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ORIGINAL ARTICLE

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고해상도 식도내압검사에서 경한 식도 운동 장애로 진단된 환자에서의 항역류 치료 효과

정준호, 김성은, 박무인, 박선자, 문원, 김재현, 정경원, 최윤정, 이준엽, 이영달
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The Effect of Anti-reflux Therapy on Patients Diagnosed with Minor Disorders of Peristalsis in High-resolution Manometry

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Background/Aims: Minor disorders of peristalsis are esophageal motility disorders categorized by the Chicago Classification (CC), version 3.0, which was announced in 2014. This study evaluated the efficacy of anti-reflux therapy in patients with minor peristaltic disorders.
Methods: Patients with minor peristaltic disorders in accordance with CC v3.0 were included. We reviewed the medical records of patients with esophageal high-resolution manometry findings, and investigated the demographic and clinical information as well as the medical therapy. Thereafter, the response to treatment was assessed after at least 4 weeks of treatment.
Results: A total of 24 patients were identified as having minor disorders of peristalsis from January 2010 to December 2015. The mean follow-up period was 497 days, and there were 17 patients (70.8%) patients with ineffective esophageal motility. In terms of anti-reflux therapy, proton pump inhibitors (PPIs) with prokinetic agents and PPIs alone were prescribed in 19 patients (79.2%) and 5 patients (20.8%), respectively. When the rate of response to the treatment was assessed, the responders rate (complete+satisfactory [≥50%] responses) was 54.2% and the non-responders rate (partial [<50%]+refractory responses) was 45.8%. Patients in the responder group were younger than those in the non-responder group (p=0.020). Among them, 13 patients underwent 24-hour multichannel intraluminal impedance-pH, and 10 patients (76.9%) were pathologic gastroesophageal reflux.
Conclusions: The majority of esophageal minor peristaltic disorders were accompanied by gastroesophageal reflux, and therefore, they might respond to acid inhibitor. Further well-designed, prospective studies are necessary to confirm the effect of anti-reflux therapy in these patients. **(Korean J Gastroenterol 2017;69:212-219)**

Key Words: Esophageal motility disorders; Manometry; Treatment outcome; Proton pump inhibitors

INTRODUCTION

Since the development of esophageal high-resolution manometry (HRM), access to the interpretation of esophageal motility disorders has been improved through the Chicago Classification (CC) system. The CC system was first announced in 2008 with major updates presented in 2011 and 2014.[1-3]

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Regarding minor disorders of peristalsis, the third version, v3.0, of the CC, has been simplified from the previous version. In the previous version, peristaltic abnormalities were divided into five parts: 1) weak peristalsis with large peristaltic breaks, 2) weak peristalsis with small peristaltic breaks, 3) frequent failed peristalsis, 4) rapid contractions with normal latency and 5) hypertensive peristalsis.[2] In the most recent version, however, minor disorders of peristalsis are classified into either ineffective esophageal motility (IEM) or fragmented peristalsis, both of which are manifested as impaired esophageal bolus transit.[3] This was done because over-classification, i.e. five categories, may be considered as counterproductive, as it makes the importance of investigating the major disorders of peristalsis pale into insignificance.

The clinical significance of minor disorders of peristalsis has been unclear and highly controversial. A few studies have proposed that IEM is related to gastroesophageal reflux disease (GERD) and that minor peristaltic abnormalities may be an early-stage characteristic of major peristaltic abnormalities, such as achalasia.[4-6] Other studies have suggested that IEM is closely associated with systematic diseases, including systemic sclerosis and chagas disease.[7-9] However, a recent study reported that there was no significant relationship between minor peristaltic disorders and symptoms. Moreover, minor disorders of peristalsis are unaffected by the management.[10] Anti-reflux therapy, such as proton pump inhibitors (PPIs) and prokinetic agents, have been suggested to treat esophageal minor disorders of peristalsis.[11] However, therapeutic options for minor disorders of esophageal peristalsis have not yet been established.

In this study, we investigated the effects of acid inhibitor in patients with minor disorders of peristalsis and attempted to determine the factors associated with treatment response.

SUBJECTS AND METHODS

1. Study population

This study retrospectively enrolled participants aged more than 18 years, who visited Kosin University Gospel Hospital between January 2010 and December 2015, underwent upper endoscopy with esophageal HRM, and were diagnosed with a minor disorder of peristalsis in accordance with the third version of CC. Endoscopic findings, such as the presence of reflux esophagitis (Los Angeles grades as A to D) and hiatal hernia were investigated by upper an endoscopy.[12] Participants were excluded if they were younger than 18 years or had a history of gastrointestinal malignancy, operations involving the upper gastrointestinal tract, esophageal stricture, prior esophageal balloon dilation, surgical myotomy at the lower esophageal sphincter (LES), or a technically insufficient manometry study. We assessed the following: Demographic information, body mass index, alcohol habits, smoking habits, most bothersome symptoms (e.g., dysphagia, chest discomfort, throat discomfort, epigastric discomfort, acid regurgitation, belching), follow-up period, and medical treatments, according to the medical records. The protocol of this study was approved by the institutional review board of the Kosin University College of Medicine.

2. Upper endoscopy

All patients underwent upper endoscopy (GIF H260; Olympus, Tokyo, Japan) to identify the status of gastroesophageal junction, including erosive esophagitis and hiatal hernia. Hiatal hernia was endoscopically confirmed when the distance from the esophagogastric junction (EGJ) to the diaphragmatic impingement was more than 2 cm.[13] All of the endoscopic photographs of the enrolled patients were reviewed by one skilled endoscopist (S.E. Kim).

3. Esophageal HRM protocol and analysis

All esophageal HRM studies were conducted by a well-trained nurse using an esophageal manometry solid-state catheter with 36 circumferential sensors of pressure spaced at 1-cm intervals (Manoscan 360; Sierra Scientific Instruments Inc., Los Angeles, CA, USA). Participants fasted overnight prior to esophageal HRM, and the catheter was calibrated and placed transnasally from the pharynx to the stomach. After equilibration, 10 swallows of 5 mL ambient temperature water with a 30-s interval were carried out in sitting position.[14]

Data were analyzed using the ManoView analysis software (Sierra Scientific Instruments Inc., Los Angeles, CA, USA). IEM and fragmented peristalsis were defined as more than 50% ineffective swallow (failed or weak contraction vigor) with distal contractile integral (DCI) <450 mmHg·s·cm but more than 50% fragmented contractions of DCI >450 mmHg·s·cm in accordance with the third version of CC.[3] The fragmented contraction patterns were defined as more than 5 cm in length of the 20 mmHg isobaric contour with DCI >450 mmHg·s·cm.

Regarding EGJ morphology, type I EGJ morphology was defined as complete overlap of the crural diaphragm and LES components with single peak; type II EGJ morphology was defined as double-peaked pressure zone with the interpeak nadir pressure greater than gastric pressure and a separation of 1-2 cm between peaks.[3] One investigator (S.E. Kim) reviewed all of the enrolled studies.

4. Ambulatory 24-hour multichannel intraluminal impedance-pH monitoring

After fasting overnight, 24-hour multichannel intraluminal impedance-pH (24-h MII/pH) monitoring was performed with a single probe combined impedance and pH (Sandhill Scientific, Highlands Ranch, CO, USA). It is composed of a 2.1 mm diameter catheter with 6 impedance areas (3, 5, 7, 9, 15 and 17 cm above the upper margin of the LES identified by HRM) and a pH-probe located 5 cm above the upper margin of LES. The date of 24-h MII/pH monitoring was analyzed using the BioView MII software (Sandhill Scientific, Highlands Ranch, CO, USA), as well as manually. Each patient recorded their meal times, postural changes, and timing of any symptoms that occurred during the 24-hour study period. All patients underwent 24-h MII/pH with off PPI. The pH parameters included acid exposure time (normal values <4.2%) and DeMeester score (normal values <14.7). Acid exposure time was defined as the percentage of total time that pH was lower than 4 in the distal probe. The impedance parameters included all reflux proximal episodes, all reflux distal episodes (normal values <73), median bolus exposure time (normal values <44.0), and all reflux percent time (normal values <1.4%). Any of the abnormal data of pH or impedance parameters, or a positive symptom index (>50%) was considered as pathologic gastroesophageal reflux (GER).

5. Medical treatment and symptom assessment

Participants with minor disorders of peristalsis were treated with PPIs (e.g., esomeprazole, rabeprazole, lansoprazole, pantoprazole, and ilaprazole) and/or prokinetic agents (e.g., mosapride, itopride, domperidone, DA-9701 [Motilitone®; Dong-A ST, Yongin, Korea]); the symptoms were assessed after at least 4 weeks of treatment. Participants were excluded if they were taking any medications prescribed by a gastroenterologist less than 2 weeks after the diagnosis of minor disorder of peristalsis. In each clinical visit, patients were asked to quantify the changes of their symptoms by percentages and compare the most bothersome symptom before and after medical therapy. The response to medical treatment was categorized as follows: Complete response (more than 80% symptom improvement), satisfactory response (more than 50% symptom improvement), partial response (less than 50% symptom improvement), or refractory response (unresponsive to medical therapy). Responders were defined as patients with a complete or satisfactory response, and non-responders were defined as patients with a partial or refractory response.[15]

6. Statistical analyses

All statistical analyses were performed with the Statistical Package for the Social Sciences for Windows (version 18.0; SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean±standard deviation or the mean (median, range) and were analyzed using the Student's *t*-test. Categorical variables were expressed as the number (%) and analyzed using a Chi-square (χ^2)-test or Fisher's exact test. p-values of less than 0.05 were considered to be statistically significant.

RESULTS

1. Participant characteristics and baseline parameters of the devices

A total of 489 patients underwent esophageal HRM between January 2010 and December 2015. Among them, 24 patients were diagnosed with a minor disorder of peristalsis in accordance with the third version of CC. The average age (mean±standard deviation) was 45.9±15.4 years (range, 21-70 years), and 14 patients (58.3%) were female. The most bothersome symptoms reported were throat discomfort (8 patients, 33.3%), epigastric discomfort (6 patients, 25.0%), acid regurgitation (4 patients, 16.7%), dysphagia (3 patients, 12.5%), chest discomfort (2 patients, 8.3%), and belching (1 patient, 4.2%).

The mean follow-up period was 497 days, and there were 17 patients with IEM (70.8%) and 7 patients with fragmented peristalsis (29.2%). With respect to medical treatment, PPIs with prokinetic agents and PPIs alone were prescribed in 19 patients (79.2%) and 5 patients (20.8%) (Table 1).

Among the 24 enrolled patients, 13 patients underwent

Table 1. Baseline Characteristics in Patients with Minor Disorders of Peristalsis

	Patients (N=24)	IEM (n=17)	Fragmented peristalsis (n=7)
Age (years, mean±SD)	45.9±15.4	48.2±15.3	40.1±15.2
Gender			
Male (%)	10 (41.7)	8 (47.1)	2 (28.6)
Female (%)	14 (58.3)	9 (52.9)	5 (71.4)
BMI (kg/m^2, mean±SD)	23.0±2.5	22.7±2.2	23.6±3.0
Cigarette smoking (%)	5 (20.8)	3 (17.6)	2 (28.6)
Alcohol intake (%)	7 (29.2)	6 (35.3)	1 (14.3)
Most bothersome symptom			
Dysphagia (%)	3 (12.5)	2 (11.8)	1 (14.3)
Chest discomfort (%)	2 (8.3)	2 (11.8)	0 (0)
Throat discomfort (%)	8 (33.3)	5 (29.4)	3 (42.9)
Epigastric discomfort (%)	6 (25.0)	5 (29.4)	1 (14.3)
Acid regurgitation (%)	4 (16.7)	2 (11.8)	2 (28.6)
Belching (%)	1 (4.2)	1 (5.9)	0 (0)
Endoscopic findings			
Reflux esophagitis			
Normal (%)	18 (75.0)	12 (70.6)	6 (85.7)
LA grade A (%)	4 (16.7)	3 (17.6)	1 (14.3)
LA grade B (%)	2 (8.3)	2 (11.8)	0 (0)
Hiatal hernia (%)	6 (25.0)	4 (23.5)	2 (28.6)
Follow-up period (days)[a]	497 (182, 30-2007)	577 (305, 30-2007)	241 (173, 61-839)
Therapeutic methods			
PPI+Prokinetic agent (%)	19 (79.2)	14 (82.4)	5 (71.4)
PPI alone (%)	5 (20.8)	3 (17.6)	2 (28.6)

IEM, ineffective esophageal motility; SD, standard deviation; BMI, body mass index; LA, Los Angeles; PPI, proton pump inhibitor.
[a]Mean (median, range).

Table 2. Baseline HRM and 24-h MII/pH Metrics in Patients with Minor Disorders of Peristalsis

	Patients (N=24)	IEM (n=17)	Fragmented peristalsis (n=7)	p-value
HRM metrics				
LES basal pressure (mmHg, mean±SD)	14.1±6.5	13.6±6.1	15.6±7.8	0.500
LES length (cm, mean±SD)	2.9±0.4	2.8±0.3	3.1±0.5	0.230
IRP (mmHg, mean±SD)	5.5±4.2	5.8±3.5	5.0±5.7	0.671
Effective swallows (%, mean±SD)	46.1±28.9	47.2±31.1	43.3±24.5	0.768
DCI (mmHg·s·cm, mean±SD)	500.9±468.3	288.4±119.0	1017.0±603.5	0.019[b]
EGJ morphology				0.643
EGJ type I, no hiatal hernia (%)	14 (58.3)	10 (58.8)	4 (57.1)	
EGJ type II, small hiatal hernia (%)	10 (41.7)	7 (41.2)	3 (42.9)	
EGJ type III, large hiatal hernia (%)	0 (0)	0 (0)	0 (0)	
pH metrics[a]				
AET (%, mean±SD)	1.8±2.4	1.4±1.9	2.7±3.3	0.347
DeMeester score (mean±SD)	7.2±8.3	6.0±7.1	9.9±11.3	0.461
Impedance metrics[a]				
All reflux proximal episodes (mean±SD)	21.5±11.9	20.4±13.8	24.0±6.7	0.640
All reflux distal episodes (mean±SD)	41.2±17.7	41.8±21.6	40.0±2.2	0.788
Median bolus exposure time (sec, mean±SD)	11.8±5.3	9.9±3.3	16.0±7.0	0.052
All reflux percent time (%, mean±SD)	1.2±0.8	1.9±1.0	1.1±0.3	0.759
Pathologic GER[a]	10/13 (76.9)	7/9 (77.8)	3/4 (75.0)	0.706

HRM, high-resolution manometry; 24-h MII/pH, 24-hour multichannel intraluminal impedance-pH; IEM, ineffective esophageal motility; LES, lower esophageal sphincter; SD, standard deviation; IRP, integrated relaxation pressure; DCI, distal contractile integral; EGJ, esophagogastric junction; AET, acid exposure time; GER, gastroesophageal reflux.
[a]Among the 24 enrolled patients, 13 patients underwent the 24-h MII/pH study. There were 9 patients in IEM group and 4 patients in fragmented peristalsis group, respectively; [b]Indicates statistical significance.

Table 3. Response to Treatment in the Patients with Minor Disorders of Peristalsis after Medical Therapy

	Patients (N=24)	IEM (n=17)	Fragmented peristalsis (n=7)
Response to treatment			
Complete (%)	6 (25.0)	3 (17.6)	3 (42.9)
Satisfactory (%)	7 (29.2)	4 (23.5)	3 (42.9)
Partial (%)	8 (33.3)	8 (47.1)	0 (0)
Refractory (%)	3 (12.5)	2 (11.8)	1 (14.3)
Response to treatment			
Responders (%)[a]	13 (54.2)	7 (41.2)	6 (85.7)
Non-responders (%)[b]	11 (45.8)	10 (58.8)	1 (14.3)

IEM, ineffective esophageal motility.
[a]Responders include patients who showed complete and satisfactory response; [b]Non-responders include patients who showed partial and refractory response.

the 24-h MII/pH study, and the proportion of pathologic GER was 76.9% (10 patients). In terms of HRM and 24-h MII/pH metrics, only DCI is significantly higher in the fragmented peristalsis group compared with the IEM group (p=0.019). However, other parameters were not significantly difference between IEM and fragmented peristalsis (Table 2).

2. Response to anti-reflux therapy

Of the 24 patients with minor disorders of peristalsis who received anti-reflux therapy, a complete response was observed in 6 patients (25.0%); satisfactory response (≥50% symptom improvement) in 7 patients (29.2%); partial response (<50% symptom improvement) in 8 patients (33.3%); and refractory response in 3 patients (12.5%). Therefore, the rate of responders (54.2%) was slightly higher than the rate of non-responders (45.8%). The response rates to medical therapy are revealed in Table 3.

3. Factors associated with response to treatment

When we analyzed patients according to the response to treatment, patients in the responders group were significantly younger than those in the non-responders group (p=0.020). Unfortunately, there were no significant differences in the most bothersome symptoms and other factors between the two groups. Six out of the seven patients (85.7%) with fragmented peristalsis were in the responders group. There was no significant difference between IEM and fragmented peristalsis; however, the treatment response of patients with fragmented peristalsis seemed to be better than that of IEM patients (p=0.078) (Table 4).

DISCUSSION

We evaluated the effect of anti-reflux therapy, such as PPIs, in patients with minor disorders of esophageal peristalsis by HRM. The rate of responders with complete response and satisfactory response was 54.2%. When we included a partial response in the responders group, the rate of responders was 87.5%. These results were associated with the characteristics of minor disorders of peristalsis. Most patients in this current study complained of typical and atypical symptoms of GERD, and 76.9% of patients showed an association with GERD in the results of the 24-h MII/pH monitoring. Therefore, we suspected that most of these disorders would be accompanied by GERD, thus minimizing its own clinical importance.

A few studies have investigated the mechanism underlying the symptoms of esophageal motility disorders. One recent study identified 135 patients with minor motor functional abnormalities, with GERD being the most common indication.[10] With respect to GERD symptoms, IEM (characterized by a pathologic number of large breaks [>5 cm length]) was significantly associated with delayed reflux clearance and higher acid exposure time in patients with GERD symptoms.[4] Another study revealed that the main presenting symptom was dysphagia in 65 patients with nonspecific esophageal motility disorders,[6] which may likely be associated with degeneration and atrophic changes in the layers of the esophageal smooth muscle.[16] One interesting study from Japan investigated the esophageal motility in patients with globus sensation who were refractory to PPI treatment. Out of the total of 119 patients who were refractory to PPI treatment, 47.9% had abnormal esophageal motility, of which 66.4%

Table 4. Comparison of Clinical Factors, HRM and 24-h MII/pH Metrics in Accordance with the Response to Treatment

	Responders (n = 13)	Non-responders (n = 11)	p-value
Age (years, mean±SD)	39.4±11.3	53.6±16.4	0.020[b]
Female (%)	8 (57.1)	6 (42.9)	1.000
BMI (kg/m^2, mean±SD)	23.6±2.8	22.2±1.7	0.178
Cigarette smoking (%)	4 (80.0)	1 (20.0)	0.327
Alcohol intake (%)	5 (71.4)	2 (28.6)	0.386
Most bothersome symptom			
Dysphagia (%)	0 (0)	3 (100.0)	0.082
Chest discomfort (%)	0 (0)	2 (100.0)	0.199
Throat discomfort (%)	4 (50.0)	4 (50.0)	1.000
Epigastric discomfort (%)	4 (66.7)	2 (33.3)	0.649
Acid regurgitation (%)	4 (100.0)	0 (0)	0.098
Belching (%)	1 (100.0)	0 (0)	1.000
Endoscopic findings			
Reflux esophagitis			0.397
Normal (%)	9 (69.2)	9 (81.8)	
LA grade A (%)	2 (15.4)	2 (18.2)	
LA grade B (%)	2 (15.4)	0 (0)	
Hiatal hernia (%)	3 (23.1)	3 (27.3)	1.000
Type of minor disorders of peristalsis			0.078
IEM (%)	7 (41.2)	10 (58.8)	
Fragmented peristalsis (%)	6 (85.7)	1 (14.3)	
HRM metrics			
LES basal pressure (mmHg, mean±SD)	15.2±6.4	12.9±6.7	0.397
LES length (cm, mean±SD)	2.9±0.5	2.9±0.3	0.951
IRP (mmHg, mean±SD)	4.9±4.4	6.3±3.9	0.438
Effective swallows (%, mean±SD)	47.9±27.5	43.9±31.7	0.742
DCI (mmHg·s·cm, mean±SD)	645.2±579.7	330.3±204.9	0.087
EGJ morphology			0.697
EGJ type I, no hiatal hernia (%)	7 (50.0)	7 (50.0)	
EGJ type II, small hiatal hernia (%)	6 (60.0)	4 (40.0)	
pH metrics[a]			
AET (%, mean±SD)	1.6±2.5	2.1±2.3	0.703
DeMeester score (mean±SD)	6.2±8.6	8.7±8.6	0.615
Impedance metrics[a]			
All reflux proximal episodes (mean±SD)	25.1±12.0	15.8±10.4	0.179
All reflux distal episodes (mean±SD)	44.8±15.1	35.4±21.9	0.378
Median bolus exposure time (sec, mean±SD)	12.9±5.7	10.0±4.6	0.365
All reflux percent time (%, mean±SD)	1.3±0.8	1.2±1.0	0.802
Pathologic GER[a]	6/8 (60.0)	4/5 (40.0)	1.000
Therapeutic methods			0.585
PPI+Prokinetic agent (%)	10 (52.6)	9 (47.4)	
PPI alone (%)	3 (60.0)	2 (40.0)	

HRM, high-resolution manometry; 24-h MII/pH, 24-hour multichannel intraluminal impedance-pH; SD, standard deviation; BMI, body mass index; LA, Los Angeles; IEM, ineffective esophageal motility; LES, lower esophageal sphincter; IRP, integrated relaxation pressure; DCI, distal contractile integral; EGJ, esophagogastric junction; AET, acid exposure time; GER, gastroesophageal reflux; PPI, proton pump inhibitor.
[a]Among the 24 enrolled patients, 13 patients underwent the 24-h MII/pH study. There were 8 patients in the responders group and 5 patients in non-responders group, respectively; [b]Indicates statistical significance.

had IEM.[17] The mechanism of esophageal motility disorders in patients with globus sensation might also be associated with GERD, because of the globus sensation is one of the atypical symptoms of GERD.

There are not many therapeutic options for patients with minor disorders of esophageal peristalsis. As mentioned above, minor disorders of peristalsis are associated with GER due to prolonged esophageal clearance and potent anti-secretory therapy, such PPIs is one of the most important methods for controlling the symptoms in these patients.[4,11] Moreover, patients with severe hypomotility disorder due to systemic sclerosis, who took high doses of PPIs twice a day,

showed significant improvements in GERD symptoms.[18] In the current study, most enrolled patients complained of typical or atypical GERD symptoms, and we also suspected that patients with minor disorders of peristalsis could be related with GERD. Therefore, treatments were focused on the symptoms of patients rather than correcting peristaltic dysfunction, and we prescribed anti-secretory therapy to these patients. With respect to the PPI dose, most patients (21 patients, 87.5%) received the standard dose of PPI, and two patients (8.3%) and one patient (4.2%) received half the standard dose and double the standard dose of PPI, respectively. Interestingly, the PPI medication period in the non-responder group was longer than the responder group (mean, 665.8 days vs. 321.2 days). It is presumed that poor treatment response might influence the treatment period of patients. However, there was no statistical difference in the symptom responses in accordance with the PPI dose (p=0.576) and PPI mediation period (p=0.164). Several studies have evaluated the efficacy of prokinetic agents, but the clinical usefulness of prokinetics in esophageal motility disorders, including minor peristaltic disorders, is still controversial.[11,19,20] Mosapride, a prokinetic agent, which is a serotonin 5-HT_4 receptor agonist, significantly increased peristaltic contraction, especially in distal esophageal segments and significantly elevated mean resting LES pressure.[19] DA-9701 is a novel prokinetic agent that is the standardized extract of Pharbitis Semen and Corydalis Tuber.[21] DA-9701 induced smooth muscle contraction in feline esophageal smooth muscle cells by binding to the 5-HT_2, 5-HT_3 and 5-HT_4 receptors.[22] However, there was no significant difference in LES resting pressures, swallow-associated relaxation, and duration or strength of peristaltic contraction between the itopride and placebo groups.[20] Nevertheless, PPIs and/or prokinetic agents are currently considered to be reasonable therapeutic options for patients with minor disorders of esophageal peristalsis depending on their clinical symptoms.

In the current study, younger age was significantly associated with the improvement of symptoms, which could be associated with the pathogenesis of minor esophageal motility disorders. There are three stages—neuropathy, myopathy, and fibrosis—in patients with esophageal hypomotility disorders.[23] First, the neuronal abnormalities are considered to be the result of arteriolar changes in the vasa nervorum. Second, focal degeneration and atrophy occur in the muscle layers due to ischemia. Lastly, the muscle tissue is changed by fibrosis with collagen deposits.[16] These changes in the smooth muscle result in absent peristalsis, as shown by the manometry, which characterized advanced esophageal motility disorders. Age could likely influence innervation and subsequent pathological progression of the esophagus. Similarly, patients with fragmented peristalsis seemed to have a better treatment response than those with IEM, although there was no significant difference in this study.

There are several limitations in this study. First, the sample size is small, and there was no control group in our study. Therefore, it is difficult to reflect the whole clinical outcomes of minor peristaltic disorders. Second, we did not perform the multiple rapid swallow (MRS) test for the diagnosis of IEM in our patients. In the third version of CC, it is unclear whether considering MRS for the diagnosis of IEM provides relevant significance clinically, because MRS could identify the peristaltic reserve in the esophagus.[3] A recent study also revealed the usefulness of MRS in patients with IEM, and IEM patients with weak MRS contraction have an increased risk of abnormal bolus clearance, transit, and exposure.[24] Third, various PPIs and prokinetic agents were used to treat these patients. Moreover, our patients did not undergo repeated HRM after the therapy to confirm whether minor peristaltic disorder has been improved. However, our detailed and specific examinations were conducted by experts, such as endoscopists and physician assistants specializing in gastrointestinal motility. In addition, the present study evaluated the relevant factors affecting symptom improvement, including epidemiologic factors and metrics of HRM. Only a few studies have verified the clinical outcomes of minor disorders of peristalsis, and there has not been a study that analyzed HRM using the third version of CC. Moreover, to the best of our knowledge, this is the first such study that targeted an Asian population.

In conclusion, most esophageal minor peristaltic disorders were accompanied by GER; therefore, they might have a reaction to anti-reflux therapy. In addition, younger age appears to be associated with good response in Korean patients with minor peristaltic disorders. However, further, well-controlled studies are necessary to evaluate the effects of anti-secretory therapy regarding esophageal minor peristaltic disorders.

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