

Clinical usefulness of esophagogastric junction distensibility measurement in patients with achalasia before and after peroral endoscopic myotomy

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ABSTRACT

Background/Aims: This study aimed to determine the clinical efficacy of measuring the esophagogastric junction (EGJ) distensibility index (DI) in patients with achalasia before and after peroral endoscopic myotomy (POEM).

Materials and Methods: Retrospective data were collected from 195 patients who underwent POEM from November 2014 to November 2017 at our clinic. The Eckardt score, high-resolution manometry, and EGJ distensibility were measured before and six months after POEM. Treatment failure was defined as a postprocedure Eckardt score >3 or patients who underwent repeat POEM.

Results: The DI (mm²/mmHg) before and after POEM was 3.42±3.55 and 11.57±6.64, respectively ($p<0.01$). There was no difference in the DI between achalasia subtypes I, II, and III (11.45±6.24 versus 15.49±11.53 versus 13.27±9.49, $p=0.22$) or previous treatment history (15.39±10.85 versus 11.10±7.25, $p=0.20$). The DI was higher in patients with reflux esophagitis after POEM, but the difference was not significant (13.59±7.15 versus 12.54±10.9, $p=0.571$).

Conclusion: This study showed that EGJ distensibility measurement is useful to assess post-POEM outcomes. These findings suggest that the functional lumen imaging probe may be a useful method for assessing clinical efficacy of POEM in patients with achalasia. However, this is a costly procedure that requires experience.

Keywords: Esophageal Achalasia, myotomy, esophagogastric junction

INTRODUCTION

Achalasia is an esophageal dysmotility disease defined as failure of esophagogastric junction (EGJ) relaxation and failure of peristalsis of the esophagus (1). Retention of food in the esophagus causes symptoms such as difficulty in swallowing, retrosternal chest pain, and weight loss (2). Currently, the goal for the treatment of achalasia is to lower the pressure at the lower esophageal sphincter (LES) (3). Current treatment options include medication, botulinum toxin, pneumatic dilatation, and laparoscopic Heller myotomy (LHM) (3, 4). Each of these methods has its advantages and disadvantages. For instance, symptom recurrence and gastroesophageal reflux (GER) are common after pneumatic dilatation. Botulinum toxin is expensive and only works in the short term. An additional fundoplication procedure may be required after surgical myotomy to prevent GER. These challenges have led physicians to explore new methods (5).

Peroral endoscopic myotomy (POEM) is a less invasive endoscopic surgery for the long-term improvement of achalasia symptoms (6). It has the advantages of an endoscopic approach with the durability of a controlled surgical myotomy in the EGJ (7). It was first described by Pasricha et al. (8) in an animal model in 2007. POEM has reported very good results in clinical and physiological improvement (7, 9, 10).

Although high-resolution manometry (HRM) is the preferred method for the diagnosis and evaluation of subtypes of achalasia, it is less suitable for the evaluation of endoscopic or surgical postoperative physiological results (11). Clinical success after the procedure is defined as Eckardt score (ES) <4. Other metrics used include improvement in esophageal emptying, lower LES pressure, and quality of life (6). These methods are useful in the diagnosis and treatment of achalasia but do not measure EGJ opening after swallowing (12, 13). The functional lu-

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men imaging probe (FLIP) is a new measuring device used for this purpose. EndoFLIP has been used to evaluate EGJ opening and pressure (14). These data are used to calculate the EGJ distensibility index (DI) (i.e., compliance in response to tension), a metric that is better correlated with postintervention symptoms than HRM findings (15).

We aimed to evaluate the clinical efficacy of EGJ distensibility measurement in patients with achalasia who were treated with POEM.

MATERIALS AND METHODS

Retrospective data were collected from 195 patients with achalasia who underwent POEM treatment from November 2014 to November 2017 at our clinic. The diagnosis of achalasia was made by the absence of peristalsis and failure of LES relaxation measured by esophageal manometry. Measurements of ES, HRM, and EGJ distensibility were performed before and six months after POEM. Treatment failure was defined as a post-POEM ES >3 or patients who underwent repeated POEM. This study was approved by the Institutional Review Board of the CHA Bundang Medical Center, Seongnam, South Korea (registration number: CHAMC 2018-07-050-001). Written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo.

POEM operative method

POEM was performed under general anesthesia. A standard carbon-dioxide-insufflator-assisted gastroscope with a cap was used. A premixed saline-based solution was injected 9–10 cm above the EGJ to make a submucosal fluid bleb. Mucosectomy was performed over the fluid bleb, and the scope was inserted into the submucosal space. Submucosal tunnel dissection was performed using the dual knife. Myotomy was performed from 6 cm above to 2.5–3 cm below the EGJ. The myotomy length was measured with the gastroscope (The EVIS LUCERA ELITE Gastrointestinal Videoscope GIF-HQ290, Olympus, Southend-on-Sea, UK) during POEM. The incision area was closed by using hemoclips.

MAIN POINTS

- The EndoFLIP system were used for measurement of EGJ distensibility.
- EGJ distensibility is higher after POEM in achalasia patients.
- The EndoFLIP may be a useful method for assessing clinical efficacy of POEM in patients with achalasia.

Symptom scores

Symptom scores were evaluated by the ES and the GerdQ score (21). If the ES was 4, the treatment was defined as successful. The GerdQ score was used to evaluate reflux symptoms. Symptom scores were measured before and one month after the POEM procedure.

Esophageal manometry (high-resolution manometry)

Achalasia was diagnosed by measuring the integrated relaxation pressure (IRP) and LES pressure, which was performed by HRM (InSIGHT Ultima system, Sandhill Scientific, Highlands Ranch, CO, USA). According to IRP and features of pressurization on the EGJ, achalasia patients were classified as type I, type II, and type III achalasia. Esophageal manometry was performed using a 32 pressure (four sensor circumferential)/16 impedance catheter.

Timed barium esophagogram

Timed barium esophagogram was used to evaluate esophageal emptying. Real-time images from 1 to 5 minutes after ingestion of gastrografin contrast agent (50 mL) were obtained. Lower esophagus shapes were classified according to esophagogram findings as sigmoid or nonsigmoid type. Timed barium esophagogram was performed before and 4 days after POEM to detect leakage occurrence at the EGJ.

EndoFLIP measurement

The EndoFLIP system (EndoFLIP; Crospon Medical Devices, Galway, UK) and probes were used for measurement of EGJ distensibility. EndoFLIP is a catheter-based probe, which consists of 17 ring electrodes placed at 5-mm intervals. In this study, the balloon was inflated to 40-mL volume, and the measurements were recorded for 30 seconds to determine intrabag pressure, luminal cross-sectional area (CSA), and EGJ distensibility. The EGJ DI was defined as the CSA divided by FLIP-bag pressure (mm^2/mmHg). EndoFLIP was performed before and one month after POEM.

Statistical analysis

Statistical analyses were performed using the Statistical Packages for the Social Sciences (SPSS) version 22 program (IBM Corp.; Armonk, NY, USA). The Pearson's Chi-squared test and the Fisher's exact test were used to analyze categorical patient variables. The Student's *t*-test was used to analyze independent samples, and the Mann-Whitney U test was used to analyze nonparametric variables. The results were given as frequency and percentages for categorical variables and mean \pm SD if the variable was normally distributed (for continuous vari-

ables). Deviation values were shown with median (minimum-maximum) values if they did not show normal dis-

Table 1. Patient baseline characteristics.

Characteristics	Number of patients (n=195)
Sex	
Male	93 (47.6%)
Female	102 (52.4%)
Age (year)	43.75±15.53
BMI (kg/m ²)	22.72±3.59
Follow-up duration (days)	288.85±255.291
Duration of disease (years)	5.72±7.87
Prior treatment	
None	110
CCB	15
Balloon dilatation	32
Botox	15
POEM	5
Surgery	4
CCB+Botox	6
CCB+balloon dilatation	4
Balloon dilatation+surgery	4
Esophageal shape	
Sigmoid type	17
Nonsigmoid type	178
Maximal diameter of esophagus (mm)	3.84±3.55
Myotomy length	8.96±2.20
Method of myotomy	
Full thickness myotomy	152
Selective myotomy	43
Type of achalasia	
Type I	83
Type II	91
Type III	21

BMI: body mass index; CCB: Calcium channel blocker; POEM: peroral endoscopic myotomy.

Table 2. Changes in variables before and after POEM.

Measuring tool	Characteristics	Preoperative values	Postoperative values	p
EndoFLIP	DI40 mL (mm ² /mmHg)	3.42±3.55	11.57±6.64	<0.01
HRM				
LES _p (mmHg)	31.64±18.66	14.82±9.21	<0.01	
IRP (mmHg)	25.55±19.49	11.75±7.61	<0.01	
Questionnaire				
Eckardt score	6.35±2.28	1.32±1.24	<0.01	
Reflux symptom (+)	36	64	0.007	

HRM: high-resolution manometry; LES_p: lower esophageal sphincter pressure; IRP: integrated relaxation pressure.

tribution. A logistic regression analysis was run (with 95% confidence intervals). Statistical significance was defined as $p < 0.05$.

RESULTS

Patients

One hundred and ninety-five patients were evaluated before and after POEM. The baseline characteristics of those patients are shown in Table 1.

High-resolution manometry

LES pressure and IRP levels decreased significantly post-POEM procedure (31.64 ± 18.66 versus 14.82 ± 9.21 , $p < 0.01$; 25.55 ± 19.49 versus 11.75 ± 7.61 , $p < 0.01$, respectively) (Table 2).

Esophagogastric junction distensibility functional lumen imaging probe

The DI (mm²/mmHg) before and after POEM was 3.42 ± 3.55 and 11.57 ± 6.64 , respectively ($p < 0.01$) (Table 2). There was no difference in the DI between achalasia subtypes or previous treatment choices. The DI was higher in patients with reflux esophagitis after POEM, but this difference was not significant (13.59 ± 7.15 versus 12.54 ± 10.9 , $p = 0.571$).

Eckardt score

There was a significant difference between pre- and postoperative ESs (6.35 ± 2.28 versus 1.32 ± 1.24 , $p < 0.01$). ESs improved significantly after the POEM (Table 2).

Reflux symptoms

Reflux symptoms according to the GerdQ score were positive in 36 patients before the POEM procedure and 64 patients after the procedure ($p = 0.007$) (Table 2). Figures 1 and 2 show endoFLIP imaging and DI levels before and after the POEM procedure, respectively.



Figure 1. EndoFLIP imaging before the POEM procedure.

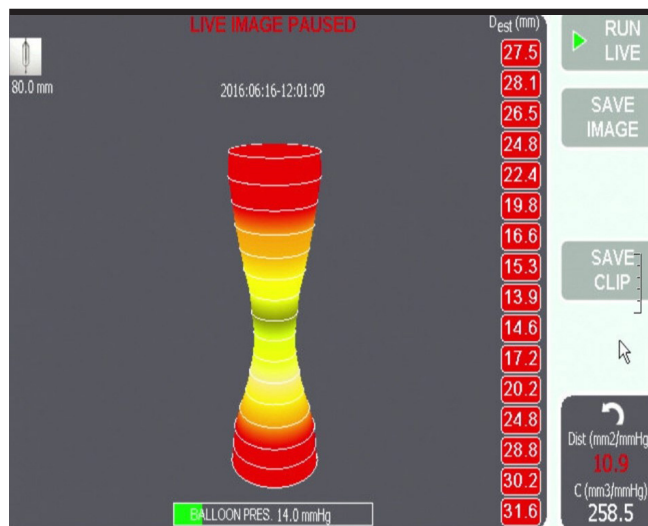


Figure 2. EndoFLIP imaging after the POEM procedure.

DISCUSSION

POEM is a novel minimally invasive endoscopic method for achalasia management. Compared to the traditional surgical myotomy, POEM has an equal dysphagia relief with less pain and shorter recovery period (7). To be the new gold standard for managing endoscopic procedure achalasia, POEM's advantages need to be documented objectively. Traditional techniques for the assessment of post-POEM results include HRM, 24-hour pH monitoring, timed barium esophagogram, and upper endoscopy. We investigated the FLIP technique to assess EGJ distensibility pre- and post-POEM. In evaluating the function of the EGJ, it is increasingly apparent that a clinical tool

that measures distensibility rather than pressure is more useful. FLIP provides information on distensibility in the esophagus and can help distinguish the difference between normal sphincters and achalasia (16). Kwiatak et al showed that FLIP data did not correlate with manometer measurements of the EGJ. This finding shows that contractility and distensibility of the EGJ are different (17).

We found that EGJ distensibility was significantly higher after POEM in achalasia patients, similar to previous studies (18-20). Two studies emphasized the usefulness of FLIP in evaluating achalasia patients before and after interventions (15, 21); both found that the EGJ DI was the highest in the control group and the lowest in the untreated group. The patients were classified according to treatment response (good treatment response if ES<3 or a poor treatment response if ES>3). The EGJ DI was significantly higher in patients with a good treatment response compared to untreated patients or patients with a poor response. FLIP measurements were found to better correlate with symptoms after treatment than IRP obtained by HRM. Riedel et al. (19) also showed that POEM immediately corrected the nonrelaxing LES in patients with achalasia, and that the EGJ distensibility assessment was useful for in-depth evaluation of the POEM procedure (19). Rohof et al showed that EGJ distensibility correlated better with postoperative esophageal emptying and symptoms than did the LES pressure. Therefore, EGJ distensibility may be an effective long-term objective follow-up method after POEM (22).

There are some studies comparing EGJ distensibility in achalasia patients after POEM and LHM. Teitelbaum et al. (24) found that submucosal tunnel and myotomy both independently increased distensibility during POEM. POEM and LHM resulted in a similar improvement in EGJ distensibility. Therefore, FLIP can be a good guide in POEM or LHM patients, as it shows real-time changes in EGJ distensibility (23). In another study from Teitelbaum et al. (24), it was shown that POEM and LHM resulted in an increased DI, although this increase was significantly better after POEM.

Our results showed that the number of patients with GER was significantly higher after POEM. Pathological changes due to reflux, such as esophagitis, were investigated by three studies using conventional white-light endoscopy pre- and post-POEM. They showed an increase of 0-6%, 0-46%, and 0-19%, respectively, in the incidence of esophagitis before and after POEM (25-27). The risk for development of iatrogenic GERD may be higher after an effective myotomy. In contrast to the study of Kwiatak et

al. (14), our study showed that EGJ distensibility was similar between the patients with and without GER symptoms.

Similar to a study by Teitelbaum et al. (24), EGJ distensibility was not different between the naive patients and previously endoscopically treated patients for achalasia. There was no significant difference in EGJ distensibility between achalasia subgroups in our study. In contrast, Teitelbaum et al. (24) found a significantly higher baseline of EGJ distensibility in type I achalasia patients than in type II patients.

There are some limitations to our study. First, this was a retrospective study from a single center. Second, the maximum follow-up duration was four years. For this reason, we do not know how the DI and ESs change in the long term. We recommend the patients who underwent POEM to also undergo follow-up exams, including upper endoscopy, FLIP, and 24-hour pH monitoring every year.

In conclusion, our results show that EGJ distensibility measurement is useful for assessing post-POEM outcomes. These findings suggest that FLIP may be a useful method for assessing clinical efficacy of POEM in patients with achalasia. However, this is a costly procedure that requires experience.

Ethics Committee Approval: Ethics committee approval was received for his study from the Institutional Review Board of the CHA Bundang Medical Center (Decision date 11.09.2018. Decision number CHAMC 2018-07-050-001).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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