의학박사 학위논문

경구 내시경 근절개술을 시행한 이완불능증 환자에서 식도 기능 내강 영상 프로브(FLIP) 파노메트리의 예측적 가치: 단일 센터 경험

Predictive value of esophageal functional luminal imaging probe(FLIP) panometry in patients with achalasia undergoing peroral endoscopic myotomy: a single-center experience

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Abstract

Background/Aims: We evaluated the clinical significance and prognostic power of FLIP (functional luminal imaging probe) panometry in patients with achalasia treated with POEM (peroral endoscopic myotomy), and examined the clinical parameters associated with symptomatic improvement and partial recovery of peristalsis (PRP) following POEM.

Methods: We reviewed the electronic medical records of patients with achalasia treated with FLIP panometry and POEM at a tertiary teaching hospital in Seoul, Republic of Korea. Follow-up examination was composed of esophageal manometry and questionnaires on symptoms. We analyzed the FLIP data by interpolating using the cubic spline method in MATLAB.

Results: We retrospectively analyzed 33 men and 35 women (mean age: 52 ± 17 y), of whom 14, 39, and 15 patients were diagnosed with achalasia types I, II, and III, respectively. The FLIP panometry diagnoses were reduced esophagogastric junction opening (REO) with a retrograde contractile response (n=43); REO with an absent contractile response (n=5); REO with a normal contractile response (n=11); and a retrograde contractile response (n=9). Overall, the patients showed improvements in Eckardt scores following POEM from 6.48 ± 2.20 to 1.16 ± 1.15 ($p<0.01$). Post-POEM symptomatic improvement was not significantly associated with any of the clinical parameters, including panometry diagnosis. Conversely, post-POEM PRP was significantly associated with the presence of repetitive antegrade contractions and achalasia subtypes (both $p<0.01$).

Conclusions: FLIP panometry can predict the clinical course following POEM and can complement manometry in the functional evaluation of esophageal motility

disorders.

Keywords: achalasia, peroral endoscopic myotomy (POEM), EndoFLIP

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INTRODUCTION

Achalasia is an esophageal motility disorder characterized by the inability of the lower esophageal sphincter (LES) to relax and a lack of esophageal body peristalsis. Treatment methods include medication, endoscopic treatment, and surgical treatment. Among them, peroral endoscopic myotomy (POEM) has become the mainstay of endoscopic treatment for achalasia.[1-3] POEM is currently being highlighted as a new treatment.

High-resolution manometry (HRM) based on a spatiotemporal plot can help diagnose esophageal motor disorders; the Chicago classification based on HRM showed a higher diagnostic yield than the previously used conventional criteria based on linear waves.[4-7] However, the Chicago classification has its limitations, including inconsistent measurements of the adequacy of the esophagogastric junction (EGJ) with integrated relaxation pressure (IRP).

As research on achalasia has increased, interest in the functional luminal imaging probe (FLIP) has also increased.[8-10] The FLIP showed a higher diagnostic yield compared to the previously used IRP in the measurement of the function of EGJ using the EGJ-distensibility index (EGJ-DI).[11-13] Moreover, FLIP panometry can mimic secondary peristalsis, and new diagnostic criteria based on panometry showed a better diagnostic yield compared to the Chicago classification.[14] However, its usefulness before POEM treatment is yet unproven, except in a small number of cases.[15] Moreover, it is unclear which parameters can predict symptomatic improvement and the regaining of esophageal peristalsis after POEM treatment.[16, 17] The aim of this study was to investigate the clinical significance of panometry before POEM and identify the predictive parameters of symptomatic improvement and regaining of esophageal peristalsis after POEM.

MATERIALS AND METHODS

Patients

We reviewed the clinical records of adult patients (age >18 y) with achalasia who had undergone FLIP panometry after the induction of general anesthesia and POEM at a tertiary referral center in Seoul, South Korea, from October 2017 to March 2020. The following clinical data were collected: age, sex, HRM, FLIP data, and pre- and post-POEM Eckardt scores. This study was approved by the institutional review board of the treating institute (approval number: S2019-1634).

POEM operative technique

POEM was performed by three expert endoscopists (HYJ, KDC, and DHK) while the patient was under general anesthesia. All of the procedures were performed using an upper gastrointestinal endoscope with a plastic cap and carbon dioxide insufflation. Landmarks, such as the LES, gastroesophageal junction, and site of incision in the mid-esophagus, were identified by endoscopy before POEM. After injecting a starch-based or saline solution into the submucosal layer to create a submucosal bleb, a mucosal incision of approximately 3 cm was made using a hook knife (Olympus, Tokyo, Japan) using the dry cut mode at 60 W with effect 5 (ERBE, Tübingen, Germany). Myotomy was performed in the posterior (5 o'clock) position with an insulated-tip knife nano (Olympus, Tokyo, Japan) using the mode at 80 W with effect 7 at the discretion of the endoscopist; the myotomy was intended to be of selective/partial thickness in all of the cases. Following the completion of myotomy, the mucosal incision site was closed with endoclips.[3]

HRM with esophageal pressure topography

Esophageal pressure topography studies of all patients were performed using a solid-state, high-resolution impedance manometry (HRIM) catheter with 32 circumferential sensors and 16 impedance sensors (InSight Ultima, Diversatek™, Highlands Ranch, CO, USA). Manometry profiles were analyzed using the Zvu® Advanced GI Diagnostic Software (Diversatek™, Highlands Ranch, CO, USA).

Manometry sensors were positioned to record data from the terminal portion of the proximal esophageal segment through the distal esophagus and into the proximal stomach. The HRIM assembly was fixed in place by taping it to the patient's nose. Esophageal HRM was performed before and after POEM. The esophageal HRM protocol included a 30-s interval without swallowing to assess the basal EGJ pressure and morphology, followed by ten 5-mL swallows of normal saline solution in the supine position.[18] Manometric data were analyzed using Zvu® Advanced GI Diagnostic Software by one investigator (KWJ).[19] Achalasia subtypes were determined based on the Chicago classification. IRP and LES resting pressure data were analyzed. The partial recovery of peristalsis (PRP) using esophageal HRM after

POEM was defined by two investigators (KWJ and LCH) after discussion.[16]

FLIP measurement protocol

The FLIP assembly was 240 cm long, with a 16-cm-long cylindrical bag mounted on the distal end of the catheter (EndoFLIP; Crospon, Galway, Ireland). The infinitely compliant bag housed 17 impedance planimetry electrodes spaced at 1-cm intervals and a solid-state pressure transducer positioned at the distal end. Impedance planimetry electrodes were used to generate cross-sectional areas (CSAs), and the intra-bag pressure was extracted from the solid-state pressure transducer.

Patients underwent general anesthesia during endoscopic intervention in the left lateral decubitus position. The FLIP catheter was inserted trans-orally and positioned under the direct endoscopic view, with one or two sensors placed distal to the EGJ. The proper placement was confirmed based on a visualized hourglass-like shape on the FLIP display; the narrowed area of the hourglass indicated the EGJ. The bag was gradually filled with normal saline from 30 to 70 mL with 10-mL intervals, with pauses for approximately 30 to 60 s at each volume. FLIP measurements were gathered before POEM during general anesthesia.

Interpretation of FLIP panometry

Continuous data measured using the FLIP obtained through the 16 sensors were extracted as ASCII files and analyzed using MATLAB™ (The Math Works, Natick, Mass, USA). The customized program for data analysis was used to construct a topography plot based on the ASCII data extracted from each sensor. For better resolution, topography plot data were interpolated with 2-mm accuracy, and volume and pressure changes were displayed to aid in the intuitive understanding of the correlation between topography plots over time. The color in the topography plot indicates the diameter.

When evaluating FLIP motility, the volume was increased by 10 mL. We evaluated each data point from 30 to 70 mL using the EGJ-DI. To obtain the EGJ-DI, the median narrowest CSA was divided by the median intra-balloon pressure (bp). The radius was obtained using the minimum diameter for each volume, and each CSA was derived using the radius. To evaluate the EGJ-DI, the median CSA for each volume was used.[20]

Each patient's FLIP panometry data were evaluated by two investigators (KWJ and LCH). The contraction that was induced by the distension pattern was evaluated for all patients in the study. Esophageal contractions were defined when an esophageal body diameter decreased by ≥ 5 mm in two or more adjacent impedance planimetry channels.

FLIP data were converted to 3-dimensional panometry data. We measured the diameter from the probe. Three-dimensional contour plots were constructed based on the measured diameter to which the color contour was applied. We painted the surface with color according to the colored 3-dimensional contour plots. Finally, 3-dimensional panometry was compared with 2-dimensional panometry (Figure 1).

Contractions were assessed based on three-dimensional panometry plots according to the diameter or direction of repetitive contractions. Occluding or non-occluding contractions were defined as those that were >6 or ≤6 mm from the nadir diameter, respectively. A repetitive contraction was defined when three or more contractions occurred in a single direction (Figure 2).[8, 21]

Outcomes

The primary outcome was treatment success defined as a post-POEM symptom score (Eckardt symptom score) ≤3 (reference Eckardt score).[22]

Secondary outcomes assessed before and after POEM included the following: the gastroesophageal reflux disease questionnaire (GerdQ), basal LES pressure, IRP, PRP based on HRM findings, procedure time, length of myotomy, EGJ-DI, and follow-up panometry.[16]

Definition of PRP after POEM

Post-POEM peristalsis was classified as a weak contraction, premature contraction, or failed contraction according to a previous study based on the Chicago classification.[7, 16] PRP was defined when weak and premature contractions were observed in follow-up HRM. The definition of a failed contraction was minimal (< 3 cm) integrity of the 20-mmHg isobaric contour distal to the proximal pressure trough; a weak contraction was defined based on a large (> 5 cm in length) or small (2–5 cm in length) break in the 20-mmHg isobaric contour. A premature contraction was defined as weak peristalsis with a small break and distal latency < 4.5 s (Supplementary figure 1).

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as number (proportion) for categorical variables. The Kruskal–Wallis test was used to compare continuous variables between the subtypes of achalasia or the FLIP topography classification. Fisher's exact test was used to compare categorical variables between the subtypes of achalasia or the FLIP topography classification. The *t*-test was used to compare variables between the "with PRP" and "without PRP" groups. A p-value <0.05 (two-tailed) was considered to be statistically significant. A receiver operating characteristic (ROC) curve was used to determine the optimum cutoff EGJ-DI with respect to the regaining of peristalsis. The cutoff was selected to maximize the trade-off between sensitivity and specificity. The sensitivity, specificity, positive and negative predictive values, and area under the ROC curve were estimated.

All statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA).

RESULTS

General characteristics of patients

A total of 68 patients, including 33 men and 35 women, with a mean age of 52 ± 17 years, who had undergone POEM and had follow-up Eckardt score data, were included in the analyses. Table 1 summarizes the patient characteristics at baseline. Table 2 summarizes FLIP topography and the motility classification as per the manometric motility diagnosis. Thirty-six of 68 patients attended follow-up HRM after POEM (Figure 3). The median follow-up length of HRM and surveys after POEM was 205 d (Interquartile range [IQR: 25th - 75th percentile], 34 to 304 days).

Primary outcome

Of the 68 patients with achalasia, 14 (20.6%) had type I, 39 (57.4%) had type II, and 15 (22.1%) had type III. However, the mean baseline Eckardt score was 6.48 ± 2.20. Two of the 68 patients showed improvement of symptoms, as revealed by the Eckardt score, although the scores were not below 3 (cutoff) despite POEM. No statistically significantt difference was found between the pre- and post-Eckardt scores according to the different achalasia subtypes (p=0.605, Table 3). Moreover, there was no statistical significance between the Eckardt score and types of FLIP panometry diagnoses (p=0.854, Table 3). There were significant differences between pre- and post-POEM EGJ-DI values (1.6 ± 1.1 vs. 8.8 ± 5.0, p<0.01).

Secondary outcome

PRP after POEM

A total of 36 patients, comprised of 18 men and 18 women, with a mean age of 53 ± 15 y, underwent follow-up HRM to determine the presence/absence of peristalsis after POEM. Twenty-four patients regained peristalsis after POEM, whereas 12 patients did not.

Supplementary figure 1 illustrates the patterns of PRP after POEM. A total of 24 patients who had PRP after POEM also had RACs. However, among the 12 patients without PRP after POEM, 8 patients showed RACs. The prevalence of PRP was significantly higher in patients with RAC than in those without RAC (with PRP group: 24/24 patients showed RACs; without PRP group: 8/12 patients showed RACs, *p*=0.008, Table 4, Figure 4). Repetitive retrograde contractions (RRCs) were observed in 18 of 24 patients with PRP and in 11 of 12 patients without PRP. There was no significant relationship between RRCs and peristalsis (with PRP group: 18/24 patients with RRCs; without PRP group: 11/12 patients with RRCs, *p*=0.384, Table 4, Figure 4).

Among the patients who had PRP after POEM, 2 (8%) had type I, 16 (67%) had type II, and 6 (25%) had type III. Among those without PRP after POEM, six (50%) had type I and six (50%) had type II. There were significant differences among the types of achalasia in PRP (*p*=0.007, Table 4, Figure 4). The panometry analysis based on the 2019 criteria did not show clinical significance with respect to PRP (*p*=0.128, Table 4).

The mean EGJ-DI in the "with PRP" group was significantly lower than that in the "without PRP" group (1.3 ± 0.9 vs. 2.1 ± 1.3, *p*=0.023). The ROC curve analysis was performed to find the cutoff EGJ-DI for PRP. According to the result of the ROC curve analysis (Figure 5), the cutoff EGJ-DI was 2.3 mm^2/mmHg; the probability of regaining peristalsis could increase (*p*=0.042).

After POEM, FLIP panometry was measured. However, no significant repetitive pattern of contraction was observed.

POEM procedure-related parameters

We investigated the relationship between clinical outcomes and procedure-related parameters (myotomy length and procedure time). There was no significant association between Eckardt scores and myotomy length (11.6 ± 2.6 cm with symptomatic improvement vs. 11.5 ± 2.1 cm without symptomatic improvement; p=0.897) or between Eckardt scores and procedure time (75.9 ± 24.1 min with symptomatic improvement vs. 81.2 ± 31.7 min without symptomatic improvement; p=0.401).

As for PRP, there was no significant association between PRP and the myotomy length (15.8 ± 9.0 cm with PRP vs. 10.7 ± 4.5 cm without PRP; p=0.281) or between PRP and procedure time (84.7 ± 32.4 vs. 71.8 ± 21.5 min; p=0.165).

GerdQ

The follow-up GerdQ was completed by 32 patients. Most patients scored less than 8, and one patient scored 8. There were no significant differences among achalasia subtypes in the number of patients who completed the GerdQ (7 in type I, 19 in type II, and 6 in type III; p=0.878). Moreover, there was no significant differences between the panometry pattern and GerdQ (20 in REO with retrograde contractile response, 2 in REO with absent contractile response, 5 in REO with normal contractile response, and 5 in retrograde contractile response; p=0.599).

DISCUSSION

All of the patients with achalasia who had undergone POEM showed significant symptomatic improvement. PRP was significantly higher in those with RAC, achalasia type II, and a low EGJ-DI. Based on our data, we observed that patients with a lower EGJ-DI showed better symptomatic responses after POEM and a higher probability of having PRP.

All manometric subtypes of achalasia in our study showed symptomatic improvement, in line with a previous report by Kim et al.[3] In previous studies, achalasia was effectively identified using real-time FLIP panometry to evaluate esophageal motility.[8, 14, 21] However, the predictive value of FLIP panometry had no statistical significance.[21] In contrast, our results showed the predictive value of the FLIP panometry pattern in the clinical course after POEM in patients with achalasia.

RACs obtained using panometry showed a predictive value for the regaining of peristalsis after POEM in patients with achalasia. An RAC is a normal physiological secondary peristalsis of the esophagus, and its presence in achalasia indicates remaining esophageal function in patients with achalasia.

In patients with achalasia, functional recovery was observed in the distal esophagus after POEM; this suggests that impaired neuronal function limited to the LES might be prominent in some patients with achalasia.[16] In our study, the presence of an RAC, a lower EGJ-DI, and achalasia subtypes were potentially predictive of PRP after POEM in patients with achalasia.

Other papers reported PRP in some patients with achalasia after myotomy. Roman et al.[16] reported that weak peristalsis after myotomy was usually characterized by a large (>5 cm in length) or small (2–5 cm in length) break in the 20-mmHg isobaric contour, and premature contractions were characterized as distal latency <4.5 s. The recovery of peristalsis after POEM might indicate inflammation of the myenteric plexus in the distal esophagus, whereas persistent aperistalsis after POEM might indicate progression to aganglionosis.[16, 23]

As the recovery of peristalsis was associated with improved symptomatic and radiographic outcomes,[24] Carlson et al. mentioned that patients with achalasia with RACs before POEM may be more likely to show recovery of peristalsis.[14] Our study concluded that RACs were associated with recovery of peristalsis after POEM. We also examined the association between the recovery of peristalsis after POEM and the EGJ-DI. A cutoff EGJ-DI of 2.3 was confirmed with the ROC curve analysis in our study, showing an area under the curve of 0.710. Although there may be differences depending on the duration and achalasia subtypes, recovery of peristalsis was likely to occur if the EGJ-DI was ≤2.3. However, the cutoff likely had statistical significance, and the sample size was simply too small to identify the clinical significance. Therefore, future prospective studies might be required to verify this.

Other intraoperative EndoFLIP studies on panometry included fewer than 50 patients and were conducted in the same hospital that invented panometery.[25-27] However, our study is meaningful as it included the largest number of patients among intraoperative EndoFLIP panometry studies to date.

This study had a limitation. We analyzed topography using specialized software, which is not widely available. However, the data and profile obtained from this panometry pattern are technically comparable to those from other studies.[8, 20]

CONCLUSION

In conclusion, this study demonstrated that the presence of RACs and the panometry pattern tended to predict PRP after POEM. These parameters may reflect pathogenic features or the degree of neurodegeneration.

REFERENCES

1. Werner YB, Hakanson B, Martinek J, et al. Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia. N Engl J Med 2019;381:2219-2229.
2. Ponds FA, Fockens P, Lei A, et al. Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation on Symptom Severity and Treatment Outcomes Among Treatment-Naive Patients With Achalasia: A Randomized Clinical Trial. Jama 2019;322:134-144.
3. Kim GH, Jung KW, Jung HY, et al. Superior clinical outcomes of peroral endoscopic myotomy compared with balloon dilation in all achalasia subtypes. J Gastroenterol Hepatol 2019;34:659-665.
4. Ghosh SK, Pandolfino JE, Rice J, Clarke JO, Kwiatek M, Kahrilas PJ. Impaired deglutitive EGJ relaxation in clinical esophageal manometry: a quantitative analysis of 400 patients and 75 controls. Am J Physiol Gastrointest Liver Physiol 2007;293:G878-885.
5. Pandolfino JE, Ghosh SK, Rice J, Clarke JO, Kwiatek MA, Kahrilas PJ. Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls. Am J Gastroenterol 2008;103:27-37.
6. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology 2008;135:1526-1533.
7. Bredenoord AJ, Fox M, Kahrilas PJ, Pandolfino JE, Schwizer W, Smout AJ. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography. Neurogastroenterol Motil 2012;24 Suppl 1:57-65.
8. Carlson DA, Gyawali CP, Kahrilas PJ, et al. Esophageal motility classification can be established at the time of endoscopy: a study evaluating real-time functional luminal imaging probe panometry. Gastrointest Endosc 2019;90:915-923.e911.
9. Carlson DA, Kou W, Lin Z, et al. Normal Values of Esophageal Distensibility and Distension-Induced Contractility Measured by Functional Luminal Imaging Probe Panometry. Clin Gastroenterol Hepatol 2019;17:674-681.e671.
10. Kwiatek MA, Pandolfino JE, Hirano I, Kahrilas PJ. Esophagogastric junction distensibility assessed with an endoscopic functional luminal imaging probe (EndoFLIP). Gastrointest Endosc 2010;72:272-278.
11. Rohof WO, Hirsch DP, Kessing BF, Boeckxstaens GE. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. Gastroenterology 2012;143:328-335.

12. Pandolfino JE, de Ruigh A, Nicodème F, Xiao Y, Boris L, Kahrilas PJ. Distensibility of the esophagogastric junction assessed with the functional lumen imaging probe (FLIP™) in achalasia patients. Neurogastroenterol Motil 2013;25:496-501.
13. Smeets FG, Masclee AA, Keszthelyi D, Tjwa ET, Conchillo JM. Esophagogastric junction distensibility in the management of achalasia patients: relation to treatment outcome. Neurogastroenterol Motil 2015;27:1495-1503.
14. Carlson DA, Lin Z, Kahrilas PJ, et al. The Functional Lumen Imaging Probe Detects Esophageal Contractility Not Observed With Manometry in Patients With Achalasia. Gastroenterology 2015;149:1742-1751.
15. Campagna RAJ, Carlson DA, Hungness ES, et al. Intraoperative assessment of esophageal motility using FLIP during myotomy for achalasia. Surg Endosc 2020;34:2593-2600.
16. Roman S, Kahrilas PJ, Mion F, et al. Partial recovery of peristalsis after myotomy for achalasia: more the rule than the exception. JAMA Surg 2013;148:157-164.
17. Foisy H, Pioche M, Chabrun E, et al. Role of Rapid Drink Challenge During Esophageal High-resolution Manometry in Predicting Outcome of Peroral Endoscopic Myotomy in Patients With Achalasia. J Neurogastroenterol Motil 2020;26:204-214.
18. Pandolfino JE, Ghosh SK, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying EGJ morphology and relaxation with high-resolution manometry: a study of 75 asymptomatic volunteers. Am J Physiol Gastrointest Liver Physiol 2006;290:G1033-1040.
19. Jung KW, Jung HY, Myung SJ, et al. The effect of age on the key parameters in the Chicago classification: a study using high-resolution esophageal manometry in asymptomatic normal individuals. Neurogastroenterol Motil 2015;27:246-257.
20. Carlson DA, Hirano I. Application of the Functional Lumen Imaging Probe to Esophageal Disorders. Curr Treat Options Gastroenterol 2017;15:10-25.
21. Carlson DA, Kahrilas PJ, Lin Z, et al. Evaluation of Esophageal Motility Utilizing the Functional Lumen Imaging Probe. Am J Gastroenterol 2016;111:1726-1735.
22. Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. Gastroenterology 1992;103:1732-1738.
23. Sodikoff JB, Lo AA, Shetuni BB, Kahrilas PJ, Yang GY, Pandolfino JE. Histopathologic patterns among achalasia subtypes. Neurogastroenterol Motil 2016;28:139-145.
24. Nicodème F, de Ruigh A, Xiao Y, et al. A comparison of symptom severity and bolus retention with Chicago classification esophageal pressure topography metrics in patients with achalasia. Clin Gastroenterol Hepatol 2013;11:131-137; quiz e115.

25. Attaar M, Su B, Wong HJ, et al. Intraoperative impedance planimetry (EndoFLIP™) results and development of esophagitis in patients undergoing peroral endoscopic myotomy (POEM). Surg Endosc 2020.
26. Holmstrom AL, Campagna RAJ, Cirera A, et al. Intraoperative use of FLIP is associated with clinical success following POEM for achalasia. Surg Endosc 2020.
27. Holmstrom AL, Campagna RAJ, Alhalel J, et al. Intraoperative FLIP distensibility during POEM varies according to achalasia subtype. Surg Endosc 2020.

TABLES

Table 1. General characteristics according to the high-resolution manometry motility diagnosis

Variables	Type I achalasia	Type II achalasia	Type III achalasia	*p*-value
Number *(n, %)*	14 (20.6)	39 (57.4)	15 (22.1)	
Age (y)	50.0 ± 14.8	49.8 ± 17.5	61.8 ± 13.1	0.045
Male (*n*, %)	6 (43%)	21 (55%)	6 (40%)	0.594
BMI (kg/m^2)	21.2 ± 4.3	22.2 ± 3.5	21.4 ± 3.1	0.355
Median IRP (mmHg)	20.0 ± 0.0	34.2 ± 13.9	33.2 ± 10.9	0.011
Basal EGJ pressure (mmHg)	14.0 ± 1.0	42.0 ± 19.4	53.1 ± 32.9	0.008
Eckardt score	6.4 ± 1.9	6.8 ± 2.4	5.8 ± 2.0	0.369
EGJ-DI (mm^2/mmHg)	2.3 ± 1.6	1.4 ± 0.9	1.6 ± 1.1	0.278
Myotomy length (cm)	11.6 ± 2.5	11.5 ± 2.8	12 ± 2.2	0.811
Procedure time (min)	78.3 ± 22.9	75.4 ± 26.1	75 ± 20.5	0.804

Abbreviations: BMI, body mass index; IRP, integrated relaxation pressure; EGJ, esophagogastric junction; EGJ-DI, EGJ-distensibility index

Table 2. FLIP topography motility classification according to the manometric motility diagnosis

HRM motility diagnosis	No. of cases	FLIP topography motility classification, *n* (%)			
		REO with retrograde contractile response	REO with absent contractile response	REO with normal contractile response	Retrograde contractile response
Type I achalasia	14	7(50%)	0(0%)	2(14.3%)	5(35.7%)
Type II achalasia	39	28(71.8%)	2(5.1%)	6(15.4%)	3(7.7%)
Type III achalasia	15	8(53.3%)	3(20%)	3(20%))	1(6.7%)

Abbreviations: FLIP, functional luminal imaging probe; HRM, high-resolution manometry; REO, reduced esophagogastric junction opening

Table 3. FLIP panometry, achalasia subtypes, and Eckardt scores before and after POEM

Variables		No. of cases	Pre-POEM Eckardt score	Post-POEM Eckardt score	*p*-value
Achalasia subtypes	Type I achalasia	14	6.43 ± 1.95	1.57 ± 1.28	
	Type II achalasia	39	6.77 ± 2.34	1.21 ± 1.17	0.605
	Type III achalasia	15	5.80 ± 1.97	0.67 ± 0.82	
FLIP topography classification	REO with retrograde contractile response	43	6.32 ± 2.37	0.90 ± 1.01	
	REO with absent contractile response	5	6.80 ± 2.86	1.60 ± 1.14	0.854
	REO with normal contractile response	11	6.82 ± 2.13	1.36 ± 1.57	
	Retrograde contractile response	9	6.67 ± 1.00	1.89 ± 0.92	

Abbreviations: FLIP, functional luminal imaging probe; POEM, peroral endoscopic myotomy; REO, reduced esophagogastric junction opening

Table 4. Comparison of variables between the “without PRP” and “with PRP” groups3

Variables		Without PRP group (n = 12)	With PRP group (n = 24)	p-value
LES pressure (mmHg)		38.2 ± 16.6	40.7 ± 14.0	0.638
IRP pressure (mmHg)		29.1 ± 14.0	32.3 ± 10.5	0.446
Myotomy length (cm)		10.7 ± 4.5	15.8 ± 9.0	0.281
Procedure time (min)		84.7 ±32.4	71.8 ± 21.5	0.165
Achalasia type	Type I achalasia	6	2	0.007
	Type II achalasia	6	16	
	Type III achalasia	0	6	
RAC	RAC(-)	4	0	0.008
	RAC(+)	8	24	
RRC	RRC(-)	1	6	0.384
	RRC(+)	11	18	
FLIP topography classification	REO with retrograde contractile response	7	17	0.128
	REO with absent contractile response	0	2	

	REO with normal contractile response	1	4	
	Retrograde contractile Response	4	1	
EGJ-DI (mm^2/mmHg)		2.2 ± 1.3	1.3 ± 0.9	0.023
Pre-POEM Eckardt score		6.00 ± 2.30	6.88 ± 2.58	0.327
Post-POEM Eckardt score		1.08 ± 0.10	1.29 ± 1.43	0.654

Abbreviations: PRP, partial recovery of peristalsis; LES, lower esophageal sphincter; IRP, integrated relaxation pressure; RACs, repetitive antegrade contractions; RRCs, repetitive retrograde contractions; FLIP, functional luminal imaging probe; EGJ-DI, esophagogastric junction–distensibility index; POEM, peroral endoscopic myotomy

FIGURES

Figure 1. Process for the conversion of FLIP data to three-dimensional panometry data

A. Based on FLIP data obtained from each channel of the probe, the values of each channel are shown in a two-dimensional plot. The X-axis shows the procedure time (s), and the Y-axis shows the diameter (mm) of each channel. B. The measured diameter data were used to convert FLIP data to three-dimensional panometry data, and the diameter between each channel was interpolated by the spline method. The spline interpolation method performs interpolation by making interpolation functions of neighboring regions match not only the functional but also the differential value. The three-dimensional contour plot was created using diameter values obtained through interpolation. C. The three-dimensional contour plot is colored according to the diameter. Depending on the diameter, the color changes from red to blue, and a few of the measured diameters less than 5 mm is set to black. D. Creating three-dimensional panometry data using the colored three-dimensional contour plot from Figure 2C. E. Dimension reduction of three-dimensional panometry data into the two-dimensional plot helps check the patient's condition. B to E) In each three-dimensional plot, the X-axis represents the procedure time (s), the Y-axis represents the probe channel, and the Z-axis represents the diameter (mm) measured at the probe.

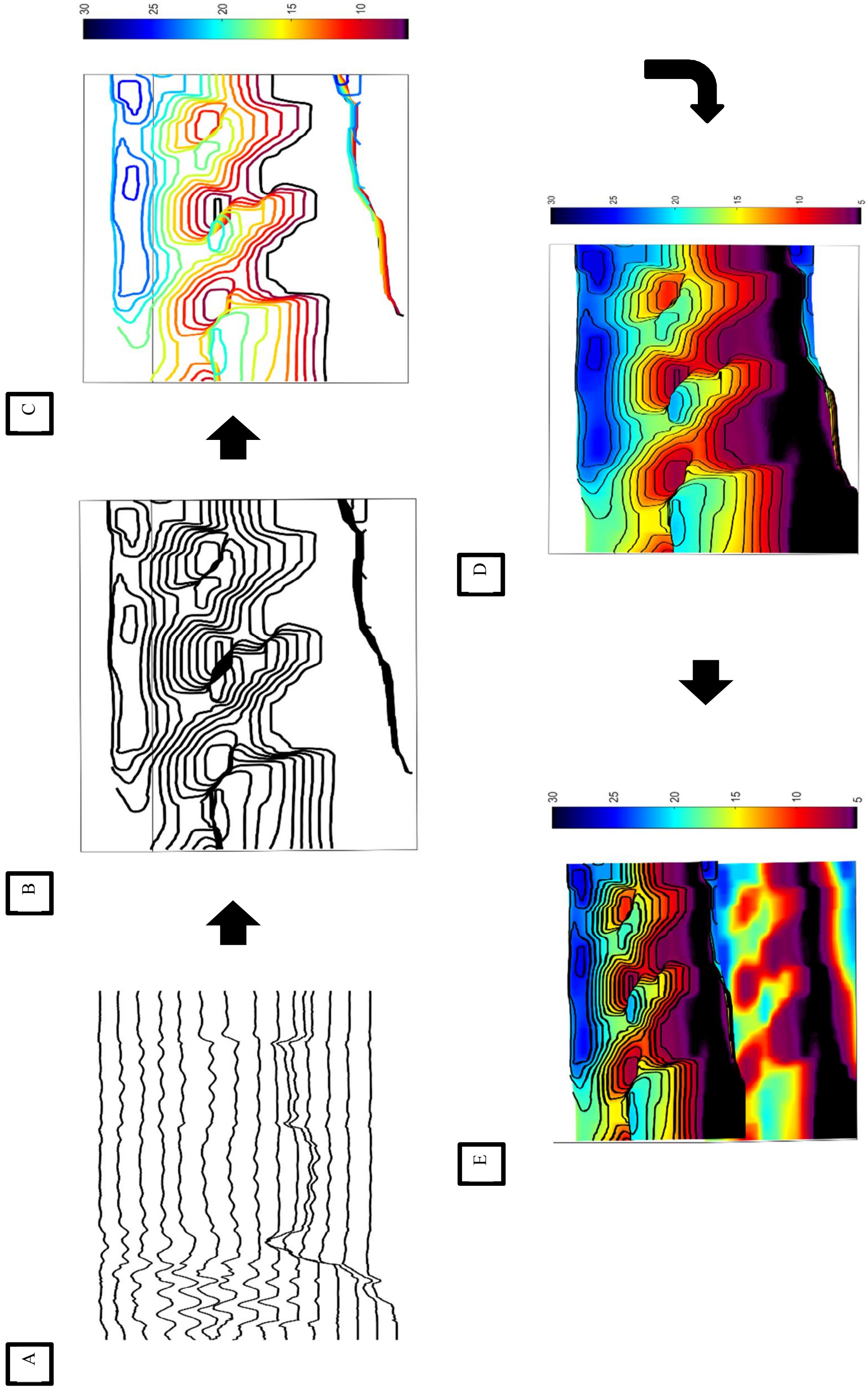

A
B
C
D
E

Figure 2. An example of the contraction types in FLIP panometry produced using the algorithm used to convert FLIP data to three-dimensional panometry data developed in this study. The X-axis represents the procedure time (s), the Y-axis represents the probe channel, and the Z-axis represents the diameter (mm) measured at the probe. A. Repetitive antegrade contraction three-dimensional panometry data. B. Repetitive retrograde contraction three-dimensional panometry data. C. Other contractility three-dimensional panometry data. D. Contractility-absent three-dimensional panometry data

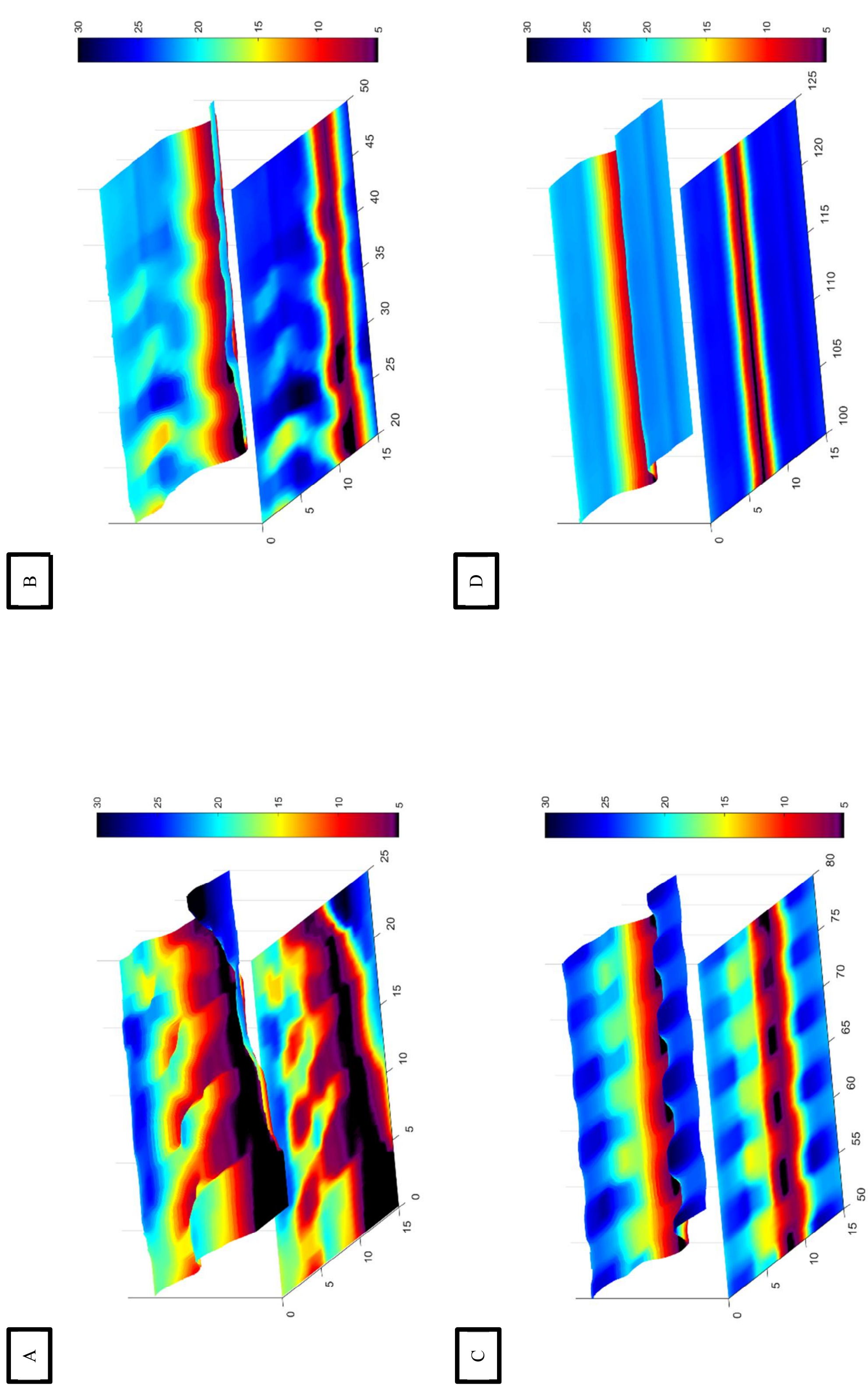

A
B
C
D

Figure 3. Flow diagram of the patient allocation process

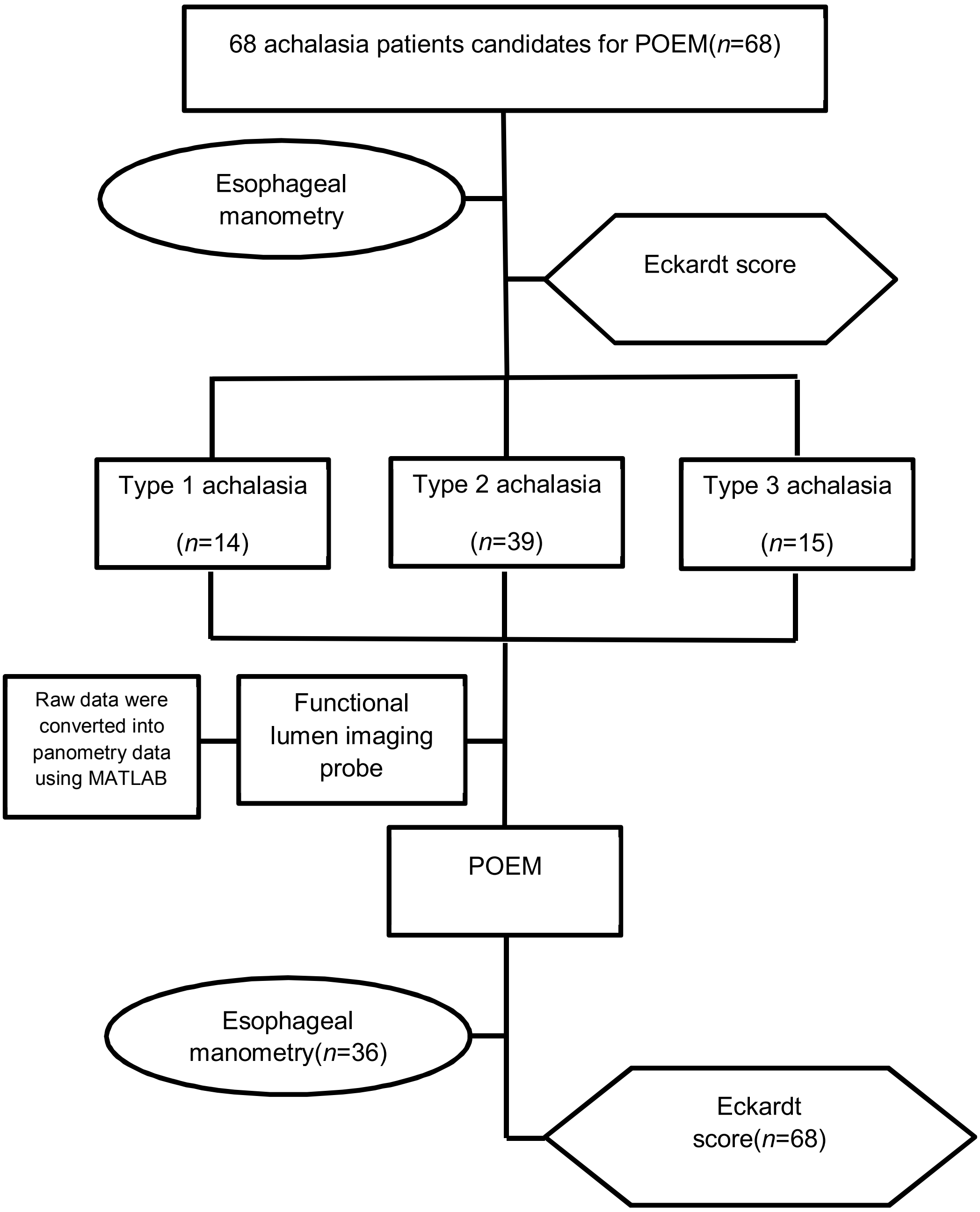
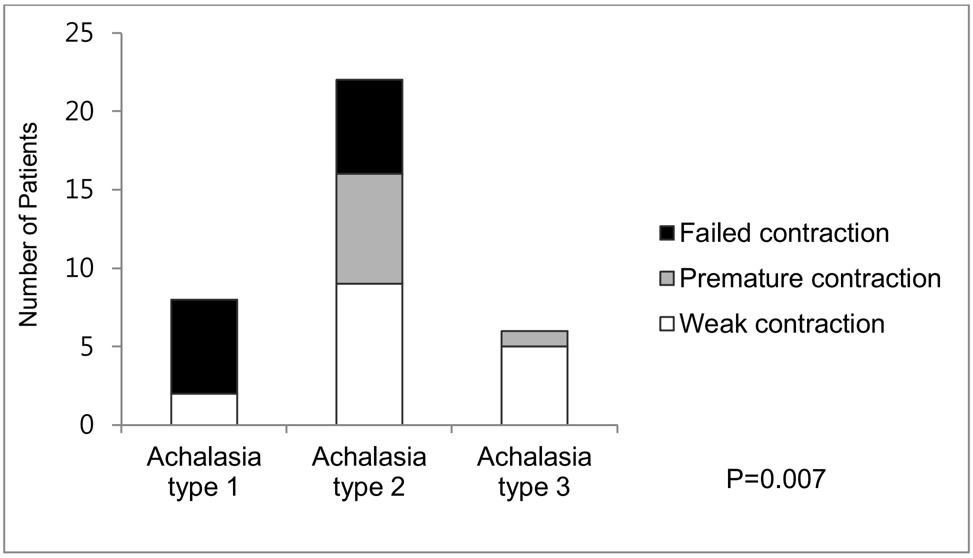
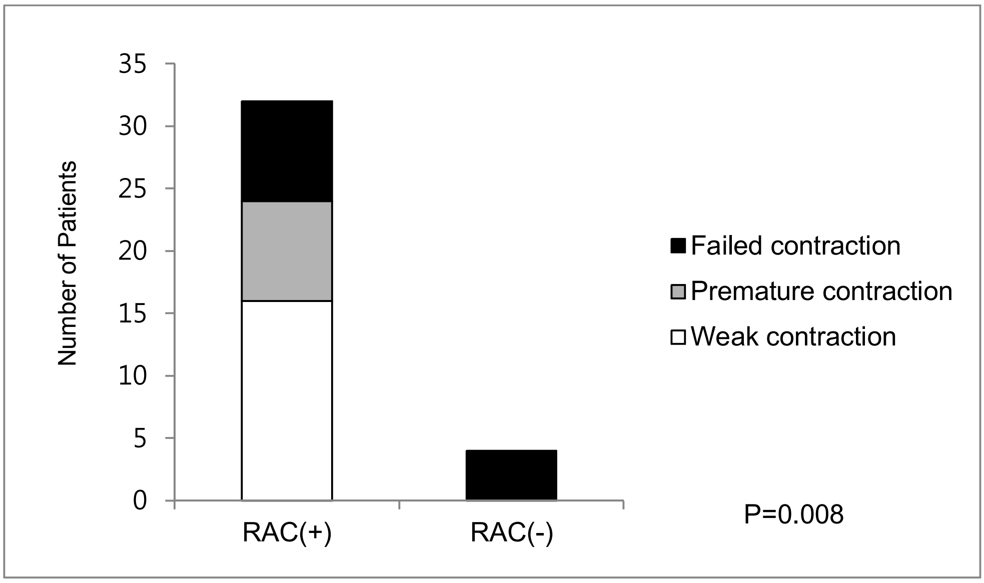


Figure 4. A. The number of patients with partial recovery of peristalsis after POEM in achalasia subtypes. B. The number of patients with PRP after POEM in the repetitive antegrade contractions group. C. The number of patients with PRP after POEM in the repetitive retrograde contractions group.

(A)



(B)



(C)

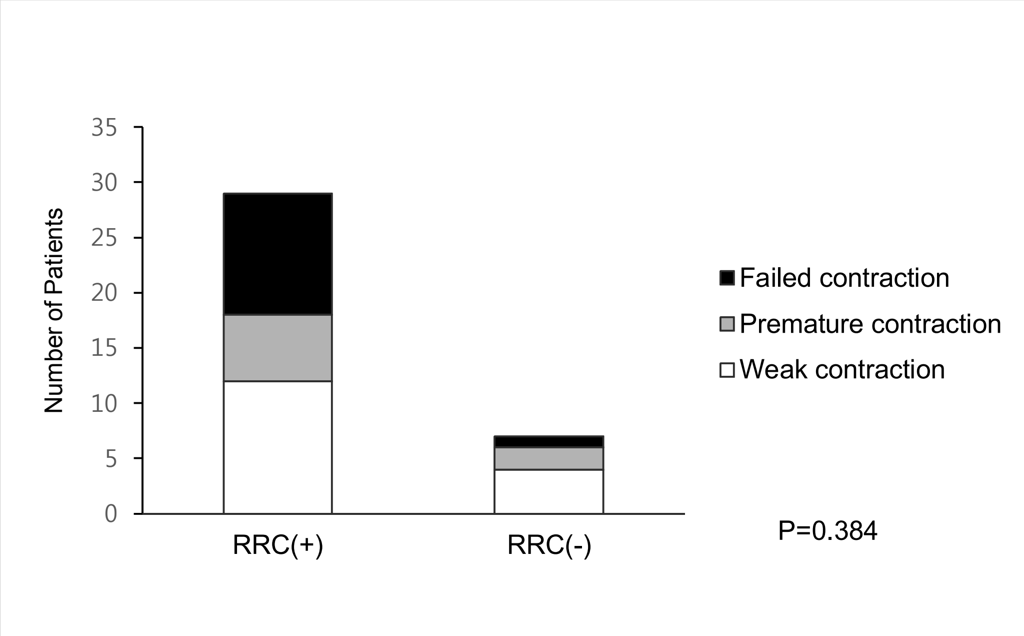
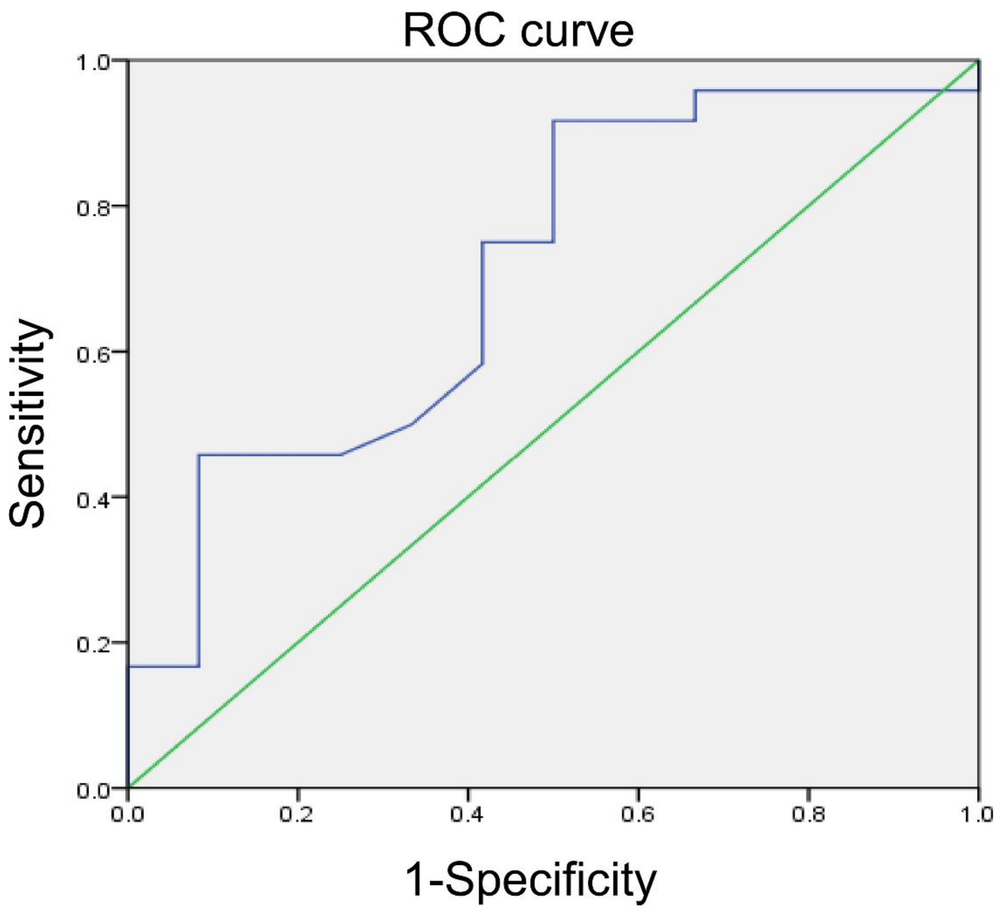
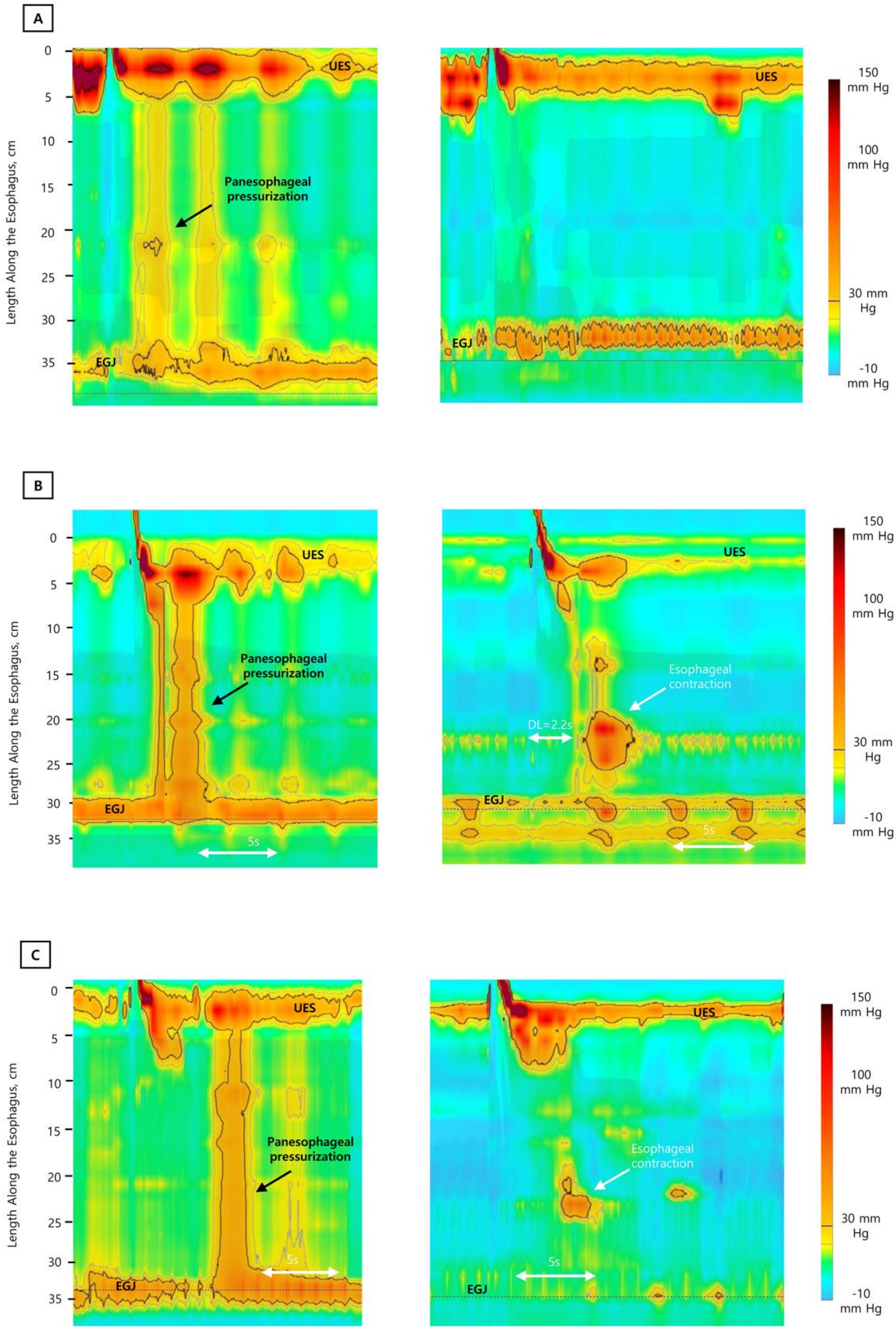

35
30
25
20
15
10
5
0
Number of Patients
RRC(+)
RRC(-)
Failed contraction
Premature contraction
Weak contraction
P=0.384

Figure 5. Receiver operating characteristic curve of the EGJ-DI. Specificity and sensitivity by the cutoff.



Supplementary figure 1. Esophageal pressure topography pre-POEM (left) and post-POEM (right). A–C Patients with type II achalasia. Esophageal pressures were recorded from the upper esophageal sphincter to the esophagogastric junction (EGJ). Pressure amplitudes are coded by color on the right. Both patients with type II achalasia were characterized by impaired EGJ relaxation and panesophageal pressurization. Patient A had failed peristalsis after POEM. The EGJ pressure of patient B had decreased after POEM, but premature contraction persisted (distal latency <4.5 s). Patient C had weak peristalsis after POEM; his post-POEM EGJ pressure was extremely low.


A
B
C
Length Along the Esophagus, cm
UES
EGJ
Panesophageal pressurization
Esophageal contraction
DL=2.2s
5s
150 mm Hg
100 mm Hg
30 mm Hg
-10 mm Hg

국문요약

연구목적: 경구 내시경 근절개술을 시행한 이완불능증 환자에서 식도 기능 내강 영상 프로브 파노메트리의 임상적 유의성과 예측적 능력을 평가하고 경구 내시경 근절개술 시행 후 증상 개선 및 연동운동의 부분적 회복과 관련된 임상변수를 분석하고자 하였다

연구방법: 본 논문은 3 차 병원에서 식도 기능 내강 영상 프로브 파노메트리와 경구 내시경 근절개술을 시행한 이완불능증 환자의 전자 의무 기록을 후향적으로 검토했다. 추적관찰은 식도 고해상도 내압 검사 및 증상에 대한 설문으로 이루어졌다. 식도 기능 내강 영상 프로브 자료는 MATLAB 에서 cubic spline 방법을 사용하여 보간하여 분석하였다.

연구결과: 남자 33 명, 여자 35 명(평균연령: 52±17 세)을 후향적으로 분석하였고, 이 중 14, 39, 15 명의 환자가 Ⅰ형, Ⅱ형, Ⅲ형 이완불능증으로 진단되었다. 식도 기능 내강 영상 프로브 파노메트리의 진단으로는 위식도 접합부 개방 감소(REO)와 역행성 수축 반응(n=43); 수축성 반응이 없는 REO(n=5); 정상적인 수축 반응을 보이는 REO(n=11); 및 역행성 수축 반응(n=9)이 있었다. 모든 환자들은 경구 내시경 근절개술 시행 후 Eckardt 점수가 6.48 ± 2.20 에서 1.16 ± 1.15 로 개선되었다($p<0.01$). 경구 내시경 근절개술 후 증상 개선은 파노메트리 진단을 포함한 어떤 임상 매개변수와도 유의한 연관성은 보이지 않았다. 경구 내시경 근절개술 후 연동운동의 부분적 회복은 반복적인 전방 수축 및 이완불능증 아형의 존재와 유의한 연관성이 있다. (모두 $p<0.01$).

결론: 식도 내강 영상 프로브 파노메트리는 경구 내시경 근절개술 후의 임상 경과를 예측할 수 있고 식도 운동 장애의 기능적 평가에서 식도 고해상도 내압 검사를 보완할 수 있다.

중심단어: 식도 이완불능증, 경구 내시경 근절개술, 식도 기능 내강 영상 프로브