

ORIGINAL PAPERS

Peroral endoscopic myotomy *versus* pneumatic dilation for achalasia in patients aged ≥ 65 years

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ABSTRACT

Background and aim: Both peroral endoscopic myotomy (POEM) and pneumatic dilation (PD) has proved to be effective for treating achalasia in patients aged ≥ 65 years. However little is known about the comparison between POEM and PD. The aim of the study was to compare the safety and efficacy of POEM and PD for the treatment of achalasia in these patients.

Methods: We retrospectively reviewed the medical records of patients aged 65 years-old or more who received POEM or PD for the treatment of achalasia at our hospital from January 2010 to December 2015, they were divided into the POEM group and the PD group. Demographics and data about safety and efficacy were collected retrospectively and compared between the two groups.

Results: A total of 31 patients were enrolled, and 21 of them received POEM, while the other 10 received PD. The treatment success (Eckardt score ≤ 3) rate of POEM and PD at 3, 6, 12, 24 and 36 months after the treatment were comparable ($p > 0.05$). Treatment failure was noticed in 3 cases, 1 of them was in the POEM group and the other 2 in the PD group, there was no significant difference ($p > 0.05$). Multivariate analysis showed that sigmoid-type achalasia was a predictive factor of treatment failure. No severe complications were observed during operation and peridical follow-up.

Conclusion: Short-term and intermediate efficacy of POEM and PD for treating achalasia in patients aged ≥ 65 years was comparable. A large scale, randomized study with long-term follow-up is necessary in order to make a definitive conclusion.

Key words: Achalasia. Pneumatic dilation. Peroral endoscopic myotomy. Old people.

INTRODUCTION

Achalasia is a rare primary esophageal dysmotility disorder, with an estimated annual incidence of 0.3-1.5 cases per 100,000 population, and the highest incidence appears in the seventh decade of life (1,2). It is characterized by failed relaxation of the lower esophageal sphinc-

ter (LES) and absent peristalsis of the distal esophagus. The symptoms of achalasia are dysphagia, regurgitation, aspiration, retrosternal pain, and weight loss (2). All therapeutic options focus on reducing the pressure gradient across the LES, and this can be achieved by pharmacological agents, endoscopic methods (botulinum toxin injection, pneumatic dilation, stent insertion) and surgical myotomy (open or laparoscopic) (2). Endoscopic methods are recommended as the first-line option due to the poly-morbidity and high risk of surgery in patients aged ≥ 65 years, and pneumatic dilation (PD) has been most commonly used (3).

Peroral endoscopic myotomy (POEM) is a novel technique for treating achalasia and has also shown exciting results in patients aged ≥ 65 years (4-6). However little is known about the comparison of safety and efficacy between POEM and PD for the treatment of achalasia in this population. In this study, we collected the clinical data of patients aged ≥ 65 years who received POEM or PD for the treatment of achalasia to compare the safety and efficacy of the two methods.

PATIENTS AND METHODS

Patients

This retrospective study was approved by the ethics committee of the Second Xiangya Hospital of Central South University. The inclusion criteria for enrollment in the study were as follows: a) achalasia diagnosed by established methods, on the basis of symptoms, high-resolution manometry (HRM), esophagogastroduodenoscopy (EGD) and barium esophagram; and b) patients at least 65 years of age. Those patients with severe cardiopulmonary disease or blood coagulation disorders were excluded from the study. Informed consent was obtained from all the patients before the procedure was performed. They were all informed of possible adverse events and other possible treatment options.

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POEM procedure

POEM was performed under general anesthesia via tracheal intubation using a standard single-channel endoscopy (GIF-Q260Z; Olympus, Tokyo, Japan) with a transparent cap (D-201-11802, Olympus) attached to the front. A carbon dioxide insufflator (UCR, Olympus) was used. Other equipment and accessories included a high-frequency generator (VIO 200D; ERBE, Tübingen, Germany), an argon plasma coagulation unit (APC300; ERBE), a hybrid knife (ERBE), a dual knife (KD-650Q; Olympus), an injection needle (NM-4L-1; Olympus), and hemostatic clips (HX-600-90; Olympus). The POEM procedure was performed as previously reported (5):

1. A submucosal injection was made into the right posterior esophageal wall at 8-10 cm above esophagogastric junction (EGJ).
2. A 2-3 cm longitudinal mucosal incision was made to create tunnel entry.
3. A submucosal tunnel was created, passing over the EGJ, and about 3 cm into the proximal stomach.
4. Myotomy was started from 2 to 3 cm below tunnel entry using a hybrid knife (ERBE) or a dual knife (KD-650Q; Olympus). Twelve patients received circular myotomy alone while another nine received full-thickness myotomy at about 3 cm above EGJ and 3 cm below EGJ.
5. Several metal clips were applied to close mucosal entry. Figure 1 describes the procedure of POEM.

PD procedure

PD was performed with the patients under conscious sedation by using a polyethylene balloon system (Rigiflex; Microvasive, Boston Scientific), and a 30 mm or 35 mm balloon was used. The patient is placed in the left lateral position. The endoscope is advanced into the stomach, the guide wire is placed in the stomach, and the endoscope is then removed. The balloon dilator was passed over the guide wire and positioned across the EGJ. The balloon

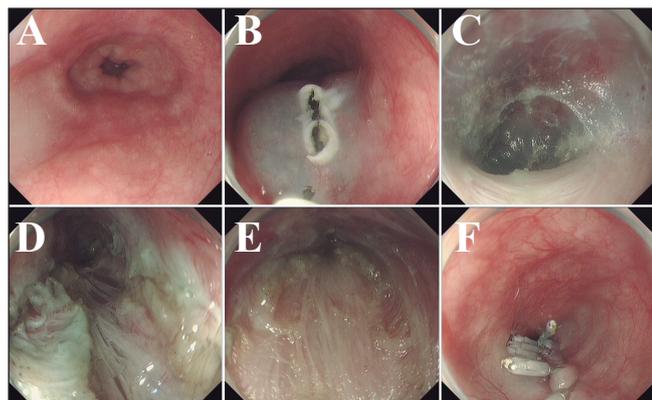


Fig. 1. Case illustration of peroral endoscopic myotomy. A. Endoscopic examination revealed an enlarged esophagus. B. Mucosal incision to make a tunnel entry. C. Submucosal tunnel. D and E. Circular myotomy. F. The mucosal entry was closed with several clips.

pressure was gradually increased, and was added according to the patients' sensation (stopped when the pain was described as unbearable, obvious or severe pain), each dilation was maintained for 1 to 2 minutes with an interval of 2-5 minutes. During the interval, endoscopy examination was performed to check for any severe complication and whether the EGJ was loose enough. The balloon was ended until confirmation of a loose EGJ, obliteration of the waist occurred, or severe complication occurred. Usually 2 to 3 sessions were performed for each patient. Figure 2 describes the procedure of PD.

Postoperative management

Patients were kept nil per os for 24 hours after POEM and 8 hours after PD, with a liquid diet for 3 days and returning gradually to a normal diet within 2 weeks. Intravenous proton pump inhibitor (PPI) was used for 3 days. At day 2 post-POEM, a thoracoabdominal X-ray was performed to check for the occurrence of emphysema, pneumothorax, pneumoperitoneum and pleural effusion, etc.

Study outcome and follow-up

The primary outcome was treatment success defined as a reduction in the Eckardt score to ≤ 3 during follow-up. Secondary outcomes were procedure-related complications. EGD was performed at 1, 3, 6 and 12 months after treatment and annually after that to check for any objective sign of reflux esophagitis or recurrence. They also underwent follow-up esophageal manometry to measure LES pressure and barium esophagram to measure esophageal diameter 6 months after treatment. Patients were contacted via telephone to assess for complications and a current Eckardt score.

Statistical analysis

Statistical analysis was performed with the SPSS 21.0 software (Chicago, USA). Quantitative variables were expressed as mean and standard deviations and analyzed by the Student's t test. Qualitative data were calculated using the chi-square test or Fisher exact test. Chi-square test or Fisher exact test was used for univariate analysis and logistic regression for multivariate analysis. A *p* value of less than 0.05 was considered to be significant.

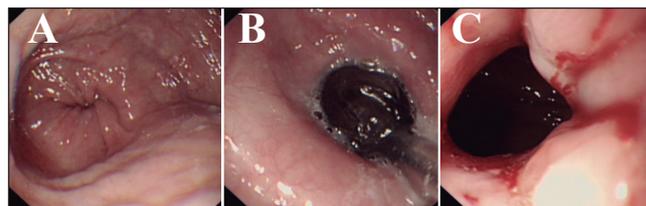


Fig. 2. Case illustration of pneumatic dilation. A. Endoscopic examination revealed a tortuous esophagus. B. The procedure of pneumatic dilation. C. The cardia was loose after dilation.

RESULTS

Patient general characteristics

A total of 31 patients were enrolled, and 21 patients received POEM therapy while the other 10 received PD. Ten patients had previous therapy, and 8 of them received prior endoscopic therapy, 1 had prior Heller myotomy and the remaining patient had pharmacological agents (calcium antagonist). Five patients had sigmoid-type achalasia. There was no significant difference between the two groups in terms of gender, age, duration of symptoms, previous therapy, sigmoid-type achalasia, achalasia type in HRM, preoperative Eckardt score, esophageal diameter, and LES pressure (Table I).

Comparison of efficacy between the two groups (Table II)

All patients received POEM or PD treatment successfully. Their symptoms were relieved after treatment, and the mean Eckardt score decreased dramatically both in the POEM group (preoperative vs postoperative, 7.7 vs. 0.76, $p < 0.05$) and the BD group (preoperative vs. postoperative, 7.3 vs. 1.1, $p < 0.05$). Sixteen patients in the POEM group and 5 in the PD group had paired manometry results, and the LES pressure decreased significantly in the two groups, so did the diameter of esophagus. There was no significant difference between the two groups in terms of postoperative Eckardt score, postoperative LES pressure and esophageal diameter ($p > 0.05$).

As for the treatment success, the success rate of POEM and PD 3, 6, 12, 24 and 36 months after the treatment were comparable ($p > 0.05$). The mean follow-up in the POEM

and PD group was 21.8 months and 35.0 months, and a total of 3 cases encountered treatment failure, which was comparable between the 2 groups [4.8% (1/21) vs. 20% (2/10) $p > 0.05$]. All three cases had symptom recurrence within 6 months. The failed patient in the POEM group received an additional PD, for the 2 cases in the PD group, 1 of them received POEM, while the other one received an additional PD. No recurrence was noticed thereafter.

We then analyzed the risk factors of treatment failure. Univariate analysis revealed that previous therapy, type III

Table I. Comparison of clinical characteristics between the two groups

Characteristics	POEM (n = 21)	BD (n = 10)	p
Age, year	67.9 ± 4.3	69.4 ± 5.4	0.413
Gender, female/male	9/12	5/5	0.709
Duration of symptoms, year	13.9 ± 11.7	16.4 ± 14.5	0.612
Previous therapy, yes/no	8/13	3/7	1.000
Combined disease, yes/no	9/12	2/8	0.262
Preoperative Eckardt score	7.7 ± 1.7	7.3 ± 1.3	0.734
Preoperative esophageal diameter, mm	51.0 ± 5.4	50.0 ± 5.8	0.626
Sigmoid-type achalasia, yes/no	4/17	1/9	1.000
Achalasia type in HRM, I/II/III	5/16/0	2/7/1	0.336
Preoperative LES pressure, mmHg	29.9 ± 3.7	30.4 ± 4.2	0.772

POEM: peroral endoscopic myotomy; BD: pneumatic dilation; LES: lower esophageal sphincter; HRM: high-resolution manometry.

Table II. Comparison of treatment efficacy and complications between the two groups

Characteristics	POEM (n = 21)	PD (n = 10)	p	
Postoperative	Eckardt score	0.77 ± 0.83	1.10 ± 0.74	0.282
	LES pressure, mmHg	10.3 ± 1.6	11.4 ± 1.8	0.098
	Esophageal diameter, mm	30.2 ± 4.7	29.1 ± 3.2	0.512
Treatment success (%)	3 months later	95.2 (20/21)	80 (8/10)	0.237
	6 months later	94.7 (18/19)	80 (8/10)	0.267
	12 months later	93.4 (15/16)	80 (8/10)	0.538
	24 months later	90 (9/10)	100 (7/7)	1.000
	36 months later	100 (4/4)	100 (6/6)	/
Complications	GERD, %	9.5 (2/21)	0 (0/10)	0.486
	Subcutaneous emphysema	4.8 (1/21)	0 (0/10)	1.000
Hospitalization costs, dollars	2,620.3	1212.6	< 0.001	

POEM: peroral endoscopic myotomy; PD: pneumatic dilation; LES: lower esophageal sphincter; GERD: gastroesophageal reflux disease.

in HRM, previous therapy, Henderson type III of esophageal diameter (7) and sigmoid-type achalasia were risk factors, and multivariate analysis showed that only sigmoid-type achalasia was risk factor for treatment failure [OR = 16.7, 95% CI (1.1, 243.7)].

Complications

No patient in any group encountered serious complications such as obvious bleeding, perforation during and after treatment. One patient in the POEM group suffered from subcutaneous emphysema, which was asymptomatic and the emphysema was absorbed spontaneously. Two patients in the POEM group suffered from gastroesophageal reflux disease, and they were noticed 2, and 8 months after treatment, respectively. EGD revealed esophagitis in both of them, and their symptoms were relieved after oral PPI therapy. There was no significant difference between the two groups with regard to complications ($p > 0.05$, Table II). Both cases of reflux in the POEM group happened in patients that received full-thickness myotomy.

DISCUSSION

In the present study, we found that the short-term to intermediate efficacy of POEM and PD were comparable for treating achalasia in patients aged ≥ 65 years. To the best of our knowledge, this is the first study comparing the safety and efficacy of POEM and PD for achalasia in patients with an age of 65-year-old or older.

The optimal treatment of achalasia in patients aged ≥ 65 years remains unclear, available methods include pharmacological and endoscopic therapy (injection of botulinum toxin, pneumatic dilation, stent insertion and POEM) and surgical myotomy (2). Pharmacological treatment with nitrates or calcium antagonists has almost been abandoned due to its poor efficacy and significant side effects (8). Although Heller myotomy (HM) is the most definitive and successful treatment, it is an invasive procedure, and often leads to complications such as perforation, esophageal reflux, and stricture. What's more, some elderly patients hold a higher risk for the surgical procedure due to their poly-morbidity, thus endoscopic treatment is recommended as the first-line option. Endoscopic botulinum toxin injection is safe and effective in aged patients, but the effect tends to attenuate over time, and repeated treatment is thus needed (9). Stent insertion is an alternative, and has demonstrated the same effective as PD, however the long-term efficacy is not that satisfactory and stent migration also occurs (10).

PD disrupts the LES by inserting a balloon across the EGJ, thus decreasing the LES pressure. PD is easier to perform, and has the advantages of a shorter hospitalization and lower cost compared with surgery and had a

better long-term efficacy than endoscopic botulinum toxin injection (9,11,12). The major concern of PD is that its long-term efficacy may not be that satisfactory (13,14). However, researchers have noticed an interesting fact: the recurrence rate after PD for achalasia inversely correlated with patient age, an older age is a favorable predictive factor for a good long-term efficacy (15-17). Recently, a multicenter randomized controlled trial in Europe comparing pneumatic dilation and laparoscopic HM reported the 5-year success rate between the two groups (PD vs. LHM, 82% vs. 84%, $p > 0.05$) (12). And they found that PD had a better 5-year efficacy than HM for patients aged > 40 years old (12). In addition, it has been demonstrated that the most cost-effective treatment for achalasia over a 5-10-year period after the procedure is PD (18,19). So, PD is recommended as an initial treatment for achalasia in elderly patients and theoretically leads to a favorable long-term outcome. In the present study, only 20% (2/10) of patients recurred after PD treatment with a mean follow-up of 35 months. Another concern of PD treatment is the risk of perforation, and the rate of perforation ranges from 0% to 14.5% (20,21). However, according to a literature review including 29 studies, the overall perforation rate was 2% and only 1% of them required surgery (22), suggesting PD is a safe method for the treatment of achalasia. In the present study, no perforation was observed.

POEM, firstly reported by Inoue et al. (4), is a novel technique for treating achalasia, and could relieve symptoms as well as improving the quality of life in adults (23,24). Only a few case report/series have been reported regarding POEM for achalasia in patients aged ≥ 65 years, and the maximum age reported was 97 years of age (5,6). Li et al. (5) reported 15 cases (aged 65-84 years old) treated with POEM and symptoms reported in all patients during a follow-up of 6-39 months, their quality of life increased, indicating a promising outcome of POEM for achalasia in this population. However, little is known about the comparison of POEM and PD. In the present study, 21 cases received POEM and 10 received PD for the treatment of achalasia, and we found that the treatment success rate of POEM and PD 3, 6, 12, 24 and 36 months after the treatment were comparable, and PD had a lower cost, suggesting a comparable short-term to immediate efficacy between POEM and PD. In order to determine whether POEM could lead to a better long-term efficacy over PD, further comparative studies with long-term follow-up are needed.

Recurrence is a major concern after endoscopic and/or surgical treatment of achalasia, and several factors have been found to be associated with treatment failure, type III in HRM, young patients (< 40 years old), males had an unfavorable outcome in PD (2,11,13,25), and incomplete myotomy, an excessively tight anti-reflux wrap and sigmoid-type achalasia were associated with treatment failure in HM (26). In the present study, three cases had a recurrence, and multiple analysis revealed that sigmoid-type

achalasia was a risk factor of treatment failure. PD is considered to be ineffective for sigmoid-type achalasia, and esophagectomy is usually indicated (2). Although POEM has demonstrated to be effective for this advanced achalasia, it could not reverse the morphological changes, so recurrence may occur (27,28). In the present study, Type pattern in HRM was not demonstrated to be a risk factor, maybe because of the relative small sample, and rarity of type III achalasia (3.2%, 1/31). Though the recurrent case in the POEM received circular myotomy only, there was no significant difference in recurrence between circular and full-thickness myotomy, but a large, comparative study with long-term follow-up is needed to determine whether incomplete myotomy will lead to a higher rate of recurrence. The limitations of the study includes its small sample size, retrospective design and relative short-term follow-up. In conclusion, the short-term to intermediate efficacy of POEM and PD were comparable in achalasia patients aged ≥ 65 years. Large scale, randomized studies are warranted to further confirm our findings and long-term follow-up is necessary to demonstrate whether POEM could lead to a better efficacy over PD.

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