The Key Timing of Pharyngeal Reflux in Patients with Laryngopharyngeal Reflux

Jeong Wook Kang[1], Young Chan Lee[2], Seong-Gyu Ko[3], and Young Gyu Eun[2]

[1]Kyung Hee University Hospital
[2]Kyung Hee univesity Hospital
[3]College of Korean Medicine, Kyung Hee University

April 16, 2024

Abstract

Objectives: To analyze the incidence of pharyngeal reflux in laryngopharyngeal reflux patients over a 24-hour period and find out the key timing of pharyngeal reflux. Design: Retrospective descriptive analysis Setting: Single institution. Participants: Sixty-nine patients with LPR and twenty-six normal controls Methods: We reviewed 69 patients who visited our clinic with LPR-related symptoms and were proven to have pharyngeal reflux via 24-hour multichannel intraluminal impedance-pH (24hr MII-pH) monitoring. Quantitative analysis was conducted for the LPR profiles, such as the acidity of reflux, nighttime reflux, and positional reflux. The time series of pharyngeal reflux episodes and mealtimes were analyzed over a 24-hour period. Also, we recruited 26 normal controls. We compared the timing of pharyngeal reflux between LPR patients and asymptomatic controls. Results: The quantitative analysis revealed that pharyngeal reflux occurred 4.88 ± 4.59 times over 24 hours. Weakly acidic pharyngeal reflux was more abundant than acidic or weakly alkaline reflux. Pharyngeal reflux occurred mainly during daytime in the upright position. The most frequent timing of pharyngeal reflux episodes was within 2 hours after meals. Additionally, there was no significant difference of the timing of post-prandial reflux between LPR patients and asymptomatic controls. Conclusion: The key timing of pharyngeal reflux in patients with LPR was post-prandial 2 hours.

The Key Timing of Pharyngeal Reflux in Patients with Laryngopharyngeal Reflux

Abstract

*Objectives***:** To analyze the incidence of pharyngeal reflux in laryngopharyngeal reflux patients over a 24-hour period and find out the key timing of pharyngeal reflux.

*Design***:** Retrospective descriptive analysis

Setting : Single institution.

Participants : Sixty-nine patients with LPR and twenty-six normal controls

*Methods***:** We reviewed 69 patients who visited our clinic with LPR-related symptoms and were proven to have pharyngeal reflux via 24-hour multichannel intraluminal impedance-pH (24hr MII-pH) monitoring. Quantitative analysis was conducted for the LPR profiles, such as the acidity of reflux, nighttime reflux, and positional reflux. The time series of pharyngeal reflux episodes and mealtimes were analyzed over a 24-hour period. Also, we recruited 26 normal controls. We compared the timing of pharyngeal reflux between LPR patients and asymptomatic controls.

*Results***:** The quantitative analysis revealed that pharyngeal reflux occurred 4.88 ± 4.59 times over 24 hours. Weakly acidic pharyngeal reflux was more abundant than acidic or weakly alkaline reflux. Pharyngeal reflux occurred mainly during daytime in the upright position. The most frequent timing of pharyngeal reflux

episodes was within 2 hours after meals. Additionally, there was no significant difference of the timing of post-prandial reflux between LPR patients and asymptomatic controls.

Conclusion: The key timing of pharyngeal reflux in patients with LPR was post-prandial 2 hours.

Keywords. Laryngopharyngeal Reflux; 24-Hour Multichannel Intraluminal Impedance pH Monitoring; Reflux Type

Keypoints

- Pharyngeal reflux episodes of laryngopharyngeal reflux (LPR) patients dominantly occur in daytime.
- Most pharyngeal reflux of LPR patients occurs during upright position.
- Pharyngeal reflux of LPR patients frequently occurs within 2 hours after mealtime.
- Acidities of post-prandial pharyngeal reflux were weakly acid and weakly alkaline.
- The fundamental timing of post-prandial pharyngeal reflux in LPR patients does not differ from normal controls.

Introduction

Laryngopharyngeal reflux (LPR) is defined as extra-esophageal reflux of gastroduodenal content to the laryngopharynx, affecting the upper aerodigestive tract.[1] LPR is similar to gastroesophageal reflux disease (GERD), in which gastric acid rises up the esophagus. Because of their similarities, gastroenterologists manage LPR patients as a subtype of GERD.[2] However, otolaryngologists consider LPR as a new disease entity because many patients with LPR-related symptoms have no GERD-associated symptoms.[3] Moreover, non-acid reflux or even gas reflux can be a disease etiology of LPR, owing to its multifactorial nature.[4]

The gastroesophageal junction consists of a lower esophageal sphincter (LES), diaphragm, and phrenoesophageal ligament.[5] The primary LES function is to allow food transit during swallowing and prevents the reflux of gastroduodenal contents back into the esophagus. Transient lower esophageal sphincter relaxation (TLESR) is defined as spontaneous LES relaxation without swallowing. The TLESR exists physiologically to prevent the swallowing of air. However, TLESR also allows gastroesophageal reflux to occur.[6] TLESR can be triggered by gastric distension after meals.[7] Since TLESR mainly occurs after meals, it has been considered as a major cause of post-prandial GERD-related symptoms.[8] A meta-analysis reported that baclofen, which inhibits TLESR, decreases the number of reflux episodes in GERD patients.[9]

'Laryngopharyngeal Reflux Study Group of Young Otolaryngologists of the International Federation of Otorhinolaryngological Societies' indicated that 24-hour multichannel intraluminal impedance-pH (24hr MII-pH) monitoring is the best way to diagnose LPR based on hypopharyngeal-esophageal reflux episodes (HREs).[10]However, to the best of our knowledge, there has been no study specifically showing whether HREs occurring in LPR actually occur frequently after meals, as shown in the TLESR phenomenon in GERD. Therefore, in this study, we tried to investigate the antecedent relationship between diet and HREs in LPR patients through diachronic analysis of 24hr MII-pH monitoring.

Materials and Methods

Subjects and study design

In this study, we retrospectively reviewed patients diagnosed with LPR via 24hr MII-pH monitoring. Examiners advised to all patients to keep their common diet during 24hr MII-pH monitoring. Patients with typical reflux symptoms and [?] 1 objective pharyngeal reflux episode were classified as LPR patients.[11] LPR symptoms were assessed using the reflux symptom index (RSI).[12] The objective pharyngeal reflux episode was assessed using 24hr MII-pH monitoring.[13] Finally, we enrolled 69 LPR patients whose test time of 24-hour MII-pH monitoring could be estimated, and raw recording files could be accessible. Additionally, we recruited normal controls without reflux-related symptom. 24hr MII-pH monitoring was performed on the healthy controls. The time of pharyngeal reflux episodes in the healthy controls was analyzed and compared with the LPR patients. This study was approved by Institutional Review Board of OOO.

24-hour multichannel intraluminal impedance-pH monitoring

All subjects underwent 24hr MII-pH monitoring using a multi-channel probe catheter for LPR (Sandhill Scientific, Inc., Highlands Ranch, CO, ZAI-BL-54, 55, 56, ComforTEC Z/PH single-use 2.3-mm-diameter probe). The catheter has four pairs of esophageal impedance electrodes, two pairs of pharyngeal impedance electrodes, and two proximal-distal-pH sensors. We placed the most proximal pharyngeal impedance electrodes 1 cm above the upper esophageal sphincter. We checked the number of pharyngeal reflux events, specific event time by 24-hour notation, and acidity of reflux contents. Mealtimes were excluded from analysis. The pharyngeal reflux was defined as any reflux episode reaching proximally to 1 cm above the upper border of UES.[14] The pharyngeal reflux includes liquid reflux, and mixed reflux.[15] Liquid reflux retrograde 50% decrease in impedance starting distally and propagating at least to the next 2 or more proximal impedance measuring segments. Mixed reflux was defined as a combination of the gas reflux and liquid reflux patterns. The number of pharyngeal reflux was manually analyzed by an otolaryngology specialist after automated pre-analysis with autoscan software (Bioview Analysis, Sandhill Scientific). We defined daytime as 06:00–18:00 and nighttime as 18:00–06:00. Pre- and post-prandial periods were defined as 2 h immediately before and after mealtime, respectively. The cut-off values of acidity classification were acid (pH $<$ 4), weakly acidic (7 $>$ pH $>$ 4), and weakly alkaline (pH $>$ 7).

Statistical analysis

Paired t-test and Wilcoxon signed rank test were used to compare pre-prandial and post-prandial pharyngeal reflux according to whether they were parametric or not. Statistical analysis was performed using the R software (https://www.R-project.org, ver. 4.1.0).

Results

A total of 69 patients were enrolled in the study. Demographic parameters and baseline reflux symptoms are summarized in **Table 1** . The male-to-female ratio was 25/43. The mean value of Age, BMI, and RSI were 55.93 +- 13.02, 24.8 +- 2.71, and 12.28 +- 6.19. The most severe reflux symptom was globus, with a mean value of 3.77 +- 1.7.

The 24hr MII-pH monitoring revealed the characteristics of pharyngeal reflux patterns. **Table 2** shows the properties of pharyngeal reflux depending on acidity, event time, and body position. The number of weakly acidic pharyngeal reflux was high (3.41 +- 3.27), while acidic and weakly alkaline reflux were 0.93 +- 2.34 and 0.55 +- 1.02, respectively. The hourly incidence of daytime reflux, 0.229 +- 0.282, was statistically more frequent than that of nighttime reflux (0.097 +- 0.13; $p < 0.001$). The reason for using hourly incidence, and not the total number of reflux, is for even statistical comparison over the same observation time. In the analysis according to body position, the hourly incidence of pharyngeal reflux was statistically higher in the upright position (0.327 +- 0.339) than during the recumbent position (0.064 +- 0.117; $p < 0.001$).

We sought to evaluate the relationship between reflux episodes and mealtimes. The common mealtimes of enrolled patients were concentrated at 9:00–10:00 and 16:00–18:00 out of 24 hours (**Figure 1A**). The high incidence of pharyngeal reflux was recorded at 10:00–11:00 and 19:00–20:00 out of 24 h (**Figure 1B**). We found that the incidence of pharyngeal reflux increased after mealtime (**Figure 1C**). Therefore, we compared the number of pharyngeal reflux episodes for 2 h before and after mealtime (**Table 3** , **Figure 2**).**Table 3** shows the comparison between pre- and post-prandial pharyngeal reflux frequency within 2 h around mealtime. All post-prandial reflux episodes (1.256 +- 0.878) were statistically more frequent than all pre-prandial reflux episodes (0.632 +- 0.548, $p < 0.001$). In classification according to acidity, the number of weakly acidic post-prandial reflux (0.853 +- 0.665) was significantly higher than that of pre-prandial weakly acidic reflux (0.433 +- 0.447, $p < 0.001$). The numbers of post-prandial acid reflux and pre-prandial acid reflux were 0.212 +- 0.420 and 0.134 +- 0.375, respectively ($p = 0.11$). The numbers of post-prandial weakly alkaline reflux and pre-prandial weakly alkaline reflux were 0.191 +- 0.390 and 0.065 +- 0.180 ($p = 0.012$), respectively. **Figure 2** shows the frequency of pharyngeal reflux for all participants based on the center zero, which represented the mealtime. The number of post-prandial pharyngeal reflux was relatively larger than that of pre-prandial pharyngeal reflux.

Twenty-six patients were recruited as a normal control group, and pharyngeal reflux episodes were found in 5 patients on 24hr-MII-pH monitoring. The mean number of pharyngeal reflux episodes in the 5 patients was 1.4 times. **Table 4** reveals whether there was a difference in the timing of post-prandial pharyngeal reflux between normal controls and LPR patients. Analyzing the time relationship between mealtime and pharyngeal reflux episodes, the timing of post-prandial reflux was 58.2 +- 61.8 minutes in the LPR patient group and 38.4 +- 34.2 minutes in the normal control group, with no statistical difference (p = 0.322).

Discussion

Since Koufman's double-probe pH monitoring study for gastroesophageal reflux disease, several studies have improved our understanding of LPR.[16] However, because 24hr MII-pH monitoring is an uncomfortable test that patients are reluctant to do, we may shorten the test time if we know when pharyngeal reflux occurs frequently. Moreover, it will be helpful in establishing an appropriate treatment strategy by adjusting the timing of drug administration, it also may improve the accuracy of the analysis of the test outcome. Our research may contribute to the diagnosis and treatment of LPR. In a recent study, it was reported that automated analysis overestimates the number of reflux episodes compared to manual analysis.[17] In our study, the hourly number of pharyngeal reflux episodes was meaningful because it was based on manual analysis by a skilled otolaryngologist.

In GERD, esophageal reflux typically occurs during the night and is called nocturnal reflux. GERD reflux usually occurs in a recumbent position. Contrasting results were obtained in this study as well (Table 2). The daytime incidence was more than two times higher than the nighttime incidence, and the frequency of pharyngeal reflux was five times higher in the upright position. Our study provides clues as to whether shortening the 24-hour monitoring period is appropriate. However, careful consideration is required in this regard because other studies have reported that nocturnal reflux is associated with disease severity.[10] Additionally, our findings lead us to rethink the usefulness of twice-daily proton-pump inhibitors (PPIs) for all LPR patients. A prospective cohort study on western patients showed that twice-daily PPIs is more efficient than once-daily PPIs.[18] However, recent another prospective cohort study on Asian patients fails to show the therapeutic advantage of twice-daily PPIs.[19] If patients have no nighttime reflux event, the second dose of PPIs may not useful.

We confirmed that pharyngeal reflux increased after meals compared to before meals (Table 3). This is similar to the esophageal reflux pattern induced by TLESR in GERD. TLESR occurs frequently in the post-prandial period, especially within 15 minutes after meals.[20] It is correlated that the distal esophageal reflux episodes in GERD typically occur in the post-prandial 1 h.[20] Since an acid pocket has formed near the cardia at that time, TLESR can increase gastric acid up to the esophagus and cause heartburn symptoms in GERD patients.[21] The incidence of TLESR in GERD patients is more than two times higher than that of normal healthy controls.[22] An esophago-pharyngeal regurgitation process is required to induce the laryngopharyngeal symptoms in LPR. A previous study found that transient upper esophageal sphincter (UES) relaxation was related to pharyngeal reflux in post-prandial 3 h.[23] The UES relaxation was not related to swallowing activity and was considered transient spontaneous relaxation. Our study also showed a doubling incidence of pharyngeal reflux in the 2 h post-prandial period compared to the pre-prandial 2 h (**Figure 2**). If post-prandial pharyngeal reflux plays an important role in the physiology of LPR, the 24-hour monitoring time could be reduced. In fact, there have been attempts to reduce the study time for GERD. A GERD study reported that post-prandial 3 h MII-pH monitoring could be used as a predictor of gastroesophageal reflux disease.[24]

Merati et al. reported that pharyngeal reflux episodes were detected in 0-33% of normal subjects in their meta-analysis.[25]Looking at the studies included in their meta-analysis, the mean number of pharyngeal reflux episodes found in normal subjects was 1-3 times. The pharyngeal reflux pattern of normal subjects involved in those study was similar to that of normal controls of this study. In this study, pharyngeal reflux episodes were detected in 19% of normal controls, and the mean numbers of their pharyngeal reflux episodes were 1.4. There was no study that revealed the timing of pharyngeal reflux in normal subjects. However, the fact that TLESR occurs mainly after meals in normal subjects is comparable to that pharyngeal reflux occurs mainly

after meals in normal controls of this study.[6,7] There was not statistical difference in the major timing of pharyngeal reflux episodes in LPR patients and normal controls, but the difference in frequency was clear. This suggests the importance of reducing the frequency of post-prandial pharyngeal reflux episode in the treatment of LPR patients.

Some potential shortcomings of this study were its retrospective design. Some patients were inevitably excluded from this study. The causes of exclusion were as follows: (1) unclear start time of 24hr MII-pH monitoring and (2) no raw data files for analysis. The dropout rate of the subjects can cause selection bias. In this study, the mealtimes of the enrolled 69 patients appeared to have a double peak shape (**Figure 1**). This could mean that patients skipped breakfast among three meals per day despite our education to keep common diet To prevent vomiting during the 24hr MII-ph probe insertion process, the insertion was performed in a fasting state. However, skipping breakfast may have resulted in a few failures in monitoring the routine 24 hours of LPR patients. Eight patients had medical history of GERD among enrolled 69 patients. Even if it is assumed that all eight patients have GERD, we thought that it was a small fraction compared to the total number of patients.

Conclusions

In conclusion, the results of this study indicate that 2 hours after meals is a very important pharyngeal reflux timing in LPR patients. Therefore, in the future, we need to think about ways to reduce pharyngeal reflux episodes that occur after meals in LPR patients.

References

1. Campagnolo AM, Priston J, Thoen RH, Medeiros T, Assuncao AR. Laryngopharyngeal reflux: diagnosis, treatment, and latest research.*Int Arch Otorhinolaryngol.* 2014;18(2):184-191.

2. Gelardi M, Ciprandi G. Focus on gastroesophageal reflux (GER) and laryngopharyngeal reflux (LPR): new pragmatic insights in clinical practice. *J Biol Regul Homeost Agents.* 2018;32(1 Suppl. 2):41-47.

3. Kim SI, Kwon OE, Na SY, Lee YC, Park JM, Eun YG. Association between 24-hour combined multichannel intraluminal impedance-pH monitoring and symptoms or quality of life in patients with laryngopharyngeal reflux.*Clin Otolaryngol.* 2017;42(3):584-591.

4. Salihefendic N, Zildzic M, Cabric E. Laryngopharyngeal Reflux Disease - LPRD. *Med Arch.* 2017;71(3):215-218.

5. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus G. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol.*2006;101(8):1900-1920; quiz 1943.

6. Lee YC, Jung AR, Kwon OE, Kang JW, Huh JH, Eun Y-G. The effect of baclofen combined with a proton pump inhibitor in patients with refractory laryngopharyngeal reflux: A prospective, open-label study in thirty-two patients. *Clinical Otolaryngology.* 2019;44(3):431-434 %U https://onlinelibrary.wiley.com/doi/abs/410.1111/coa.13297.

7. Holloway RH, Hongo M, Berger K, McCallum RW. Gastric distention: a mechanism for postprandial gastroesophageal reflux.*Gastroenterology.* 1985;89(4):779-784.

8. van Wijk MP, Blackshaw LA, Dent J, Benninga MA, Davidson GP, Omari TI. Distension of the esophagogastric junction augments triggering of transient lower esophageal sphincter relaxation. *Am J Physiol Gastrointest Liver Physiol.* 2011;301(4):G713-718.

9. Li S, Shi S, Chen F, Lin J. The effects of baclofen for the treatment of gastroesophageal reflux disease: a meta-analysis of randomized controlled trials. *Gastroenterol Res Pract.* 2014;2014:307805.

10. Lechien JR, Bobin F, Dapri G, et al. Hypopharyngeal-Esophageal Impedance-pH Monitoring Profiles of Laryngopharyngeal Reflux Patients.*The Laryngoscope.* 2021;131(2):268-276 %U

https://onlinelibrary.wiley.com/doi/210.1002/lary.28736.

11. Kim SI, Jeong SJ, Kwon OE, et al. Pharyngeal reflux episodes in patients with suspected laryngopharyngeal reflux versus healthy subjects: a prospective cohort study. *Eur Arch Otorhinolaryngol.*2021.

12. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice.* 2002;16(2):274-277.

13. Hoppo T, Sanz AF, Nason KS, et al. How much pharyngeal exposure is "normal"? Normative data for laryngopharyngeal reflux events using hypopharyngeal multichannel intraluminal impedance (HMII). *J Gastrointest Surg.* 2012;16(1):16-24; discussion 24-15.

14. Wang AJ, Liang MJ, Jiang AY, et al. Gastroesophageal and laryngopharyngeal reflux detected by 24-hour combined impedance and pH monitoring in healthy Chinese volunteers. *J Dig Dis.*2011;12(3):173-180.

15. Kawamura O, Kohata Y, Kawami N, et al. Liquid-containing Refluxes and Acid Refluxes May Be Less Frequent in the Japanese Population Than in Other Populations: Normal Values of 24- hour Esophageal Impedance and pH Monitoring. *J Neurogastroenterol Motil.* 2016;22(4):620-629.

16. Kuo C-L. Laryngopharyngeal Reflux: An Update. *Archives of Otorhinolaryngology-Head & Neck Surgery.* 2019;3(1 %U https://scitemed.com/article/2594/scitemed-aohns-2019-00094).

17. Kang HJ, Park JM, Choi SY, et al. Comparison Between Manual and Automated Analyses in Multichannel Intraluminal Impedance: pH Monitoring for Laryngopharyngeal Reflux. *Otolaryngol Head Neck Surg.*2021:1945998211006929.

18. Park W, Hicks DM, Khandwala F, et al. Laryngopharyngeal reflux: prospective cohort study evaluating optimal dose of proton-pump inhibitor therapy and pretherapy predictors of response.*Laryngoscope.* 2005;115(7):1230-1238.

19. Yoon YH, Park KW, Lee SH, Park HS, Chang JW, Koo BS. Efficacy of three proton-pump inhibitor therapeutic strategies on laryngopharyngeal reflux disease; a prospective randomized double-blind study. *Clin Otolaryngol.* 2019;44(4):612-618.

20. Pandolfino JE, Zhang QG, Ghosh SK, Han A, Boniquit C, Kahrilas PJ. Transient lower esophageal sphincter relaxations and reflux: mechanistic analysis using concurrent fluoroscopy and high-resolution manometry.*Gastroenterology.* 2006;131(6):1725-1733.

21. Moonen A, Aguilera-Lizarraga J, Bisschops R, Moonen P, Tack J, Boeckxstaens GE. 24-hour multi-pH recording of the postprandial acid pocket and the nocturnal acid distribution at the esophagogastric junction in healthy volunteers. *Neurogastroenterology & Motility.* 2019;31(11 %U https://onlinelibrary.wiley.com/doi/abs/10.1111/nmo.13694).

22. Schneider JH, Kuper MA, Konigsrainer A, Brucher BL. Transient lower esophageal sphincter relaxation and esophageal motor response. *J Surg Res.* 2010;159(2):714-719.

23. Szczesniak MM, Williams RB, Cook IJ. Mechanisms of Esophago-Pharyngeal Acid Regurgitation in Human Subjects. *PLoS ONE.* 2011;6(7):e22630 %U https://dx.plos.org/22610.21371/journal.pone.0022630.

24. Gourcerol G, Verin E, Leroi AM, Ducrotte P. Can multichannel intraluminal pH-impedance monitoring be limited to 3 hours? Comparison between ambulatory 24-hour and post-prandial 3-hour recording: Three-hour pH-impedance monitoring. *Diseases of the Esophagus.*2014;27(8):732-736 %U https://academic.oup.com/dote/article-lookup/doi/710.1111/dote.12161.

25. Merati AL, Lim HJ, Ulualp SO, Toohill RJ. Meta-analysis of upper probe measurements in normal subjects and patients with laryngopharyngeal reflux. *Ann Otol Rhinol Laryngol.*2005;114(3):177-182.

Table 1. Baseline characteristics of 69 enrolled subjects with laryngopharyngeal reflux

Parameter	Baseline
Patient, n	69
Male	26
Female	43
Age, y	55.93 ± 13.02
Height, cm	163.13 ± 9.71
BW, kg	65.58 ± 12.16
BMI, kg/m^2	24.8 ± 2.71
RSI	
Voice	1.38 ± 1.55
Throat	2.62 ± 2.02
PND	0.42 ± 1.14
Swallow	0.31 ± 0.74
Cough-supine	0.19 ± 0.69
Dyspnea	0.58 ± 1.33
Cough	0.58 ± 1.21
Globus	3.77 ± 1.7
Heartburn	1.65 ± 1.7
Total	12.28 ± 6.19

Data are shown as mean ± SD; BW, body weight; BMI, body mass index; RSI, reflux symptom index; PND, post-nasal drip.

Table 2. Characteristics of pharyngeal reflux of 24-hour multichannel intraluminal impedance-pH monitoring.

	Pharyngeal reflux	p-value
Acidity, n		
Acid	0.93 ± 2.34	
Weakly acidic	3.41 ± 3.27	
Weakly alkaline	0.55 ± 1.02	
All reflux	4.88 ± 4.59	
Time, REs/h		< 0.001
Daytime	0.229 ± 0.282	
Nighttime	0.097 ± 0.13	
Body position, REs/h		< 0.001
Upright	0.327 ± 0.339	
Recumbent	0.064 ± 0.117	

Data are shown as mean ± SD; RE, reflux event; Daytime, 6:00 AM–6:00 PM; Nighttime, 6:00 PM–6:00 AM

Table 3. Comparison between pre- and post-prandial pharyngeal reflux within 2 hours according to acidity in 24-hour multichannel intraluminal impedance-pH monitoring.

	Pharyngeal Reflux	Pharyngeal Reflux	P-value
	Pre-prandial	Post-prandial	
Within 2 hours, n			
Acid	0.134 ± 0.375	0.212 ± 0.420	0.110
Weakly acidic	0.433 ± 0.447	0.853 ± 0.665	< 0.001*

	Pharyngeal Reflux	Pharyngeal Reflux	P-value
Weakly alkaline	0.065 ± 0.180	0.191 ± 0.390	0.012*
All reflux	0.632 ± 0.548	1.256 ± 0.878	< 0.001*

Data are shown as mean ± SD.

Table 4. Comparison between patients with laryngopharyngeal reflux and normal controls.

	LPR patients (N = 69)	Normal controls (N = 26)	P-value
Age (y)	55.93 ± 13.02	44.23 ± 13.87	
Male : Female (n)	26:43	6:20	
Positive of pharyngeal reflux (n)	69/69 (100%)	5/26 (19%)	
Timing of post-prandial reflux (min)	58.2 ± 61.8	38.4 ± 34.2	0.322

Data are shown as mean ± SD.

FIGURE LEGENDS

Figure 1. Cumulative distribution of meal and pharyngeal reflux episodes in total 69 enrolled subjects. (A) Histogram of meal; (B) Histogram of pharyngeal reflux; (C) Probability density plot of pharyngeal reflux episodes over 24 h.

Figure 2. Histogram of pharyngeal reflux episodes from pre-prandial 2 hours to post-prandial 2 hours in a total of 69 enrolled subjects. The x-axis means the relative time from mealtime represented as zero.