randomized controlled trail is needed to evaluate the GERD-HRQL scores for QoL between LHM and POEM.

Our study has a number of limitations that should be considered. First, due to follow-up time of the included studies was relatively short, our meta-analysis could not analyze the long-term follow-up results. Second, only one of involved studies reported AE-18 and SF-12; therefore, it could not be meta-analyzed. Third, due to most of the studies, we reviewed were retrospective or cohort studies and few randomized controlled trials were available. It may result in selection bias and reporting bias. Finally, some included studied lost data on variables we were interested in, such as means and standard deviation of QoL for patients, which could not allowed us to carry out a more comprehensive meta-analysis.

Conclusion

Our current evidence suggests there is significant improvement in QoL after POEM procedure treatment

achalasia. Further studies with larger sample are warranted to explore the influences of POEM to QoL during the long-term follow-up.

Authors' Contributions

Study conception and design: Xiaowei Tang. Drafting of manuscript: Chunyu Zhong and Shali Tan. Acquisition of data and critical revision: Yutang Ren. Revision of manuscript and final approval of manuscript: Muhan Lü, Yan Peng, Xiangsheng Fu, and Xiaowei Tang.

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Disclosure Statement

Dr. Chunyu Zhong, Dr. Shali Tan, Dr. Yutang Ren, Dr. Muhan Lü, Dr. Yan Peng, Dr. Xiangsheng Fu, and Dr. Xiaowei Tang all have no conflicts of interest or financial ties to disclose.

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