Original Article / Çalışma - Araştırma

The importance of voice analysis in evaluating the effectiveness of reflux treatment

Reflü tedavisinin etkililiğinin değerlendirilmesinde ses analizinin önemi

Ayşegül Batıoğlu-Karaaltın, MD.,[1] Ömer Necati Develioğlu, MD.,[2]
Özge Tarhan, MD.,[1] Mehmet Külekçi, MD.[2]

[1]Department of Otolaryngology, İstanbul University, Cerrahpaşa Medical Faculty, İstanbul, Turkey
[2]Department of Otolaryngology, Gaziosmanpaşa Taksim Traning and Research Hospital, İstanbul, Turkey

ABSTRACT

Objectives: This study aims to investigate the effects of reflux treatment in voice disorders in laryngopharyngeal reflux (LPR) patients using acoustic analyses and the relationship between scoring systems.

Patients and Methods: A total of 84 LPR patients (18 males, 66 females; mean age 43.1±11.3 years; range 18 to 73 years) were evaluated using reflux symptom index (RSI), reflux findings score (RFS), videolaryngostroboscopic examination, and acoustic analysis with Dr. Speech 4 before LPR treatment and at the first and third months after treatment.

Results: Maximum phonation time, fundamental frequency (F0), jitter, and shimmer scores did not show any statistically significant alteration at the posttreatment period according to pretreatment scores (p>0.05). However, the alteration in Harmonics-to-Noise ratio and Signals-to-Noise ratio scores were statistically significant (p=0.017 and p=0.003, respectively). Reflux symptom index results showed significant positive correlation with F0 at the pretreatment, and at posttreatment first and third month evaluations (Spearman's rank correlation coefficient [rho]=0.246, p=0.024; rho=0.300, p=0.006; rho=0.305, p=0.005, respectively).

Conclusion: The relationship between the parameters of acoustic analysis and RSI and RFS values seems to be controversial for diagnosis and follow-up of LPR patients, requiring further investigations.

Keywords: Laryngopharyngeal reflux; reflux scoring system; voice analysis.

ÖZ

Amaç: Bu çalışmada akustik analizler kullanılarak larengofarengeal reflü (LPR) hastalarındaki ses bozukluklarında reflü tedavisinin etkileri ve skorlama sistemleri arasındaki ilişki araştırıldı.

Hastalar ve Yöntemler: Toplam 84 LPR hastası (18 erkek, 66 kadın; ort. yaş 43.1±11.3 yıl; dağılım 18-73 yıl) reflü semptom indeksi (RSİ), reflü bulgu skoru (RBS), videolaringostroboskopik inceleme ve Dr. Speech 4 ile akustik analiz kullanılarak LPR tedavisi öncesinde ve tedavi sonrası birinci ve üçüncü ayda değerlendirildi.

Bulgular: Maksimum fonasyon zamanı, temel frekans (F0), jitter ve shimmer skorları tedavi öncesi skorlara göre tedavi sonrası dönemde istatistiksel olarak anlamlı değişiklik göstermedi (p>0.05). Fakat harmonik gürültü oranı ve sinyal gürültü oranı skorlarındaki değişiklik istatistiksel olarak anlamlı idi (sırasıyla p=0.017 ve p=0.003). Reflü semptom indeksi bulguları tedavi öncesi ve tedavi sonrası birinci ve üçüncü ay değerlendirmelerinde F0 ile anlamlı pozitif ilişki gösterdi (sırasıyla Spearman'ın sıralama korelasyon katsayısı [rho]=0.246, p=0.024; rho=0.300, p=0.006; rho=0.305, p=0.005).

Sonuç: Akustik analiz parametreleri ve RSİ ve RBS değerleri arasındaki ilişki LPR hastalarının tanısı ve takibi için tartışmalı gözükmekte ve ileri araştırmalar gerektirmektedir.

Anahtar Sözcükler: Larengofarengeal reflü; reflü skorlama sistemi; ses analizi.

Available online at
www.kbbihtisas.org
doi: 10.5606/kbbihtisas.2016.80688
QR (Quick Response) Code

Received / *Geliş tarihi:* January 21, 2016 Accepted / *Kabul tarihi:* April 06, 2016

Correspondence / İletişim adresi: Ayşegül Batıoğlu-Karaaltın, MD. İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Kulak Burun Boğaz Hastalıkları Anabilim Dalı, 34098 Cerrahpaşa, Fatih, İstanbul, Turkey.

Tel: +90 532 - 776 03 85 e-mail *(e-posta):* batioglu@yahoo.com

Gastroeosophageal reflux disease (GERD) is an entity with heartburn, regurgitation, chest and stomach pain and the feeling of gastric acid coming up.[1] Laryngopharyngeal reflux (LPR) refers to backflow of gastric contents above the level of the upper esophageal sphincter and it has been implicated in the pathogenesis of several voice disorders such as vocal fold nodules,[2,3] Reinke's edema[3] laryngeal true vocal fold granuloma[2-4] and other otolaryngologic disorders such as globus pharyngeus,[5-7] subglottic and laryngotracheal stenosis,[2,5,8] and laryngopharyngeal carcinoma.[5,9,10] The symptoms of LPR include hoarseness, sore throat, dysphagia, globus pharyngeus, chronic cough and difficulty in breathing with or without classical GERD symptoms.[5,11]

Laryngopharyngeal reflux is a disease that gives rise to subjective and objective changes in voice quality.[12,13] It is important to describe the effect of LPR in voice disorders. There are different methods to diagnose and follow treatment such as the voice handicap index and objective voice analysis techniques[11,14] but utilization of these techniques is controversial, because the relation between LPR and voice problems is relatively new.

The aim of this study was to find out the changes in acoustic analyses and the correlation the acoustic analyses and the scoring system with medical treatment in LPR patients to show the effectiveness of reflux treatment.

PATIENTS AND METHODS

Our study included 84 patients (18 males, 66 females; mean age 43.1±11.3 years; range 18 to 73 years) who were diagnosed with laryngopharyngeal reflux disease at a tertiary referral center in Istanbul, Turkey. The study protocol was approved by the Taksim Education and Research Hospital Ethics Committee. Written informed consent was obtained from each patient before study enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki. The exclusion criteria were having vocal fold nodule, vocal fold cyst or polyp, intracordal hemorrhage, leukoplakia and suspected malignancy.

All patients were examined before the treatment, at the first month of treatment, and at the third month of treatment. Before all examinations, patients filled out the Reflux Symptom Index (RSI) form. A 70° rigid scope (Karl Storz Laryngostrobe, Tuttlingen, Germany) was used to confirm that the patients did not have any additional laryngeal findings such as nodule, polyp, and dysplasia that may cause voice changes, and a Reflux Finding Score (RFS) was obtained. The Dr. Speech 4 program (Tiger Electronics, Seattle, WA) was used for acoustic analysis. All examinations were conducted by a single physician who was blinded to the RSI results and had a special interest in laryngology.

All patients with symptoms of chronic cough, voice disturbances such as hoarseness and throat cleaning, sore throat, and globus pharyngeus were examined and 84 patients were included in the study with a diagnosis of laryngopharyngeal reflux by having an RSI above 13 and an RFS above seven. These two tests are defined and validated by Belafsky et al.[15] Acoustic analysis with Dr. Speech (Tiger Electronics, Seattle, WA) was performed for each patient after standardization with three different 10 seconds of 'a' voice recorded from a distance of 15 cm from the mouth with an angle of 45 degrees in a sound isolated room for sounds below 50 dB.

After the analysis patients received a treatment of 30 mg PPI (lansoprazole) twice a day. A follow-up of three months for patients provided three RSI values, three RFS values by scoring of the videostroboscopic images and three acoustic analysis reports: before treatment, at the first month of treatment, and at the third month of treatment.

Objective voice analysis included six different criteria: Maximum phonation time, fundamental frequency, jitter, shimmer, Harmonics-to-Noise ratio (HNR) and Signal-to-Noise ratio (SNR). Maximum phonation time is a criterion for aerodynamic analysis for voice and phonation. A stable 'a' voice is recorded after a proper inspiration and the duration of the sound while stable was recorded. The normal interval is between 25-35 seconds for men and 15-25 seconds for women.[16] Fundamental frequency is a criterion for vocal vibration, indicating the amount of vocal vibration during one second and its unit is Hertz (Hz). Jitter is a frequency perturbation parameter which is the index of fundamental frequency changes. Shimmer is

Table 1. Changes in reflux symptom index score and reflux findings score during treatment

	Before treatment			1st month of treatment			3rd month of treatment			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
RFS			9.5±2.2			7.3±2.2			6.0±1.7	<0.001
RFS improvement (<7)				28	33.3		47	56		<0.001
RSI			23.5±7.2			19.2±7.0			17.3±6.1	<0.001
RSI improvement (<13)				10	11.9		18	21.4		<0.001

SD: Standard deviation; RFS: Reflux findings score; RSI: Reflux symptom index.

an amplitude perturbation parameter defined in decibels (dB) and indicates the amplitude changes between two following voice periods. The HNR and SNR are spectral parameters of voice analysis. Harmonics-to-Noise ratio is an index of fundamental frequency and its harmonics-to-noise energy. Signal-to-noise is an index of measurable signals-to-noise energy.[17]

Statistical analysis

The statistical analysis was made using IBM SPSS software version 19.0 (IBM Corporation, Armonk, NY, USA). Comparison of more than two dependent numerical variables was done using Friedman test. Subgroup analyses were done by using Wilcoxson test and were interpreted by Bonferroni rectification. Statistical significance was accepted at the p<0.05 level.

RESULTS

Before treatment, the RFS index average was 9.50±2 and RSI average was 23.5±7.2. The RFS and RSI average score differences were statistically significant before and after treatment at the first and third month (p<0.001, p<0.001, p<0.001, p<0.001). The improvement (means RFS under 7 and RSI under 13) in RFS was 33.3% at the first month and 56% at the third month of treatment. The improvement in RSI was 11.9% at the first month, and 21.4% at the third month of treatment (Table 1).

When acoustic analysis results were evaluated, F0, jitter, shimmer, maximum phonation time (MPT) scores did not show any statistically significant alteration at the first and third month of treatment compared to before treatment scores. But the alterations in HNR and SNR scores were statistically significant (p=0.017, p=0.003). The difference between third month HNR and SNR scores and before treatment scores was statistically significant (p<0.001, p<0.001) (Table 2).

When we compared the results of follow-up examinations RSI results showed significant positive correlation with F0 at the before treatment, first and third month evaluations (rho=0.246 p=0.024; rho=0.300 p=0.006; rho=0.305 p=0.005) and significant negative correlation with shimmer (rho= -0.275 p=0.011) at the first month evaluation.

To show the importance of voice analysis in evaluating the effectiveness of reflux treatment,

Table 2. Evaluation of aerodynamic and acoustic analysis data

	Before treatment	1st Month	3rd Month	
	Mean±SD	Mean±SD	Mean±SD	*p*
Fundamental frequency	199.9±42.5	199.8±43.9	200.7±42.2	0.492
Jitter	0.3±0.2	0.3±0.2	0.3±0.2	0.647
Shimmer	0.4±0.5	0.5±1.7	0.4±0.4	0.256
Harmonics-to-Noise ratio	22.0±4.1	22.9±4.2	23.8±4.0*	0.017
Signal-to-Noise ratio	20.8±4.0	23.8±18.9	22.6±3.9*	0.003
Maximum phonation time	13.6±5.6	13.9±5.3	14.4±5.0	0.098

SD: Standard deviation; * 3rd month Harmonics-to-Noise ratio and Signal-to-Noise ratio scores different from before treatment score (p<0.001, p<0.001).

the parameters of acoustic analysis were compared between improved RSI and RFS values and the RSI and RFS values that did not have any improvement.

The difference between F0 (205.5±41.1, 206.6±40.9, 206.9±41.5) of the patients whose RSI values decreased under 7 (improved reflux symptoms) and F0 (179.3±40.9, 173.7±43.8, 179.2±42.1) of the patients whose RSI values did not decrease under 7 (non improved reflux symptoms) for before treatment, first and third month were statistically significant (p=0.011 p=0.004 p=0.029). For the other parameters of acoustic analysis, there was no statistically significant difference for this group. On the other hand mean HNR and SNR score of the patients that did not have any improvement in RSI values showed statistically significant difference between the third month of treatment (HNR: 23.7±3.9; SNR: 22.6±3.8) and before treatment (HNR: 21.6±4.1; SNR: 20.5±4.1) (p=0.006, p=0.005).

The difference between any parameters of acoustic analysis of the patients whose RFS values decreased under 13 (improved reflux findings) and the patients whose RFS values did not decrease under 13 (non improved reflux findings) for before treatment, first and third month were not statistically significant (p>0.05). However mean SNR score of the patients that did not have any improvement in RSI values showed statistically significant differences between third month of the treatment (SNR: 22.9±3.8) and before treatment (SNR: 21.1±3.6) (p=0.015).

DISCUSSION

In generally, LPR patients have lower quality voices than healthy people and they show restricted phonation capabilities.[13,18] When voice analysis data of LPR patients were compared to healthy subjects significant deterioration was showed for MPT, jitter, shimmer, and glottal noise in LPR patients.[12,18] F0 is not affected by most laryngeal disorders and Pribuisiene et al.[12] found no difference for mean F0 between suspected LPR patients and controls. Increased jitter and shimmer may reflect degenerative changes in laryngeal tissue but shimmer seems to be a more sensitive parameter than jitter in LPR patients.[13,18,19,20] The HNR changes in LPR patients were shown as well. Some authors found statistically significant changes for HNR values[18,19,21] but others did not find any differences.[18]

On the other hand, it is still controversial whether voice parameters improve with medical treatment or not. Some authors reported improvement in acoustic parameters with medical treatment[22,23] but others showed no significant improvement.[20,21] In 1996 Shaw and Searl[23] have performed a study including acoustic analysis and LPR treatment and they have claimed that improvement in acoustic parameters are seen after treatment if there was hoarseness before treatment. In our study F0, jitter, shimmer, MPT scores did not show any statistically significant alteration at the first and third month of treatment compared to pre-treatment scores. But the alteration in HNR and SNR scores were statistically significant.

Today, 24-hour pH monitoring is accepted as the most powerful diagnostic test for LPR diagnosis but various practical issues limit the usage of pH monitoring; the test is expensive, the results are controversial and some patients cannot tolerate the use of these system.[5,24] Although recent studies have showed some promising methods for diagnosis of LPR such as laryngeal sensory testing and control of blood pepsin levels,[25] the diagnosis of LPR is made clinically. For instance omeprazole test means empirical treatment in patients with potential LPR has a sensitivity and specificity of 89%[26] and preferred by many clinicians as a diagnostic test. The RFS and RSI which were defined by Belafsky et al.[27] are sensitive, specific, easily applicable, and patient-oriented methods. The RFS is superior to other scoring systems in evaluating the response to treatment because it is troublesome to evaluate the response after a short-term treatment due to parameters such as nodule, granuloma and polyp that require longer recovery periods. The RFS and RSI could be used effectively in the diagnosis and follow-up of LPR.[28] We evaluated the availability of diagnostic tool of alteration in acoustic parameters with treatment by comparing them with the already widely used RSI and RFS.

In our patient group, RFS declined below 7 in 56% of the patients at the third month of treatment. The RSI declined below thirteen in 21.4% of patients at the third month of

treatment. According to these data, finding scores declined earlier than symptom scores in our patient group, and this is contradictory to other studies in literature.[29,30] But RFS and RSI average score differences were statistically significant before and after treatment at first and third month.

Jin et al.[28] proposed a significant correlation between jitter and RSI and secondary correlation between shimmer and RSI. Our RSI results showed significant positive correlation with F0 at the before treatment, first and third month evaluations. The differences between F0 of the patients whose RSI values improved and did not improve were statistically significant. The differences between any parameters of acoustic analysis of the patients whose RFS values improved and did not improve were not statistically significant. Controversially, HNR and SNR scores of the patients that not have any improvement at RSI values showed statistically significant difference between third month of the treatment and SNR score of the patients that not have any improvement at RSI values showed statistically significant differences between the third month of the treatment.

We tried to show the correlation between the parameters of acoustic analysis and improved RSI, RFS values. The RSI and RFS scales, aerodynamic and acoustic analyses have been performed but the statistical analyses are far from satisfactory. Acoustic analysis techniques are important for testing laryngeal benign neoplasms, or vocal fold paralysis, or functional laryngeal abnormalities, but our study and the other recent studies showed that objective and subjective voice analysis techniques are far from providing an accurate diagnosis and follow-up criteria for laryngopharyngeal reflux.

The treatment of GERD with correct diagnosis has satisfactory results and otolaryngological examination with RFS and RSI are valuable for accurate diagnosis. At the same time there are significantly different acoustic analysis values for LPR patients than control subjects, but the limited data to date show no clear picture of whether acoustic parameters are useful indicators of treatment efficacy in LPR disease.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Jailwala JA, Shaker R. Supra-oesophageal complications of reflux disease. Dig Liver Dis 2000;32:267-74.
2. Koufman JA, Amin MR, Panetti M. Prevalence of reflux in 113 consecutive patients with laryngeal and voice disorders. Otolaryngol Head Neck Surg 2000;123:385-8.
3. Toohill RJ, Kuhn JC. Role of refluxed acid in pathogenesis of laryngeal disorders. Am J Med 1997;103:100-6.
4. Olson NR. Laryngopharyngeal manifestations of gastroesophageal reflux disease. Otolaryngol Clin North Am 1991;24:1201-13.
5. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 1991;101:1-78.
6. Hill J, Stuart RC, Fung HK, Ng EK, Cheung FM, Chung CS, et al. Gastroesophageal reflux, motility disorders, and psychological profiles in the etiology of globus pharyngis. Laryngoscope 1997;107:1373-7.
7. Woo P, Noordzij P, Ross JA. Association of esophageal reflux and globus symptom: comparison of laryngoscopy and 24-hour pH manometry. Otolaryngol Head Neck Surg 1996;115:502-7.
8. Bain WM, Harrington JW, Thomas LE, Schaefer SD. Head and neck manifestations of gastroesophageal reflux. Laryngoscope 1983;93:175-9.
9. Price JC, Jansen CJ, Johns ME. Esophageal reflux and secondary malignant neoplasia at laryngoesophagectomy. Arch Otolaryngol Head Neck Surg 1990;116:163-4.
10. Ward PH, Hanson DG. Reflux as an etiological factor of carcinoma of the laryngopharynx. Laryngoscope 1988;98:1195-9.
11. Ulualp SO, Toohill RJ. Laryngopharyngeal reflux: state of the art diagnosis and treatment. Otolaryngol Clin North Am 2000;33:785-802.
12. Pribuisiene R, Uloza V, Kupcinskas L, Jonaitis L. Perceptual and acoustic characteristics of voice changes in reflux laryngitis patients. J Voice 2006;20:128-36.
13. Oguz H, Tarhan E, Korkmaz M, Yilmaz U, Safak MA, Demirci M, et al. Acoustic analysis findings in objective laryngopharyngeal reflux patients. J Voice 2007;21:203-10.
14. Ali Mel-S. Laryngopharyngeal reflux: diagnosis and treatment of a controversial disease. Curr Opin Allergy Clin Immunol 2008;8:28-33.
15. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). J Voice 2002;16:274-7.
16. Maslan J, Leng X, Rees C, Blalock D, Butler SG. Maximum phonation time in healthy older adults. J Voice 2011;25:709-13.
17. Kılıç MA, Evaluation of the patient with voice problem by objective and subjective methods, Curr Pract ORL 2010;6:257-26.

18. Ross JA, Noordzji JP, Woo P. Voice disorders in patients with suspected laryngo-pharyngeal reflux disease. J Voice 1998;12:84-8.
19. Akyildiz S, Ogut F, Varis A, Kirazli T, Bor S. Impact of laryngeal findings on acoustic parameters of patients with laryngopharyngeal reflux. ORL J Otorhinolaryngol Relat Spec 2012;74:215-9.
20. Hamdan AL, Sharara AI, Younes A, Fuleihan N. Effect of aggressive therapy on laryngeal symptoms and voice characteristics in patients with gastroesophageal reflux. Acta Otolaryngol 2001;121:868-72.
21. Selby JC, Gilbert HR, Lerman JW. Perceptual and acoustic evaluation of individuals with laryngopharyngeal reflux pre- and post-treatment. J Voice 2003;17:557-70.
22. Hanson DG, Jiang JJ, Chen J, Pauloski BR. Acoustic measurement of change in voice quality with treatment for chronic posterior laryngitis. Ann Otol Rhinol Laryngol 1997;106:279-85.
23. Shaw GY, Searl JP. Laryngeal manifestations of gastroesophageal reflux before and after treatment with omeprazole. South Med J 1997;90:1115-22.
24. Branski RC, Bhattacharyya N, Shapiro J. The reliability of the assessment of endoscopic laryngeal findings associated with laryngopharyngeal reflux disease. Laryngoscope 2002;112:1019-24.
25. Komatsu Y, Kelly LA, Zaidi AH, Rotoloni CL, Kosovec JE, Lloyd EJ, et al. Hypopharyngeal pepsin and Sep70 as diagnostic markers of laryngopharyngeal reflux: preliminary study. Surg Endosc 2015;29:1080-7.
26. Siupsinskiene N, Adamonis K. Diagnostic test with omeprazole in patients with posterior laryngitis. Medicina (Kaunas) 2003;39:47-55.
27. Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope 2001;111:1313-7.
28. Jin bJ, Lee YS, Jeong SW, Jeong JH, Lee SH, Tae K. Change of acoustic parameters before and after treatment in laryngopharyngeal reflux patients. Laryngoscope 2008;118:938-41.
29. DelGaudio JM, Waring JP. Empiric esomeprazole in the treatment of laryngopharyngeal reflux. Laryngoscope 2003;113:598-601.
30. Hanson DG, Kamel PL, Kahrilas PJ. Outcomes of antireflux therapy for the treatment of chronic laryngitis. Ann Otol Rhinol Laryngol 1995;104:550-5.