Phonetic Approaches of Laryngopharyngeal Reflux Disease: A Prospective Study

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Summary: Objectives. The study aimed to explore the impact of the selection of the analyzed time interval on the significance of acoustic measurements used to investigate laryngopharyngeal reflux (LPR) treatment efficacy, and based on these results to develop an alternative statistical approach in data analysis focusing on individual patient vocal behavior.

Study Design. This is a prospective case series.

Methods. From September 2013 to July 2015, 41 patients with a reflux finding score (RFS) > 7 and a reflux symptom index (RSI) > 13 were enrolled and treated with pantoprazole 20 mg twice daily and diet behavioral changes for 3 months. Voice recordings were performed at baseline and after 3 months of treatment. Most stable time intervals of 1, 2, 3, 4, and 5 seconds, and a 1-second time interval positioned at mid-production, were subjected to acoustic analysis. Based on the latter, we developed an "informativeness coefficient" for each acoustic parameter that aimed at assessing its sensitivity to clinical resolution in the case of LPR disease.

Results. Significant clinical improvement (RSI and RFS) was observed after treatment ($P < 0.05$). The acoustic analysis revealed that acoustic parameters significantly improving from pre- to posttreatment varied across time intervals. The duration and the position of the analyzed time interval in the production yielded considerable differences in the results. Analysis of the informativeness coefficient indicated that jitter, jitter percent, relative average perturbation (RAP), pitch perturbation quotient (PPQ), shimmer (ShdB), shimmer percent (Shim), amplitude perturbation quotient (APQ), and smoothed amplitude perturbation quotient (sAPQ) were the indices most sensitive to medical treatment efficacy, with a coefficient ranging from 75.86% to 86.21%.

Conclusions. Depending on the selection of the time interval over which the acoustic parameters are measured, the potential effect of the treatment may or may not be statistically demonstrated. Future studies are needed to establish standardized methodological procedures for acoustic data analysis.

Key Words: laryngopharyngeal reflux–reflux laryngitis–acoustic–voice–hoarseness.

INTRODUCTION

Laryngopharyngeal reflux (LPR) is defined as the back flow of gastric contents to the laryngopharynx, where it comes in contact with the tissues of the upper aerodigestive tract.[1] It concerns 10% of patients in ENT consultation[2,3] and is involved in up to 75% of patients with refractory ENT symptoms.[4] The LPR irritation leading to hoarseness may also be accompanied by abnormal perceptual voice characteristics, such as musculoskeletal tension, hard glottal attack, glottal fry, vocal forcing, forcing sensations, clamping, vocal fatigue, prolonged voice warm-up time, and restricted tone placement.[5,6] However, some authors claim the existence of two different LPR patient profiles according to the presence or absence of perceptual dysphonia.[7] On this subject, it is well known that subtle voice changes may be even more difficult to detect by the usual subjective assessment by the clinician. This leads to the development of several acoustic parameters to study the pathophysiology or to measure the effectiveness of treatment, especially in LPR disease.[8–11] Nowadays, the various acoustic studies conducted in LPR disease are using different methods, leading to partially inconsistent results.

In a previous report, we addressed the issue of the effect of a 3-month proton pump inhibitor (PPI) twice-daily treatment on the voice disorders of LPR subjects.[12] Before and after treatment, subjects were instructed to sustain the vowel /a/ three times for a time corresponding to the maximum phonation time. An extended acoustic analysis was performed over the most stable 1-second time interval of these productions, which was defined as the interval exhibiting the lowest percent jitter, percent shimmer, and noise to harmonic ratio (NHR) values. The results showed that both subjective (according to reflux symptom index [RSI] and reflux finding score [RFS] indices) and objective (acoustic parameters) voice disorders improved after treatment. However, the specifics of the acoustic results could not be easily compared with the relevant literature due to methodological factors. Indeed, a methodological uncertainty characterizes most studies as to the method to be used to measure acoustic parameters in cohorts of LPR patients.[7,9,13–15] First, although it is well accepted that the analysis of acoustic measures must be made on a sustained oral vowel (often [a]),[16] it seems that the measure

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Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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of the main acoustic parameters may significantly vary depending on the chosen vowel ([i], [a], [u]).[17] Second, a recent meta-analysis reported a significant variability between acoustic studies of voice quality in the method used to select the time interval subjected to acoustic analysis, and the duration of that interval,[18] although the results obtained using *MDVP* have been shown to differ according to the choice and the duration of the time interval over which the analysis is performed.[19] The only consensus in the literature concerns the exclusion from the analysis of the onset and offset of the speech signal, given the instability related, respectively, with the warm-up and shutdown of the vocal folds vibration process.[20] Depending on the choice made and rarely justified, the analyzed time interval may be either the whole speech signal[11] or a selection, positioned simply at the middle of the production[15] or more often in its most stable portion. However, the "most stable" interval is not yet defined, so that some authors choose the most stable portion based on visual observation of the acoustic signal,[18] whereas others have attempted an objective approach using acoustic values, such as jitter, shimmer, and NHR, to determine stability.[12,14] Concerning the duration of the analyzed time interval, it may vary between 500 ms[14] and 5 s[11] in the LPR literature.

Given the high methodological variability for measuring acoustic parameters in different LPR studies and its potential impact on the results, we conducted this study. Thus, the aim of the present paper was to draw on the large dataset collected in the above-mentioned study[12] in order to address some of the methodological issues that may impact the outcome of the acoustic analysis of voice disorders. Our specific goals were (1) to explore the impact of changes in the nature and duration of the analyzed time interval on the significance of the acoustic measurements, and (2) based on these results to develop a novel statistical approach in data analysis largely bypassing the interval selection problem and focusing on individual patient evolution, which may in time allow to consider different profiles of LPR disease.

MATERIALS AND METHODS

Fifty-four subjects with suspected LPR were recruited from September 2013 to September 2015 at the Otolaryngology Department of EpiCURA Hospital (Belgium). LPR diagnosis was performed using both RSI > 13 and RFS > 7. Indeed, Belafsky et al have demonstrated that these thresholds were correlated with pathologic pH monitoring (pH < 4).[21] In this context, other groups used the same thresholds in other papers.[22,23] Exclusion criteria included smoking or alcohol addiction, pregnancy, neurologic disease, psychiatric illness, upper tract infections within the last month, an antacid treatment already started, previous history of cervical surgery, traumatism, benign vocal fold lesions, malignancy, ENT radiotherapy, seasonal allergies, asthma, PPI hypersensitivity, untreated thyroid disease, prior antireflux surgery, or chemical exposure causing laryngitis. The study protocol was approved by the local ethical committee of the EpiCURA Hospital (n° A2014/001). From the 54 patients identified as candidates, 41 completed the study. There were 18 men (44%) and 23 women (56%), and the mean age of the subjects was 50 years (50 in the women subgroup [24–72] and 51 in the men subgroup [19–86]). Patients were treated with diet and lifestyle measures and twice-daily pantoprazole (20 mg). The RSI, RFS, and voice recordings (among others, for details see Lechien JR et al[12]) were performed at baseline and after 3 months of treatment by the same practitioner. Concerning the speech task, subjects were instructed to sustain three times the production of the vowel /a/ for as long as possible (maximum phonation time). Voice recordings were conducted in a sound-treated room with a high-quality microphone (Sony PCM-D50; New York, NY) placed at a distance of 30 cm from the patient's mouth. Acoustic measurements were carried out using the *MDVP* software (KayPENTAX, Montvale, NJ), and include a measurement of standard deviation of F0 (STD), fundamental frequency variation (vF0), absolute jitter (Jita), jitter percent (Jitt), relative average perturbation (RAP), pitch perturbation quotient (PPQ), smoothed pitch perturbation quotient (sPPQ), phonatory fundamental frequency range (PFR), fundamental frequency tremor (Fftr), shimmer (ShdB), shimmer percent (Shim), amplitude perturbation quotient (APQ), smoothed amplitude perturbation quotient (sAPQ), amplitude frequency tremor (Fatr), peak-to-peak amplitude variation (vAm), NHR, voice turbulence index (VTI), soft phonation index (SPI), F0 tremor intensity index (FTRI), and amplitude tremor intensity index (ATRI).

Acoustic parameters measured in the productions of the patients before and after treatment were analyzed in two different ways. First, a group analysis was performed to investigate how the assessment of medical treatment efficacy by acoustic parameters is mediated by time interval selection. Six different time intervals were selected in one of the three /a/ productions before and after treatment, including a 1-second interval positioned at mid-production, as well as five "most stable" (ie, exhibiting the lowest Jitt, Shim, and NHR values) time intervals of, respectively, 1-, 2-, 3-, 4-, and 5-second duration. Changes in acoustic parameters from pre- to posttreatment were calculated for the overall group of 41 patients using Wilcoxon matched-pairs signed-ranks tests for each time interval, and the results were compared across time intervals.

Second, a per subject analysis was developed in order to bypass the time interval selection problem and to find the acoustic parameters that are most sensitive to the resolution of the LPR disease. After excluding the onset and offset of the speech signals, all successive 1-second intervals of the three /a/ productions before and after treatment were included in the analysis. For each patient, changes in acoustic parameters from pre- to posttreatment were calculated using Mann-Whitney tests (pre- and posttreatment productions had to be considered as independent samples as they were of different sizes depending on the length of the productions). From these data, an "informativeness coefficient" was determined for each acoustic parameter, which was defined as the percentage of cured patients (RSI < 13 and RFS < 7) for whose that particular acoustic parameter significantly improved from pre- to posttreatment.

Third, we also conducted a correlation study among the RFS total score, vocal folds edema, diffuse laryngeal edema, and relevant acoustic parameters at baseline (defined by a significant improvement of the values after treatment in >1 interval time analysis).