



Clinical Implications of the Gastroesophageal Reflux Disease Questionnaire and Reflux Symptom Index in Patients With Suspected Laryngopharyngeal Reflux Symptoms

Young Dong Kim,¹ Cheol Min Shin,^{1*} Woo-Jin Jeong,^{2*} Yang Jin Kim,¹ Hyuk Yoon,¹ Young Soo Park,¹ Nayoung Kim,¹ and Dong Ho Lee¹

Departments of ¹Internal Medicine and ²Otorhinolaryngology-Head and Neck Surgery, Seoul National University Bundang Hospital, Seongnam, Gyeonggi-do, Korea

Background/Aims

To evaluate the usefulness of gastroesophageal reflux disease questionnaire (GerdQ) and reflux symptom index (RSI) for diagnosis of gastroesophageal reflux disease (GERD) in patients with suspected laryngopharyngeal reflux (LPR) symptoms (cough, hoarseness, globus, and throat pain).

Methods

A total of 98 patients with LPR symptoms were incorporated from either gastroenterology or otorhinolaryngology clinic. Patient's laryngoscopic findings were graded by reflux finding score (RFS), and RFS ≥ 7 was considered as positive LPR. Erosive esophagitis on endoscopy or abnormal results on ambulatory impedance-pH monitoring were used as diagnostic criteria for GERD. Esophageal motor function was evaluated using high-resolution esophageal manometry.

Results

Ninety-three (94.9%) of the 98 subjects were diagnosed as LPR by RFS, but only 15 (15.3%) had GERD. For GerdQ, the cutoff value of 9 showed the highest area under curve (AUC) to diagnose GERD by receiver operating curve analysis (AUC = 0.565); the sensitivity, specificity, positive predictive value, and negative predictive value were unsatisfactory (50.0%, 70.7%, 22.6%, and 89.2%, respectively.) RSI also showed poor performance in diagnosing GERD; the cutoff value of 25 showed the highest yield (AUC = 0.581); the sensitivity, specificity, positive predictive value, and negative predictive value were 42.9%, 79.3%, 26.1%, and 89.0%, respectively. Ineffective esophageal motility was frequently observed (69 of 98, 70.4%), but there was no difference in esophageal motility parameters between GERD and non-GERD patients.

Conclusions

In patients with LPR symptoms, significant discrepancies are observed between laryngoscopic diagnosis and GERD. In this population, neither GerdQ nor RSI is useful in diagnosing GERD.

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Key Words

Gastroesophageal reflux questionnaire; Laryngopharyngeal reflux; Reflux finding score; Reflux symptom index

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*Correspondence: Cheol Min Shin and Woo-Jin Jeong are equally responsible for this study.

Cheol Min Shin, MD, PhD

Department of Internal Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam, Gyeonggi-do 13620, Korea

Tel: +82-31-787-7057, Fax: +82-31-787-4052, E-mail: scm6md@gmail.com

Woo-Jin Jeong, MD, PhD

Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Bundang Hospital, 82 Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam, Gyeonggi-do 13620, Korea

Tel: +82-31-787-7409, Fax: +82-31-787-4057, E-mail: safar@snuh.org

Introduction

Gastroesophageal reflux disease (GERD) is one of the most common functional gastrointestinal disorders.¹ The prevalence of GERD is between 9.0-26.0% in Western countries and 1.1-7.1% in Eastern countries.^{2,3} Although the prevalence of GERD is relatively lower in Asia, the prevalence of GERD is increasing in Korea.^{4,5}

There is no gold standard in the diagnosis of GERD. According to the Montreal agreement, GERD has been defined as a condition that develops when the gastric refluxate causes troublesome symptoms and/or complications.⁶ The diagnosis of GERD is based on the symptoms such as heartburn and regurgitation.⁷ In clinical practice, GERD is empirically diagnosed and treated based on the clinician's assessment of typical GERD symptoms, but GERD can also cause atypical symptoms such as cough, hoarseness, globus, and throat pain.⁸ So it is often difficult to distinguish GERD from other similar conditions in clinical primary care settings.^{9,10} Laryngopharyngeal reflux (LPR) is a distinct clinical entity that may result from GERD but require additional treatment.^{11,12} It is apparent that the pathophysiology of LPR is different to that of classical GERD.¹³ Also, there is wide discrepancy among experts on the diagnosis of LPR.¹⁴ Some of LPR symptoms appear to be over-diagnosed, and not actually caused by GERD.

Diagnostic procedures such as endoscopy, pH-metry, esophageal impedance monitoring, are invasive and uncomfortable to the patient. So the diagnostic method using questionnaires has been tried to improve the diagnostic accuracy of the questionnaire.¹⁵⁻¹⁷ Among them, gastroesophageal reflux disease questionnaire (GerdQ) is a self-administered diagnostic questionnaire consisting of 6 items.¹⁸ Recently, it was validated in Korean GERD patients.¹⁹ Similarly, Belafsky et al²⁰ developed the reflux symptom index (RSI), a validated, self-administered, 9-item scoring system, designed to assess the symptoms related to LPR.

The aims of this study are to evaluate the diagnostic yield of the

GerdQ and RSI for GERD in patients with suspected LPR symptoms, and to provide a comparison of endoscopic findings, 24-hour ambulatory esophageal impedance-pH monitoring parameters, and high-resolution esophageal manometry (HREM) parameters between patients with and without GERD.

Materials and Methods

Ethics Statement

This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (Seongnam, Gyeonggi-do, Korea); the approval number is B-2003/598-104. The study was given exemption from written informed consents by the Institutional Review Board. We conducted a retrospective study.

Study Subjects

In this study, we enrolled 98 patients with suspected LRP symptoms (cough, hoarseness, globus, and throat pain) in either gastroenterology or otorhinolaryngology clinic. All the study subjects responded to the GerdQ (Supplementary Table 1). All of them underwent HREM and multichannel intraluminal impedance and ambulatory pH (MII-pH) monitoring. They also had esophago-gastroduodenoscopy within 6 months before enrollment at Seoul National University Bundang Hospital or an outside clinic, and their endoscopic images were reviewed to check reflux esophagitis (RE). RE was graded by the Los Angeles (LA) classification. All study subjects underwent laryngoscopic examination at the time of enrollment. They filled in the RSI questionnaire to evaluate LPR symptoms.

Gastroesophageal Reflux Disease Questionnaire

GerdQ consists of 6 items (Supplementary Table 1).²¹ A 4-graded Likert scale (0-3) is used to score the frequency of heartburn, regurgitation, sleep disturbances due to gastroesophageal

reflux, or the use of over-the-counter medications to relieve reflux symptoms in the last 1 week. A reversed Likert scale is used for 2 questions such as frequency of epigastric pain and nausea. The result of GerdQ ranges from 0 to the highest score 18. We used a Korean version of GerdQ questionnaire in this study.¹⁹ The most meaningful cut-off value of GERD probability was determined in the study population.

Reflux Finding Score

A single otorhinolaryngologist (W.J.J.) checked the larynx area with a 4 mm diameter, 70-degree laryngeal endoscopy with knowledge of the patient's symptoms. Each patient's findings were filled out by the reflux finding score (RFS) form (adapted from Belafsky et al).²² RFS is graded by (1) subglottic edema, (2) ventricular obliteration, (3) erythema and/or hyperemia, (4) vocal fold edema, (5) diffuse laryngeal edema, (6) posterior commissure hypertrophy, (7) granule and/or granulation tissue, and (8) thick endo-laryngeal mucus (Supplementary Table 2). The score ranges from 0 (minimum score) to 26 (maximum score). RFS ≥ 7 was considered as positive.²²

Reflux Symptom Index

RSI is a self-administered, 9-item scoring system, published by Belafsky et al.²⁰ It was designed to assess LPR symptoms, including (1) hoarseness or voice problems, (2) throat clearing, (3) excess throat mucus or postnasal drip, (4) swallowing difficulty, (5) coughing related to eating or lying down, (6) breathing difficulties, (7) troublesome or annoying cough, (8) sensation of something sticking or a lump in the throat, and (9) heartburn, chest pain, indigestion, or stomach acid coming up, with a maximum total score of 45 (Supplementary Table 3). We used a Korean version RSI questionnaire in this study.²³ The cutoff value of RSI in diagnosing GERD for patients with suspected LPR symptoms was evaluated in this study.

Multichannel Intraluminal Impedance pH Monitoring

The patients underwent combined MII-pH monitoring-esophageal manometry after at least 6 hours of fasting. A pH-impedance catheter (Sandhill Scientific Inc, Highlands Ranch, CO, USA) was inserted trans-nasally; the pH electrode was placed at 3 cm above the lower esophageal sphincter (LES). Esophageal impedance was measured at 3, 5, 7, 9, 15, and 17 cm above the LES. During the procedure, patients were encouraged to everyday living as usual and to eat usual meals. The patients were instructed to keep in an upright position for the daytime and lie down only during bedtime. The result was analyzed using BioVIEW analysis

software (Sandhill Scientific Inc). Total 24-hour esophageal acid exposure time (AET, %) was defined as the percentage of time of a pH below 4. Abnormal AET was defined as an intra-esophageal pH of < 4 for more than 4.2% during the inspection period. A DeMeester score (DMS) of > 14.72 was defined as positive.

In this study, baseline impedance (BI) levels were assessed every 2-hours at both proximal BI is the mean BI of 15 cm and 17 cm above LES (proximal BI) and that of 3 cm and 5 cm above LES (BI) manually. A 30-second period was selected, and the BI during this period was calculated. Finally, the 2-hourly BI values were averaged for the entire 24-hour measurement.²⁴

Definition of Gastroesophageal Reflux Disease

GERD, including both erosive esophagitis and non-erosive reflux disease, was defined as being diagnosed if any one of the followings were present: (1) AET $> 4.2\%$, (2) DMS > 14.72 , (3) number of reflux episode > 73 , and (4) RE (LA classification grades A-D) on endoscopy.⁸

High-resolution Esophageal Manometry

The patient's esophageal motor function was evaluated by using HREM.²⁴ HREM was performed by just 1 operator (InSIGHT HRiM system, Sandhill Scientific Inc). It was performed after at least 6 hours of fasting in the upright position; any medications which may affect esophageal motor function should be discontinued for more than 7 days before the study. A catheter with a total of 32 circumferential pressure transducers spaced 1 cm apart was used to measure the esophageal pressure. Before each study, calibration of the catheter was done, equilibrated to atmospheric pressure. The HREM protocol included a 5-minute period of the basal sphincter pressure measurement, and 10 swallows of 5 mL water. The data analysis was performed using BioVIEW software (Sandhill Scientific Inc).

Pressure was visualized into color topographic plots. Continuous pressure picture was provided throughout the segment. Transitional zone defect (TZD) is a break between the end of the proximal esophageal segment and the beginning of the distal esophageal segment in the 20-mmHg isobaric contour. The TZD length is measured as the vertical distance between the 2 segments. If another break is observed around the distal pressure troughs, it is also measured as the vertical distance (distal break [DB]). Ineffective swallow includes (1) weak contraction: $100 \leq$ distal contractile integral (DCI) < 450 mmHg-sec-cm, (2) failed peristalsis: DCI < 100 mmHg-sec-cm, and (3) fragmented swallow: TZD of peristalsis > 5 cm in the setting of a DCI ≥ 450 mmHg-sec-cm. Inef-

fective esophageal motility (IEM) was defined as more than 70% of swallows as ineffective, or $\geq 50\%$ failed peristalsis, following the Chicago classification version 4.0.

Statistical Methods

Statistical analyses were performed using R software (version 4.0.3). Differences were considered statistically significant at a level of $P < 0.05$. All statistical analyses were 2-sided. The characteristics of the study subjects were presented using the Student's *t* test or χ^2 test when appropriate. The optimal cutoff value of each questionnaire was determined by using the "RO" and "epi.tests" functions in the "epiR" package in R (<https://cran.r-project.org/web/pack>

Table 1. Characteristics of the Study Subjects According to the Presence or Absence of Gastroesophageal Reflux Disease

Characteristics	GERD (n = 15)	Non-GERD (n = 83)	P-value
Male	9 (60.0)	47 (56.6)	0.808
Age (yr)	53.1 ± 11.7	55.5 ± 12.9	0.513
BMI (kg/m ²)	24.7 ± 2.9	22.6 ± 3.1	0.011
Main complaints			
Globus	10 (66.7)	63 (75.9)	0.072
Hoarseness	3 (20.0)	15 (18.1)	
Throat pain	0 (0.0)	4 (4.8)	
Cough	2 (13.3)	1 (1.2)	
Endoscopic findings ^a			
No RE	10 (66.7)	83 (100)	NA
LA-A	4 (23.5)	0	
LA-B	1 (11.8)	0	
Laryngopharyngeal reflux ^b	15 (100.0)	78 (94.0)	0.428
GerdQ score	8.1 ± 3.0	7.6 ± 2.2	0.533
RSI score	19.4 ± 10.0	18.1 ± 8.7	0.600
Impedance-pH monitoring parameters			
DeMeester score	13.9 ± 14.3	2.9 ± 2.5	0.010
DeMeester score > 14.72	5 (33.3)	0 (0.0)	< 0.001
Acid exposure time (%)	4.3 ± 4.3	0.7 ± 0.8	0.007
Acid exposure time > 4.2%	5 (33.3)	0 (0.0)	< 0.001
Reflux activity	62.6 ± 24.5	38.0 ± 15.5	0.002
Reflux activity > 73	7 (46.7)	0 (0.0)	< 0.001
Reflux activity			
< 40	3 (20.0)	50 (60.2)	< 0.001
40-79	7 (46.7)	33 (39.8)	
> 80	5 (33.3)	0 (0.0)	
Proximal extent of reflux ^c (n)	34.5 ± 14.8	20.0 ± 11.3	< 0.001
Proximal BI ^d (Ω)	2073.9 ± 464.0	2461.7 ± 618.4	0.023
Distal BI ^e (Ω)	1818.9 ± 841.6	2779.4 ± 784.7	< 0.001
Proximal to distal BI ratio ^f	1.6 ± 1.4	0.9 ± 0.3	0.104

ages/epiR/index.html), and sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each diagnostic method were calculated.

Results

Characteristics of the Study Participants

The characteristics of 98 subjects were as follows. The median age was 55.1 years (range: 21-83 years); 56 patients (57.1%) were men; the median body mass index (BMI) was 22.9 kg/m² (range: 17.2-32.4). Their main complaints included globus (n = 73, 74.5%), hoarseness (n = 18, 18.4%), throat pain (n = 4, 4.1%), and cough (n = 3, 3.1%).

Table 1. Continued

Characteristics	GERD (n = 15)	Non-GERD (n = 83)	P-value
HREM parameters			
Resting LES pressure (mmHg)	22.8 ± 9.2	20.3 ± 13.7	0.499
IRP (mmHg)	11.3 ± 4.7	12.9 ± 6.8	0.376
Resting UES pressure (mmHg)	78.8 ± 39.1	77.2 ± 39.4	0.885
Distal contractile integral (mmHg-sec-cm)	1158.7 ± 952.2	1058.5 ± 1081.5	0.738
TZD length (cm)	5.8 ± 4.3	6.4 ± 4.4	0.635
DB length (cm)	0.5 ± 0.6	0.7 ± 1.1	0.415
TZD + DB length (cm)	6.3 ± 4.5	7.1 ± 4.6	0.520
Ineffective esophageal motility	8 (53.3)	61 (73.5)	0.132

^aThere were no patients with severe erosive esophagitis (Los Angeles [LA] classification grade C or D) in this study.

^bLaryngopharyngeal reflux was defined as reflux finding score ≥ 7 by laryngoscopic exam.

^cProximal extent of reflux is the number of reflux events reaching 15 cm above the low esophageal sphincter (LES).

^dProximal baseline impedance (BI) is the mean baseline impedance of 15 cm and 17 cm above LES.

^eDistal BI is mean baseline impedance of 3 cm and 5 cm above LES.

^fProximal to distal ratio was calculated as proximal BI/distal BI.

GERD, gastroesophageal reflux disease; BMI, body mass index; RE, reflux esophagitis; GerdQ, GERD questionnaire; RSI, reflux symptom index; BI, HREM, high-resolution esophageal manometry; IRP, integrated relaxation pressure; UES, upper esophageal sphincter; TZD, transitional zone defect; DB, distal break; NA, non-applicable.

P-values were calculated using Student's *t* test or χ^2 -test. $P < 0.05$ was considered statistically significant.

Data are presented as n (%) or mean ± SD.

Laryngopharyngeal Reflux and Gastroesophageal Reflux Disease in Patients With Suspected Laryngopharyngeal Reflux Symptoms

In this study, LPR was defined as RFS score of 7 or higher. According to the criterion, 93 of the 98 patients (94.9%) were diagnosed to have LPR. The characteristics of the patients according to the presence or absence of LPR are summarized in Supplementary Table 4. Interestingly, although the number of subjects without LPR was too small to draw any significant results, the patients with LPR showed significantly higher levels of the total reflux episodes than patients without LPR (reflux activity, 42.6 vs 29.2, $P = 0.003$).

In contrast, only 15 of 98 (15.3%) were diagnosed as GERD (Table 1). The GERD patients had a higher BMI than the non-GERD patients (mean BMI, 24.7 kg/m² vs 22.6 kg/m², respectively; $P = 0.011$). As for 24-hour MII-pH monitoring parameters, DMS was significantly higher in the GERD patients than in the non-GERD patients (13.9 vs 2.9, $P = 0.010$). Also, there were significant differences between the 2 groups in terms of total reflux events, proximal extent of reflux, and distal and proximal baseline impedance levels. That is, the mean acid exposure time % were 4.3 and 0.7 in the GERD group and non-GERD group, respectively ($P = 0.007$). The mean total reflux episodes (reflux activity) were 62.6 and 38.0 in the GERD group and non-GERD group, respectively ($P = 0.002$). The patients with GERD showed a significantly lower levels of both the proximal baseline impedance

and the distal baseline impedance levels than those without GERD (proximal and distal baseline impedance levels, 2073.9 and 1818.9 vs 2461.7 and 2779.4 Ω ; $P = 0.023$ and < 0.001 , respectively). However, the GerdQ score of the GERD patients was 8.1 while that of the non-GERD patients was 7.6, which was statistically insignificant ($P = 0.533$).

When esophageal motor function was evaluated using HREM, 69 of 98 (70.4%) patients had IEM. However, there were no significant differences between the GERD and non-GERD patients in terms of IEM, resting LES pressure, resting upper esophageal sphincter (UES) pressure, integrated relaxation pressure, TZD length, DB length, and TZD + DB length (Table 1). Similarly, there were no significant differences between patients with or without LPR (Supplementary Table 4).

Optimal Cutoff Value of the Gastroesophageal Reflux Disease Questionnaire and Reflux Symptom Index Scores to Diagnose Gastroesophageal Reflux Disease in Patients With Suspected Laryngopharyngeal Reflux Symptoms

The distribution of GerdQ scores of the patients is presented in Figure 1. To diagnose GERD in patients with suspected LPR, the sensitivity, specificity, PPV, and NPV of GerdQ according to each cutoff value are presented in Table 2. We found that the GERD cutoff value of 9 showed the highest area under curve (AUC) by receiver operating curve analysis (AUC = 0.565; Fig. 2); the sensitivity, specificity, PPV, and NPV were 50.0%, 70.7%, 22.6%, and 89.2%, respectively (Table 2).

Also, RSI showed poor performance in diagnosing GERD.

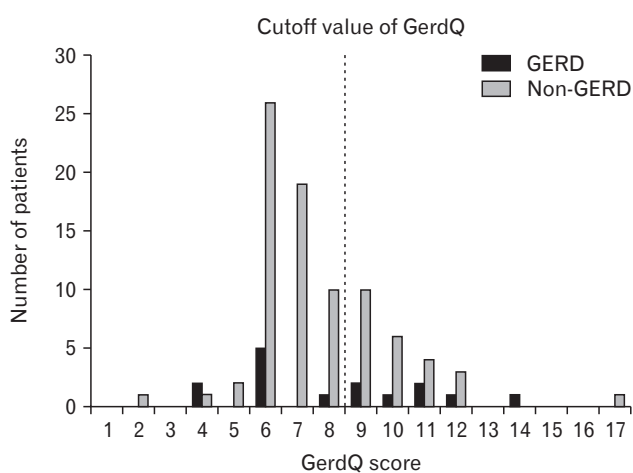


Figure 1. The distribution of Korean version of the gastroesophageal reflux disease questionnaire (GerdQ) scores (sum of 6 items, 0-18). The number of patients with gastroesophageal reflux disease (GERD, black bars) and without GERD (grey bars) by GerdQ scores are presented.

Table 2. Test Characteristics According to the Cutoff Value of Gastroesophageal Reflux Disease Questionnaire Score to Diagnose Gastroesophageal Reflux Disease in Patients With Suspected Laryngopharyngeal Reflux Symptoms

Cutoff score of GerdQ	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)
7	57.1 (28.9-82.3)	36.6 (26.2-48.0)	13.3 (5.9-24.6)	83.3 (67.2-93.6)
8	57.1 (28.9-82.3)	58.5 (47.1-69.3)	19.0 (8.6-34.1)	88.9 (77.4-95.8)
9	50.0 (23.0-77.0)	70.7 (59.6-80.3)	22.6 (9.6-41.1)	89.2 (79.1-95.6)
10	35.7 (12.8-64.9)	82.9 (73.0-90.3)	26.3 (9.2-51.2)	88.3 (79.0-94.5)

GerdQ, gastroesophageal reflux questionnaire; PPV, positive predictive value; NPV, negative predictive value.

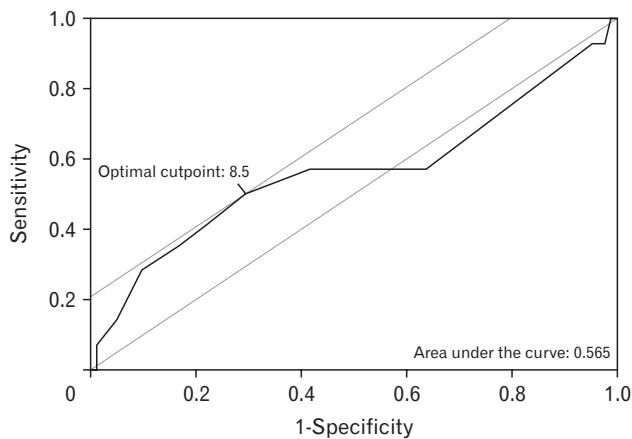


Figure 2. Receiver operating characteristic curve of the gastroesophageal reflux disease questionnaire in the diagnosis of gastroesophageal reflux disease.

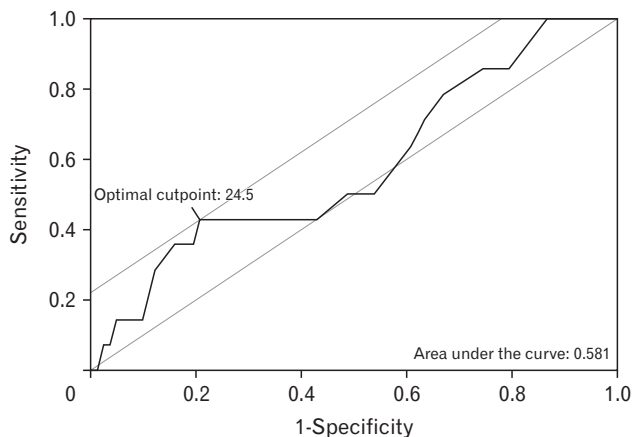


Figure 3. Receiver operating characteristic curve of the reflux symptom index in the diagnosis of gastroesophageal reflux disease.

The cutoff value of RSI score 25 showed the highest diagnostic yield (AUC = 0.581; Fig. 3). The sensitivity, specificity, PPV and NPV were 42.9%, 79.3%, 26.1%, and 89.0%, respectively (Table 3).

Discussion

In this study, we evaluated the validity of the GerdQ and RSI questionnaire in diagnosing GERD in patients with suspected LPR symptoms. The patients with suspected LPR symptoms visited the gastroenterology or otorhinolaryngology clinic. Interestingly, in our study, most patients with LPR symptoms were diagnosed with LPR at the otorhinolaryngology clinic, while the proportion of patients diagnosed with GERD was low in the Korean population.

Table 3. Test Characteristics According to the Cutoff Value of Reflux Symptom Index Score to Diagnose Gastroesophageal Reflux Disease in Patients With Suspected Laryngopharyngeal Reflux Symptoms

Cutoff score of RSI	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)
23	42.9 (17.7-71.1)	69.5 (58.4-79.2)	19.4 (7.5-37.5)	87.7 (77.2-94.5)
24	42.9 (17.7-71.1)	75.6 (64.9-84.4)	23.1 (9.0-43.6)	88.6 (78.7-94.9)
25	42.9 (17.7-71.1)	79.3 (68.9-87.4)	26.1 (10.2-48.4)	89.0 (79.5-95.1)
26	35.7 (12.8-64.9)	80.5 (70.3-88.4)	23.8 (8.2-47.2)	88.0 (78.4-94.4)
27	35.7 (12.8-64.9)	84.1 (74.4-91.3)	27.8 (9.7-53.5)	88.5 (79.2-94.6)

RSI, Reflux symptom index; PPV, positive predictive value; NPV, negative predictive value.

Diagnosis of GERD can be made symptomatically, pathologically, or physiologically.²⁵ However, there are no clear guidelines for diagnosing GERD. Recent Lyon consensus defined the “conclusive GERD” with concrete evidence for reflux including severe erosive esophagitis (LA classification grades C and D) or long-segment Barrett’s mucosa or peptic strictures on endoscopy, or distal esophageal acid exposure time > 6% or reflux activity more than 80 times on ambulatory pH monitoring.²⁶ However, it is controversial whether the Lyon consensus can be applied in Asians. A recent 2020 Seoul Consensus Guidelines of GERD suggested a value of total esophageal acid exposure time value of ≥ 4% as an abnormal finding for the Asian population.²⁵

In the present study, we applied the GERD diagnostic criteria of a previous study which evaluated the diagnostic value of 24-hour ambulatory esophageal pH impedance in patients with typical LPR symptoms to compare the results of our study with that of the previous study.^{8,27} Although not statistically significant in this study in part because there were very few patients without LPR (n = 5), parameters associated with gastroesophageal reflux tended to be high in patients with LPR. Since reflux activity was increased in patients with LPR, LPR symptoms are thought to be at least associated with abnormal increased gastroesophageal reflux (P = 0.003). So it is justified to administer anti-secretory agents for the treatment of LPR patients.²⁸ However, the large discrepancy between GERD diagnosed through endoscope or 24-hour MII-pH monitoring and LPR diagnosed through laryngoscopic exam means that these 2 conditions have different etiologies other than increased gastroesophageal reflux.¹³ This can also explain why the proton pump

inhibitor (PPI) responsiveness in LPR patients is lower than that in typical GERD patients.

A recent study reported that patients with LPR symptoms had lower proximal BI levels (1997 ± 51 vs 2245 ± 109 , $P < 0.05$) and a lower proximal-to-distal ratio (1.28 ± 0.05 vs 1.53 ± 0.09 , $P < 0.05$) than controls; patients with $RFS \geq 7$ had lower proximal baseline impedance levels than controls (1970 ± 63 vs 2245 ± 109 , $P < 0.05$).⁸ In this study, baseline impedance levels were significantly lower in GERD patients than in non-GERD patients, not only in the distal esophagus, but also in the proximal esophagus (Table 1), which is consistent with the results of previous studies.^{26,29} However, neither proximal baseline impedance nor distal baseline impedance was different between LPR positive ($RFS \geq 7$) and negative ($RFS < 7$) groups, which may be due to the insufficient number of LPR negative patients for the analysis ($n = 5$; Supplementary Table 4). Alternatively, as the average acid exposure time % in the GERD group as well as the non-GERD group was lower than that in Western studies, negative results of this study may be associated with Korean GERD patients showing less severe acid reflux and more pronounced esophageal hypersensitivity. Most of the patients with LPR symptoms have esophageal hypersensitivity, and low esophageal baseline impedance is an indicator of esophageal hypersensitivity as well as gastroesophageal reflux.²⁴

Recently, the Korean version of the GerdQe was validated for the diagnosis of GERD; its cutoff value was 8 with a sensitivity of 64.9% and a specificity of 71.4%.¹⁹ In this study, the diagnostic yield of the GerdQ was lower than that of the Korean validation study (Table 2 and Fig. 2). The low sensitivity in this study (50.0%) may be because the previous study included patients with both typical and atypical GERD symptoms, whereas this study only included patients with LPR symptoms. In fact, our findings are consistent with previous studies regarding the usefulness of GerdQ in patients with atypical symptoms of GERD.³⁰ Unlike previous studies, however, this study evaluated the presence of pathologic gastroesophageal reflux and esophageal motor function more comprehensively by looking at endoscopic and HREM findings and 24-hour MII-pH monitoring, as well as GerdQ. These findings suggest that the role of pathologic gastroesophageal reflux is limited in patients with LPR symptoms, and that the development of a more reliable GERD questionnaire is necessary for patients with extraesophageal symptoms.

The RSI questionnaire is regarded as an easily administered and highly reproducible method in diagnosing LPR, and exhibits excellent construct-based and criterion-based validity.²⁰ The cut-off value of RSI may vary depending on which population the

questionnaire is conducted. $RSI > 13$ is generally considered as a diagnostic criterion for LPR.^{14,20} In the allergy patient population, however, the cut-off value of RSI for LPR diagnosis was reported to be 19.³¹ In this study, we could not evaluate the usefulness of RSI in diagnosing LPR because most of the study participants were LPR positive. Instead, RSI of ≥ 25 yielded the highest yield in diagnosing GERD (Table 3 and Fig. 3), but the performance of RSI in the diagnosis of GERD was also disappointing. RSI score was not different between GERD and non-GERD groups (Table 1). Although RSI score was higher in LPR positive patients than in LPR negative patients (18.5 ± 9.0 vs 15.2 ± 5.0), this did not reach a statistical significance (Supplementary Table 4). Our findings were inconsistent with the results of previous studies. It is also attributable to the small sample size of LPR negative subjects. As mentioned above, however, the RSI questionnaire was initially developed to predict the laryngoscopic evidence of LPR, not for diagnosing GERD. Nevertheless, like GerdQ, RSI may have only limited roles in diagnosing GERD in individuals with suspected LPR symptoms.

Hypocontractility or IEM is considered as the most common esophageal motor abnormality in GERD.^{32,33} Impaired clearance of the esophageal refluxate can be caused by IEM.^{34,35} Esophageal peristaltic dysfunction is reportedly more prevalent in patients with severe GERD symptoms.^{32,36-38} Also, the correlation between IEM and GERD has been shown previously.³⁹ In this study, 50 of 111 (45.5%) patients had IEM, thus abnormal esophageal motor function is common among patients with LPR symptoms. However, there was no difference in esophageal motility parameter between GERD and non-GERD groups (Table 1). Similarly, previous studies have reported that elevated UES pressure may result in globus symptoms.⁴⁰⁻⁴² Most of the patients in this study had globus symptoms. However, only 17 of 111 (15.3%) patients had elevated UES pressure (≥ 118.0 mmHg), and UES pressure was not significantly correlated with the 24-hour MII-pH monitoring parameters including % acid exposure, % impedance total reflux, reflux activity, proximal extent of reflux, and distal and proximal baseline impedance levels (data not shown). Therefore, elevated UES pressure may not be associated with globus pharyngeus. More studies are necessary to clarify this issue.

Our study has several limitations. First, there were no controls (individuals without LPR symptoms) in this study. Second, the number of patients diagnosed with GERD was small to derive more significant findings. Third, PPI responsiveness could not be measured in the study subjects. The PPI test is modestly sensitive and specific for diagnosing GERD.^{25,43} However, the use of PPI

test in patients with extraesophageal symptoms has shown little benefit.⁴⁴ Nevertheless, since our study could not evaluate the response to the PPI treatment, clinical implications may be limited. Therefore, further studies are warranted in the future.

Nevertheless, our study is meaningful because it was the first study to evaluate the validity of GerdQ in patients with extraesophageal symptoms in the Asian population. Also, unlike previous studies, we comprehensively examined endoscopy, HREM, and 24-hour MII-pH monitoring to diagnose GERD.

In conclusion, pathological gastroesophageal reflux is infrequent among patients with suspected LPR symptoms. In this population, the sensitivity of GerdQ appears to be low thus it has a limited role in diagnosing GERD. Thus, additional diagnostic evaluation may be required.

Supplementary Materials

Note: To access the supplementary tables mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at <http://www.jnmjournal.org/>, and at <https://doi.org/10.5056/jnm21235>.

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