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Original Article

Is the Impedance Baseline Helpful in the Evaluation of Globus Patients?

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Background/Aims

Gastroesophageal reflux disease (GERD) has been suggested to be responsible for 23-68% of globus cases. The impedance baseline (IB) acquired by 24-hour multichannel intraluminal impedance monitoring has been proven to represent esophageal mucosal integrity. We aimed to investigate whether the IB is helpful for evaluating globus patients.

Methods

Twenty-four-hour multichannel intraluminal impedance pH tracings (MII-pH) were evaluated in globus patients. Differences in the IB between the acid reflux, non-acid reflux, and no reflux groups were analyzed. Receiver operating characteristic (ROC) curves were obtained to determine the optimal measurement point from the lower esophageal sphincter (LES).

Results

A total of 62 patients were analyzed. MII-pH showed that acid reflux, non-acid reflux, and no reflux were present in 13, 5, and 44 patients, respectively. The acid reflux group had a significantly lower IB than the other groups at a location 3 cm from the LES. ROC curve analysis revealed that placement at a position 3 cm from the LES resulted in moderate diagnostic accuracy (area under the curve = 0.88). When we set 2500 Ω as the cut-off value for acid reflux at a position 3 cm from the LES, the additional diagnostic yield for acid reflux was increased by 19.4% compared with that obtained by MII-pH.

Conclusions

IB is complementary to pH findings enabling identification of a subset of patients with co-existing acid reflux. Catheter placement at a location 3 cm from the LES and a cut-off value of 2500 Ω may be reasonable criteria for estimating acid reflux. **(J Neurogastroenterol Motil 2015;21:390-397)**

Key Words

Electric impedance; Esophageal pH monitoring; Gastroesophageal reflux disease; Globus

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Introduction

Globus, which is a persistent or intermittent non-painful sensation of a lump or foreign body in the throat, is a well-defined clinical symptom that is usually long-lasting and, difficult to treat, and has a tendency to recur. This symptom frequently improves with eating and is generally unaccompanied by dysphagia or odynophagia.[1] Although relevant data are limited, recent studies have focused on gastroesophageal reflux disease (GERD),[2-5] abnormalities of the upper esophageal sphincter,[6-8] psychological and psychiatric disorders, and stress[9-11] as major factors contributing to the globus sensation. Gastroesophageal reflux has been suggested to represent a major etiology of this symptom, potentially accounting for 23-68% of globus cases.[2-5] However, there is currently no standard tool for evaluating GERD as the cause of globus. To date, 24-hour dual-probe ambulatory pH monitoring has been widely used in the clinical assessment of supraesophageal GERD. However, this technology has not yet been standardized, and its utility for defining a clinically relevant association of the globus symptom with GERD is under debate. Another technique, namely, 24-hour multichannel intraluminal impedance and pH monitoring (MII-pH), is currently used for the detection of reflux episodes in GERD patients. However, data on MII-pH in patients with globus symptoms are lacking.

The impedance baseline (IB) has been suggested to serve as a numerical estimate of very subtle mucosal change. The esophageal wall directly contacts the MII-pH sensor catheter when there are no episodes of swallowing or reflux. As a result, the impedance value reflects the intrinsic electrical conductivity of the esophageal wall, or the so-called esophageal IB.[12] Farré et al[13] evaluated the IB in vivo and in vitro in rabbits and healthy human participants and reported that mucosal damage after esophageal acid exposure causes a decrease in the IB. In rabbits, the IB decreases by approximately one-third when the esophagus is exposed to acid, compared with healthy controls.[13] Furthermore, Kessing et al[14] demonstrated lower IBs in a consistent group of erosive and non-erosive patients compared with those observed in healthy subjects. These researchers also confirmed the close relationship between the IB and acid exposure times by means of a repeated MII-pH performed before and during acid suppression in a sub-group of patients who were, non-responders to proton pump inhibitors (PPIs).[14] However, no study has investigated the diagnostic value of IB in globus patients. In the present study, we aimed to evaluate the potential value of the IB in identifying the causes of globus.

Materials and Methods

Subject

Patients who visited Seoul St. Mary's Hospital, which is a tertiary university hospital, due to the globus symptom, from September 2009 to May 2013, were investigated in the present study. The patients who did not undergo any of the following investigations were excluded: (1) 24-hour MII-pH tracings, (2) esophagogastroduodenoscopy, (3) high-resolution manometry, (4) laryngoscopy, and (5) Symptom Checklist 90-Revised.[15] Patients with a primary or secondary esophageal motility disorders shown by high resolution manometry were excluded. This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital.

Typical Reflux Symptom

Typical reflux symptoms included heartburn and regurgitation. The presence of one of these 2 symptoms in the preceding week without the administration of PPIs was defined as typical reflux, regardless of severity or incidence.

Globus Symptom Intensity and Psychosomatic Symptom Score

Patients scored the intensity of their globus symptoms over the preceding week using a 10 cm visual analog scale that ranged from 0 to 10 (0 = no sensation to 10 = maximum intensity). To assess psychosomatic symptoms, we used the Symptom Checklist 90-Revised,[15] which is a psychiatric self-report inventory. The 90 items in the questionnaire are scored on a 5-point Likert scale ranging from 0 = not at all to 4 = significant. This scale is intended to measure symptom intensity on nine different subscales, including somatization, obsessive-compulsive behavior, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and a category of "additional items." This metric is one of the most widely used measures of psychological distress in clinical practice and research. In our study, the psychosomatic symptom score was calculated as the sum of 3 subscale scores as follows: the somatization subscale (12 items), depression subscale (13 items), and anxiety subscale (10 items). Therefore, psychosomatic symptom scores ranged from 0 to 140 points.

Laryngoscopic Examination

All patients underwent laryngoscopic examinations by a specialist who had more than 10 years of experience. During laryngoscopy, mucosal lesions in four laryngeal regions were evaluated, including the arytenoids, intra-arytenoid notch, vestibular folds, and vocal cords. Three types of mucosal lesions were evaluated, namely, alterations in the epithelium (reduced mucosal light reflex, hypertrophy, roughness, and granuloma), erythema, and edema. If any laryngeal mucosal lesions were identified, a diagnosis of pathological laryngeal change was made.[16]

Esophageal Mucosal Changes as Shown by Esophagoduodenogastroscopy

The endoscopic assessment of esophageal mucosal changes in the patients was performed under conscious sedation. We used the Los Angeles classification to evaluate mucosal changes as follows: grade A, one or more mucosal breaks no longer than 5 mm, none of which extend between the tops of the mucosal folds; grade B, one or more mucosal breaks longer than 5 mm, none of which extend between the tops of 2 mucosal folds; grade C, mucosal breaks that extend between the tops of 2 or more mucosal folds but involve less than 75% of the esophageal circumference; and grade D, mucosal breaks that involved at least 75% of the esophageal circumference.[17,18]

Twenty-four-hour Multichannel Intraluminal Impedance pH Tracings

The patients fasted for at least 8 hours prior to MII-pH monitoring. Before the procedure, a pH electrode of a MII-pH catheter was calibrated using pH 4 and pH 7 buffer solutions. PPIs and all other drugs potentially affecting gastrointestinal motility and secretion were discontinued at least 2 weeks prior to the study. Esophageal impedance-pH monitoring was performed using an ambulatory MII-pH monitoring system (Sandhill Scientific Inc, Highlands Ranch, CO, USA). The 6-channel impedance pH catheter was introduced through the nose under topical anesthesia and attached at a location 5 cm above the manometrically localized lower esophageal sphincter (LES) to record pH values at 5 cm and impedances at 3, 5, 7, 9, 15, and 17 cm proximal to the LES. The pH and impedance signals were stored in a data-collection device. The patients were encouraged to maintain their usual activities, sleep schedules, and consumption of ordinary meals. They were instructed to keep a careful diary, recording meal times, body position (upright or recumbent), daily activities, and the timing of any symptoms. The data from the impedance channels and the pH electrodes were stored on a portable data recorder (Sleuth®, Sandhill Scientific Inc). At the end of the 24-hour recording period, all data were downloaded onto a computer and analyzed using dedicated software (BioView Analysis®, Sandhill Scientific Inc), and the data from each study were manually reviewed.

Twenty-four-hour Multichannel Intraluminal Impedance pH Interpretation

The parameters recorded included the following: (1) the percentage of total time that the pH was < 4; (2) the percentage of upright time associated with a pH < 4; (3) the percentage of supine time associated with a pH < 4; (4) the number of reflux events; (5) the number of reflux events longer than 5 minutes; (6) the longest reflux event; (7) the total number of impedance-detected reflux episodes; (8) the number of impedance-detected reflux episodes in the recumbent position; and (9) the number of impedance-detected reflux episodes in the supine position. The recorded MII-pH data were classified into 3 groups according to the following definitions: acid reflux, the percentage of total time that the pH was < 4 was $> 4\%$, the DeMeester score was > 14.7, or the positive symptom index was $> 50\%$; non-acid reflux, the percentage of bolus retention time was $> 1.4\%$ or the non-acid positive symptom index was $> 50\%$; and no reflux, non-specific findings as shown by MII-pH monitoring. An abnormal reflux episode was defined as total numbers of reflux episodes at the distal and proximal esophagus of > 73 and > 31, respectively.

Impedance Baseline Calculation

The IB was assessed every hour in the all impedance channel, located 3, 5, 7, 9, 15, and 17 cm above the LES. A 30-second time period was selected, and the IB was calculated by averaging the raw impedance values during this time period. Thereafter, the hourly IBs were averaged to determine the mean IB levels for the entire 24-hour period. The investigators were blinded to the study groups.

Statistical Methods

Statistical analysis was performed using the Statistical Package for Social Sciences software (SPSS version 16.0, Chicago, IL, USA). In addition to the tests described above, we recorded age, gender, the body mass index (BMI). One-way analysis of variance (ANOVA) was used to compare the IB values between the acid reflux, non-acid reflux, and no reflux groups; then, post hoc testing was used to determine the differences between the subgroups. Receiver operating characteristic curves were obtained to evaluate the diagnostic accuracy of the IB at each position using Sigma Plot version 10.0 (Systat Software Inc, Chicago, IL, USA). Moreover, the identification of the most useful IB cut off value for acid reflux at a specific position was achieved by calculating the sensitivity and specificity. The categorical variables were compared using Fisher's exact test and the χ^2 test. The continuous variables were compared using Student's t test. Statistical significance was set at $P < 0.05$. Diagnostic accuracy based on the area under the curve (AUC) was described as follows: AUC = 1.0, perfect diagnostic accuracy; 0.9 < AUC < 1.0, high diagnostic accuracy; 0.7 < AUC ≤ 0.9, moderate diagnostic accuracy; 0.5 < AUC ≤ 0.7, low diagnostic accuracy; and AUC = 0.5, very low diagnostic accuracy.

Results

Patients

We consecutively enrolled 72 patients who underwent pH and impedance monitoring for evaluation of globus symptoms. Ten patients were excluded due to the following: immeasurable IB in 3 cases and unavailable symptom check list in 7 patients. Finally, a total of 62 patients with the globus symptom were analyzed. Analysis was therefore completed for 62 patients. Typical reflux symptoms were identified in 48 (77.4%) patients. The mean globus symptom intensity was 5.5 ± 2.9, and the mean psychosomatic symptom score was 27.3 ± 23.4. Acid reflux, non-acid reflux, and no reflux were observed in 13 (21.0%), 5 (8.0%), and 44 (71.0%) patients based on MII-pH, respectively (Table 1). There were no differences in the presence of typical reflux symptoms, globus symptom intensity, or psychosomatic symptom scores between the 3 groups. Pathological laryngeal changes was observed in 49 (79.0%) patients with no differences between the 3 groups. Most patients (59 of 62, 95.2%) showed no mucosal break at the distal esophagus. Mucosal breaks were identified in only 3 patients, as follows: 1 grade A esophagitis and 1 grade B esophagitis in the acid reflux group and 1 grade A esophagitis in the no reflux group. There were no significant differences among the 3 groups with respect to age, gender or BMI.

Comparison of Impedance Baselines Between the Acid Reflux, Non-acid Reflux, and No Reflux Groups

The acid reflux group showed a lower IB compared with the no reflux group at 3 cm (1612.85 ± 656.66 Ω vs 3087.73 ± 854.76 Ω, $P < 0.001$) and 5 cm (1738.31 ± 547.93 Ω vs 2642.45 ± 667.70 Ω, $P < 0.001$) (Fig. 1A). The IB in the acidic reflux group was also lower than that in the non-acid reflux group at a location 5 cm (1738.31 ± 547.93 Ω vs 2794.20 ± 554.56 Ω, $P = 0.008$) from the LES. However, there was no difference in the IB between the non-acid reflux group and the no reflux group at any positions. The IB of the acid reflux group at a position 15 cm from the LES was lower than those of the non-acid reflux and no reflux groups, although the differences were not significant (1909.05 ± 551.08 Ω vs 2725.57 ± 1172.01 Ω, $P = 0.151$; and 1909.05 ± 551.08 Ω vs 1992.90 ± 5 97.95 Ω, $P = 0.852$). The IB of the acid reflux group at a position 17 cm from the LES was

Table 1. Comparison of the Acid Reflux, Non-acid Reflux, and No Reflux Groups in Patients With ghe Globus Symptom (N = 62)

	Acid reflux (n = 13)	Non-acid reflux (n = 5)	No reflux (n = 44)	*P*-value
Age (mean ± SD, yr)	56.6 ± 11.7	48.2 ± 14.6	53.6 ± 11.8	0.405
Male (n [%])	3 (23.1)	0 (0.0)	13 (29.6)	0.576
Body mass index (mean ± SD, kg/m^2)	24.2 ± 2.3	23.0 ± 2.1	22.6 ± 2.8	0.576
Typical reflux symptom (n [%])	11 (84.6)	4 (80.0)	33 (75.0)	0.747
Globus symptom intensity (mean ± SD)	5.8 ± 3.3	4.8 ± 2.3	5.4 ± 2.8	0.156
Psychosomatic symptom score (mean ± SD)	26.5 ± 21.8	30.3 ± 30.4	28.5 ± 24.3	0.056
Pathological laryngeal change (n [%])	9 (69.2)	5 (100.0)	35 (79.5)	0.209
Presence of esophagitis (n [%])	2 (15.4)	0 (0.0)	1 (2.3)	0.560
LA grade A	1	0	1	
LA grade B	1	0	0	
LA grade C	0	0	0	

LA, Los Angeles.

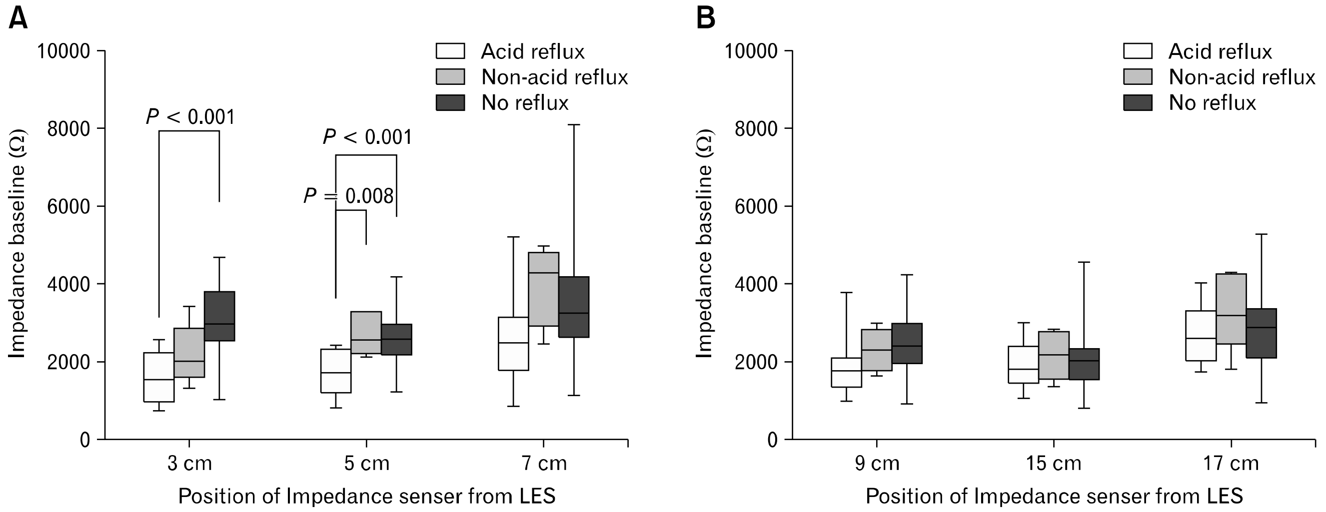

Figure 1. Comparison of impedance baselines (IB) between the acid reflux, non-acid reflux, and no reflux groups. (A) The acid reflux group showed a lower IB compared with the no reflux group at positions 3 cm (1612.85 ± 656.66 Ω vs 3087.73 ± 854.76 Ω, $P < 0.001$, respectively) and, 5 cm (1738.31 ± 547.93 Ω vs 2642.45 ± 667.70 Ω, $P < 0.001$, respectively). The IB in the acid reflux group was also lower than that in the non-acid reflux group at a position 5 cm (1738.31 ± 547.93 Ω vs 2794.20 ± 554.56 Ω, $P = 0.008$) from the lower esophageal sphincter (LES). However, there was no difference in the IB between the non-acid reflux group and the no reflux group at any positions. (B) The IB of the acid reflux group at a position 15 cm from the LES was lower than those of the non-acid reflux and no reflux groups, although this difference was not significant (1909.05 ± 551.08 Ω vs 2725.57 ± 1172.01 Ω, $P = 0.151$; 1909.05 ± 551.08 Ω vs 1992.90 ± 597.95 Ω, $P = 0.852$, respectively). The IB of the acid reflux group at a position 17 cm from the LES was also lower than those of the non-acid reflux and no reflux groups, but these differences were not statistically significant (2668.69 ± 714.58 Ω vs 3321.00 ± 1009.10 Ω, $P = 0.140$; 2668.69 ± 714.58 Ω vs 2764.02 ± 939.37 Ω, $P = 0.737$, respectively).

also lower than those of the non-acid reflux and no reflux groups, but this decrease was not statistically significant (2668.69 ± 714.58 Ω vs 3321.00 ± 1009.10 Ω, $P = 0.140$; 2668.69 ± 714.58 Ω vs 2764.02 ± 939.37 Ω, $P = 0.737$) (Fig. 1B).

When the acid reflux group was compared with the other groups (non-acid reflux + no reflux), the acid reflux group showed a lower IB compared with the others, at 3 cm (1612.85 ± 656.66 Ω vs 3026.92 ± 847.59 Ω, $P < 0.001$), 5 cm (1738.31 ± 547.92 Ω vs 2657.94 ± 653.58 Ω, $P < 0.001$), 7 cm (2541.06 ± 1143.69 Ω vs 3417.68 ± 1235.49 Ω, $P = 0.024$), and 9 cm (1957.33 ± 884.56 Ω vs 2441.76 ± 706.10 Ω, $P = 0.041$) from the LES. However, there was no difference in the IB between the acid reflux and the other group at 15 cm (1909.05 ± 551.07 Ω vs 2067.66 ± 696.40 Ω, $P = 0.451$) and 17 cm (2668.69 ±7 14.51 Ω vs 2820.73 ± 951.03 Ω, $P = 0.594$) from the LES.

Receiver Operating Characteristic Curves for Diagnostic Accuracy of the Impedance Baseline for Acid Reflux

The AUCs at each point were as follows: 3 cm from the LES, 0.88 (Fig. 2); 5 cm from the LES, 0.67; 7 cm from the LES, 0.58; 9 cm from the LES, 0.62; 15 cm from the LES, 0.52 and 17 cm from the LES, 0.53. When we used a cut-off value of 2500 Ω at a position 3 cm from the LES for the diagnosis of acid reflux, the sensitivity was 0.81 (95% confidence interval [CI], 0.57-0.94), and the specificity was 0.85 (95% CI, 0.70-0.94). We

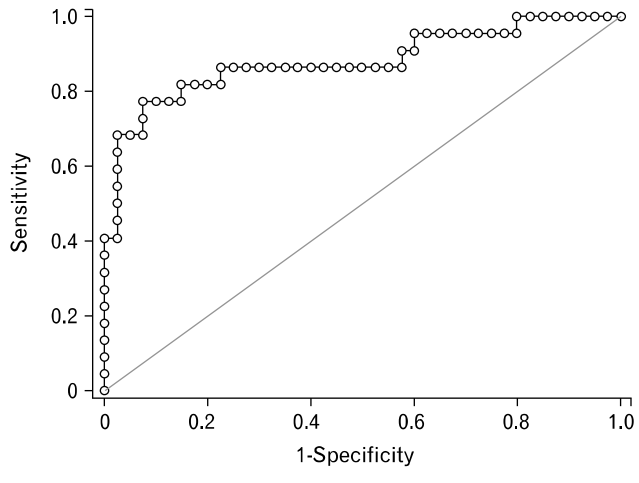

Figure 2. Receiver operating characteristic curve of the impedance baseline at a position 3 cm from the lower esophageal sphincter (LES) for acid reflux assessment. The area under the curve at a position 3 cm from the LES was 0.88, indicating moderate diagnostic accuracy.

defined an IB of ≤ 2500 Ω at a position 3 cm from the LES as low IB-3 and an IB of > 2500 Ω at a position 3 cm from the LES as high IB-3.

Difference Between the Low Impedance Baseline Group (≤ 2500 Ω) and High Impedance Baseline Group (> 2500 Ω) at a Position 3 cm From the Lower Esophageal Sphincter in Globus Patients

Reflux, as assessed by MII and acid reflux, as assessed by MII-pH were significantly more frequently observed in the low IB-3 group compared with the high IB-3 group (73.9% vs 12.8%, $P < 0.001$; and 47.8% vs 5.1%, $P < 0.001$, respectively) (Table 2). However, no differences were found in age, gender, BMI, pathologic laryngeal change, presence of typical reflux symptoms, and endoscopic findings between the 2 groups. Furthermore, there were no differences in the psychosomatic score or globus symptom intensity.

Diagnostic Yield of the Impedance Baseline for Acid Reflux

The overall diagnostic yield of the IB for acid reflux was defined according to an IB of ≤ 2500 Ω at a position 3 cm from the LES without acid reflux as assessed by MII-pH. A total of 11 patients (17.7%) with acid reflux possessed an IB of ≤ 2500 Ω at a position 3 cm from the LES. Additionally, 4 patients (6.5%) with non-acid reflux and 8 patients (12.9%) with no reflux showed an IB of ≤ 2500 Ω at a position 3 cm from the LES. Therefore, this IB was achieved in 12 (19.4%) of the participants (Table 3).

Discussion

Because the IB has been proposed as a sensitive marker of esophageal mucosal integrity,[19] the present study aimed to assess whether the measurement of esophageal IB, in addition to MII-pH variables, is helpful in investigating acid reflux in patients with

Table 2. Difference Between the Low Impedance Baseline Group (≤ 2500 Ω) and High Impedance Baseline Group (> 2500 Ω) at a Position 3 cm From the Lower Esophageal Sphincter in Globus Patients (N = 62)

	Low IB-3 (n = 23)	High IB-3 (n = 39)	*P*-value
Age (mean ± SD, yr)	56.6 ± 12.4	52.2 ± 11.5	0.161
Male (n [%])	8 (34.8)	8 (20.5)	0.242
Body mass index (mean ± SD, kg/m^2)	23.1 ± 3.0	22.9 ± 2.5	0.753
Typical reflux symptom (n [%])	18 (78.3)	30 (76.9)	0.903
Pathological laryngeal change (n [%])	19 (82.6)	30 (76.9)	0.697
Presence of esophagitis (n [%])	2 (8.7)	1 (2.6)	0.549
Reflux in MII, n (%)	17 (73.9)	5 (12.8)	< 0.001
Acid reflux in MII-pH, n (%)	11 (47.8)	2 (5.1)	< 0.001
Globus symptom intensity, mean ± SD	34.7 ± 30.0	28.0 ± 24.1	0.347
Psychosomatic symptom score, mean ± SD	29.4 ± 29.5	32.9 ± 25.1	0.618

Low IB-3, Impedance baseline ≤ 2500 Ω at a position 3 cm from the lower esophageal sphincter; high IB-3, impedance baseline > 2500 Ω at a position 3 cm from the lower esophageal sphincter; MII-pH, 24-hour multichannel intraluminal impedance pH tracings.

Table 3. Proportion of Patients With Acid Reflux If Acid Reflux Is Defined As ≤ 2500 Ω of Impedance Baseline at 3 cm From the Lower Esophageal Sphincter

Findings	Patients (n/N [%])
Impedance baseline ≤ 2500 Ω at 3 cm from the LES	23/62 (37.1)
Impedance baseline ≤ 2500 Ω at 3 cm from the LES with acid reflux on MII-pH	11/62 (17.7)
Impedance baseline ≤ 2500 Ω at 3 cm from the LES with non-acid reflux	4/62 (6.5)
Impedance baseline ≤ 2500 Ω at 3 cm from the LES with no reflux	8/62 (12.9)
Incremental diagnostic yield of the impedance baseline ≤ 2500 Ω at 3 cm from the LES	12/62 (19.4)

MII, multichannel intraluminal impedance; LES, lower esophageal sphincter.

globus.

In our study, the IB of the distal esophagus at a position 3 cm from the LES in the acid reflux patients was significantly lower than that in the no reflux patients, and the IB at a position 5 cm from the LES in the acid reflux patients was lower than that in the non-acid reflux patients. However, there were no differences in the IB between the non-acid reflux group and the no reflux group. These results are in accordance with those of a previous study.[14,19,20] The exposure of the esophageal epithelium to reflux contents results in tissue injury and symptoms. Acid is the key reflux component that leads to the production of esophagitis and microscopic alterations. According to Zhong et al,[12] acid is the most important reflux component affecting IB. These authors demonstrated a negative correlation between epithelial intercellular spaces and the IB, suggesting that a low IB can reflect subtle structural changes in the epithelium. Acid perfusion in the esophagus can provoke a dilated intercellular space,[13,21,22] and most patients achieve recovery from this dilation after PPI therapy.[23,24] Thus, it can be easily speculated that the low IB of the distal esophagus in globus patients is the consequence of acid injury to the esophageal mucosa.

In addition to the lower IB of the distal esophagus, the IB values in the proximal esophagus at positions 15 and 17 cm from the LES in the acid reflux patients were lower than those in the other 2 groups, although these findings were not statistically significant. We believe that a larger number of enrolled patients could yield statistical significance. These findings indicate that the proximal esophagus was affected by acid reflux and that mucosal integrity was impaired as a result. We hypothesized that low impedance baseline at the distal/proximal esophagus might be associated with globus. However, our results were insufficient to support our hypothesis and low impedance baseline just can indicate pathologic acid reflux in the distal/proximal esophagus. Further prospective study comparing with healthy controls might be needed to clarify this.

We generated receiver operating characteristic curves and calculated the AUCs at each point to evaluate the diagnostic accuracy of this modality for acid reflux. The value of the AUC at a position 3 cm from the LES was between 0.7 and 0.9, which corresponds to a moderate diagnostic value for acid reflux.[25,26] The cut-off value of 2500 Ω had moderate sensitivity and specificity. When we applied this value to the estimation of acid reflux in the globus patients, its diagnostic yield increased, although it was an estimation.

The limitation of this study are the sample size and the absence of control healthy subjects, which were not sufficient to generate robust conclusions. Globus sensation causes some discomfort, but it is usually not life threatening. Thus, the number of patients who decided to undergo MII-pH was inevitably small. However, the proportions of patients in the present study were similar to those in previous studies despite the small sample size, with 13 patients in the acid reflux group and 5 patients in the non-acid reflux group out of a total of 62 patients. Therefore, this study can be assumed to have good reliability. Our study suggests that low IB detects reflux in a sub-group of patients in which reflux is not demonstrated by reflux pattern by impedance change across multiple sensors nor pH measurements alone. However, this study does not demonstrate that measuring IB in globus patients leads to altered treatment plan or improved patient outcomes.

The IB represents a new parameter that can aid in the understanding of the impairment of mucosal integrity. However, the practical application of this tool in the clinical field has not yet been established. In the present study, we revealed that the IB values for the distal esophagus were lower in the acid reflux group than in the other groups, demonstrating the potential for this parameter to provide additional diagnostic yield for acid reflux in patients with globus. We cautiously suggest that the IB can be applied to acid reflux estimation in these patients.

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