

Lateral Phase Mucosal Wave Asymmetries in the Clinical Voice Laboratory

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Summary: Anecdotally, in some persons it has been observed by the Senior Author (K.K.) that asymmetries of the mucosal wave exist when examined videostroboscopically. In the vast majority of these people, no pathology is ever discovered. Mucosal wave asymmetries could cause concern for the otolaryngologist, who may consider them to be a forewarning of subclinical pathology and subject the patient to unnecessary, expensive, and anxiety-provoking investigations or interventions. The purpose of this study was to establish the prevalence of mucosal wave asymmetries in an asymptomatic population lacking laryngeal pathology. Acoustic spectral analysis is also utilized to determine if the presence of subharmonics might be associated. A hospital-based, cross-sectional study design was used. The subjects had no known vocal or medical pathologies, and were nonsmoking. The study group was composed of 30 males aged 35–50 years and 30 women between 22–55 years. Each of the males underwent acoustic spectral analysis; and all subjects completed a medical questionnaire, subjective talkativeness rating, and videostroboscopic laryngeal examination. 10.5% of the subjects (exact 95% CI = 4.0–21.5%) exhibited mucosal wave variations at stroboscopy, characterized as periodic lateral phase asymmetries found consistently in both the modal and upper registers. There was no association with the chosen acoustic spectral parameters, talkativeness scales, or questionnaire-based variables. Mucosal wave asymmetries may be a variance of normal, and are likely to be far more common in the general population than previously believed. The prevalence detected here is expected to be important in the clinical laryngology practice, where these asymmetries may be frequently encountered and influencing management decisions. There has been little normative data published for variations of the mucosal wave specifically for

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epidemiological purposes. Clinically, in the absence of such data, otolaryngologists may over interpret videostroboscopic findings, leading to unnecessary investigations or interventions.

Key Words: Voice—Mucosal wave—Vocal fold—Videostroboscopy—Asymmetry.

INTRODUCTION

Stroboscopic examination of the vocal folds is an indispensable part of the evaluation of patients with vocal complaints. Integrity of the vibratory margin of the vocal fold is essential for the complex motion required to produce good voice quality.¹ Videostroboscopy has proven essential to the accurate identification of voice pathology,^{2,3} and its use may result in a change of diagnosis, thus altering management in a number of patients.⁴ Authors have stressed the role of stroboscopy in differentiating benign lesions requiring surgery, from those that do not.^{5,6} Von Leden reported its usefulness in detecting early stages of carcinoma.⁷

Clinical interpretation of stroboscopic images usually follows a standard assessment protocol.^{8,9} Features analyzed typically include symmetry of amplitude and phase, periodicity, glottic closure, amplitudes and waveforms of individual vocal folds, and the presence of adynamic segments or pathology. Once limited to the voice laboratory, stroboscopic examination is now becoming commonplace. With this comes a large body of primarily anecdotal experience. For example, during stroboscopic examination of the vocal folds, phase asymmetries of the mucosal wave may be noted. This may cause concern for the otolaryngologist who may consider this asymmetry to be a sign of subclinical or impending pathology. This may be especially true in a professional voice user, where a phase asymmetry might be erroneously considered responsible for being the cause of the complaint. The concern is not unfounded. It has been well documented⁹⁻¹¹ that certain pathologic conditions of the vocal folds manifest as phase asymmetries of the mucosal wave. These asymmetries may occur despite grossly normal vocal folds. However, an extensive workup may not be indicated in all individuals with mucosal wave asymmetries examined stroboscopically for vocal complaints. These asymmetries may be a variance

of normal, and not related to the patient's vocal complaints, or the presence of subclinical pathology. In other words, even gross asymmetry does not necessarily indicate abnormality. It is possible that this phenomenon represents a physiologic asymmetry. To date, there have been few published databases on normal variations of the mucosal wave in a healthy, asymptomatic population.¹² Miller et al¹³ in an excellent review of videostroboscopic variations in a normal population stop short of determining the prevalence or incidence of the parameters evaluated. Differences in gender factors and voice training were their focus, and were noted. Elias et al¹⁴ have reported normal stroboscopic variations in professionally trained singers, and go on to emphasize the importance of obtaining a normal database against which abnormal findings can be compared. In the absence of such data, clinicians may overinterpret videostroboscopic findings, leading to unnecessary investigations, interventions, and significant patient anxiety.

METHOD

A cross-sectional study design was used. Two populations were studied, each containing thirty nonsmoking subjects with no known medical or vocal pathology. All subjects were recruited from the primary, and ancillary service providers at our institution via hospital-based advertisements. The first group consisted of males with an age range of 35–50 (median 37 years; SD 3.8). The second group consisted of females 22–55 years of age (median 29 years; SD 6.2). All subjects were asked to complete a medical questionnaire to identify smokers, and those individuals with a history of dysphonia, vocal pathology, and/or previous vocal surgery. Subjects were excluded if they had a history of persistent vocal complaints within the last 6 months (ie, hoarseness, loss of voice, or excessive throat

clearing), laryngeal pathology (ie, vocal nodules, malignancy/dysplasia, or sulci), or prior laryngeal surgery/radiation therapy. Seven-point occupational, and social subjective talkativeness scales were also obtained.¹⁵ None of the subjects had extensive professional vocal training, or were employed as singers.

Male subjects were first recorded in an office setting using a professional-grade condenser microphone (Dynamic Mic, Sony MTL F-96), which was held at a distance of 3 cm from the mouth. Voice signals were digitized at 22.05 kHz directly into a personal computer system, using a built-in sound card with a 16-bit A/D converter. All subjects were asked to sustain the vowel /i/ for at least 2 seconds at comfortable pitch and loudness level (chest register), and at high pitch and comfortable loudness level (head register). Three repetitions of each phonation were normalized to their maximum amplitude and were retained for spectral analysis. Narrow-band spectrograms (FFT size = 2048 samples, displayed dynamic range = 60 dB) were produced and examined by a single investigator. The presence of subharmonic components was noted according to the following rule of thumb: subharmonics were considered significant when their magnitudes were less than 40 dB below the fundamental. In addition to their magnitude, subharmonics were notable only when they were formed throughout the phonation, but not necessarily continuously.

All subjects completed videostroboscopic examination of the glottis while seated. A 70° rigid endoscope was used, during which subjects were asked to sustain the vowel /i/ in their chest register at a comfortable intensity for 5–10 seconds while the mucosal wave and phonation frequencies were recorded. This was repeated 3–5 times, until 3 adequate videotaped segments were obtained. Subjects were then recorded similarly while phonating in their upper register. The techniques for stroboscopic examination have been discussed in detail elsewhere.⁸ Flexible fiberoptic laryngoscopes were infrequently required to obtain satisfactory recordings in subjects who could not tolerate rigid examination, or in whom anatomy prevented adequate visualization of the glottis. All flexible examinations were comparable to the rigid examinations in their ability to reveal the phenomena of interest.

Qualitative analyses of the examinations for the presence or absence of lateral phase mucosal

wave asymmetry were made by two investigators independently with the senior investigator (K.K.) having extensive experience with stroboscopy. A subject was considered positive stroboscopically if the following criteria were met: readily apparent, stable (periodic) asymmetry in lateral phase existing in both the chest and head registers, lasting for a time segment constituting $\geq 75\%$ of the subject's phonation effort (maximum phonation time), with a minimum duration of three seconds; independent investigator agreement; and reproducible in two of three trials. The reliability of subjective analysis of videoed stroboscopic examinations has been well-established.^{16,17} Other qualitative measurements (glottic closure, vocal fold physical characteristics, for example) were also taken. No subject exhibited characteristics consistent with vocal pathology in any of these parameters (ie, masses, adynamic segments, leukoplakia).

Phonations were also digitized from the audio portion of the videotaped stroboscopic examination. Their spectrograms were produced and examined in the manner described above.

RESULTS

Thirty males and 30 females completed the examination. Three male subjects were subsequently excluded: one for a recent smoking history, and two others for incomplete examinations. No female subjects were excluded. The data are summarized in Table 1. Fisher's Exact Test was used to determine

TABLE 1.

	Males	Females
N =	27	30
Age	35–50 (median 37; SD 3.8)	22–55 (median 29; SD 6.2)
Flexible exams	5	5
Occupational Talkativeness Scale	Mean 6.1; SD 0.6	Mean 6.0; SD 0.8
Social Talkativeness Scale	Mean 6.0; SD 0.6	Mean 6.2; SD 0.7
Asymmetry in Both Registers	3 (11%)	3 (10%)
Asymmetry in Upper Register Alone	10 (37%)	10 (33%)

statistical significance. Two-tailed p values were used in all cases.

In total, 10.5% of subjects (exact 95% CI = 4.0–21.5%) exhibited gross, stable mucosal wave lateral phase asymmetry in both registers (see Figure 1). Eleven percent of males, and 10% of women were positive in each group. 36.5% of subjects (37% of males, and 33% of females) demonstrated lateral phase asymmetries in the head register alone. None of the subjects had asymmetries in the chest register alone; therefore, the 10.5% are a subset of the 36.5%. In all positive examinations the lateral phase asymmetry was noted in each of the three trials. No examinations were indeterminate (eg, those which met some, but not all of the criteria, except those which were noted in the head register alone). Small amplitude asymmetries were present in subjects in

both groups, but were neither quantified, nor qualified. One female demonstrated a previously unknown inclusion cyst of the epiglottis. No other laryngeal pathology or conditions were found in any of the remaining subjects.

The medical questionnaire revealed four conditions in several subjects known or suspected to affect vocal fold function (Table 2). Two men stated a history of occasional reflux laryngitis. Neither of the men had a recent event, or were taking scheduled anti-reflux medication. One male, and three females reported a recent upper respiratory tract infection (URTI) in the prior two weeks. All four had self-medicated with over-the-counter cold preparations. Four females taking second-generation antihistamines under medical supervision for seasonal allergies. 10 females were using oral contraceptive

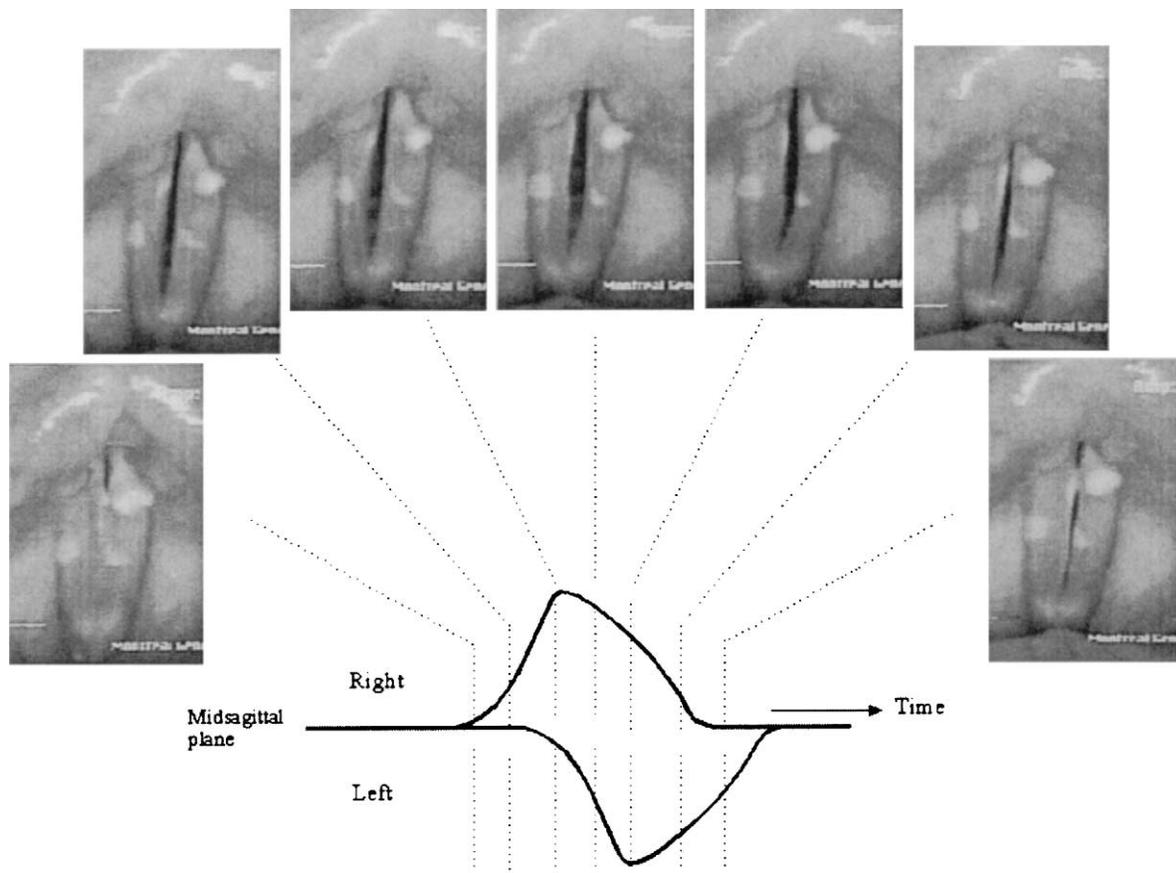


FIGURE 1. Single glottic cycle of a subject with an asymmetric mucosal wave. The line diagrams the excursion of the mucosal wave from the midline over time. Note that the mucosal wave of the right vocal fold precedes that of the left. This represents a lateral phase difference. The amplitude is bilaterally symmetrical.

TABLE 2.

	Males with Asymmetry*	Males Without	Females with Asymmetry*	Females Without
G-E Reflux	0	2	0	0
Recent URTI	0	1	0	3
Antihistamine Usage	0	0	0	4
Oral Contraceptive Usage	0	0	1	9

*Only subjects with asymmetry in both registers are included here (Table 1, row 6).

medication. Stratification was done to determine if a history of gastroesophageal reflux, recent URTI, antihistamine or oral contraceptive medication usage were associated with the presence of lateral phase asymmetry in both registers. For each of these variables $P = 1$.

The mean subjective talkativeness ratings (Table 3) for each group lay between 6–6.2. To determine the association between “excessive” talkativeness and the asymmetry, respondents reporting 1–6 were compared to those reporting 7 (greater than + 1 SD in each case). For both occupational, and social talkativeness, $P = 1$. When each gender was evaluated individually, none of the parameters reached statistical significance.

Subharmonics were noted in the recordings of 1 of the 3 males stroboscopically positive in both registers (6 of 10 stroboscopically positive in upper register alone) and in 4 otherwise unremarkable males (Table 4). Overall, subharmonics were especially notable in upper register phonations and their magnitude was more than 30 dB below the fundamental. Two of the men exhibited significant subharmonics with a magnitude of 20 dB below the

fundamental. Spectrographic analysis of the audio portion of the videotaped examinations revealed subharmonics in phonations of only 2 male subjects (one positive in both registers, one positive in upper register alone). These are the same subjects that had exhibited significant subharmonic components in the independent (“live”) spectral analysis. These persons had been identified as asymmetrical during stroboscopy. Because the presence of subharmonics did not seem to be predictive of asymmetry in both registers ($P = 0.47$), or in the upper register alone ($P = 0.10$) this parameter was not acquired on the female subjects.

When stratified by gender, there were no statistically significant differences in the presence of asymmetry in both registers ($P = 1$), or the upper-register alone ($P = 0.79$).

DISCUSSION

The prevalence of lateral phase mucosal wave asymmetries in a population lacking laryngeal pathology has not been reported. In prior studies^{14,18} mucosal wave abnormalities were described in the presence of abnormalities. Without normal population parameters, sample-size calculations for cross-sectional studies are somewhat arbitrary, and often limited by practical factors (ie, availability of funding, or facilities). The intent of this study was to determine a (rough) baseline prevalence, which will provide an estimate for future sample-size calculations. This information has been used in our institution to design the next phase of the research, which is to determine the prevalence of variations of the mucosal wave in the normal population.

Although the asymmetries found were not quantified, several salient features were noted. Each of

TABLE 3.

	Subjects with Asymmetry*	Subjects Without
Occupational Talkativeness Scale = 1–6	5	44
Occupational Talkativeness Scale = 7	1	7
Social Talkativeness Scale = 1–6	5	1
Social Talkativeness Scale = 7	1	10

*Only subjects with asymmetry in both registers are included here (Table 1, row 6).

TABLE 4.

	Males Asymmetric Both Registers	Males Without Asymmetry in Both Registers	Male Asymmetric Upper Register Alone	Males Without Asymmetry in Either Register
Subharmonics	1	4	6	4
Absent	2	20	4	13

the asymmetries in this study represented periodic lateral phase asymmetries (see reference¹³ for a description of different phase asymmetries). In what has traditionally been considered the “normal” (symmetric) glottic cycle, the right and left mucosal waves are mirror images about a midsagittal line at each time-point in the glottic cycle. As demonstrated in Figure 1, with lateral phase asymmetry, the mucosal wave of one vocal fold precedes that of the other. However, the amplitudes of each of the vocal folds are bilaterally symmetrical, and successive glottic cycles are identical, ie, the phenomenon is periodic. In this phase-shift asymmetry, a stable temporal relationship exists, and the vocal folds are considered to be vibrating synchronously, albeit out-of-phase. The fact that all of the asymmetries were characterized by a phase shift is not unexpected. From a mechanical standpoint, gross amplitude asymmetries, or aperiodic/chaotic waves imply a significant difference in mass or viscoelastic properties between the right and left vocal folds.¹⁹ The magnitude of difference that is required to result in a significant amplitude asymmetry is less likely in the absence of pathology. Minute asymmetries in amplitude certainly do exist, as do horizontal, and vertical phase differences, but are not readily apparent on routine stroboscopic examination, except to the highly experienced clinician. Any lesion which affects the viscoelastic properties of one vocal fold versus the other would likely result in asymmetry of phase, amplitude or both. For example, a paresis in the distribution of the superior laryngeal nerve might be sufficient to result in a lateral phase asymmetry.²⁰ Small temporal and spatial asymmetries reflect a natural vocal quality and are not disturbing the regularity of phonation. As a result, small, brief vibratory irregularities observed stroboscopically are usually ignored. It is possible that variations in the physical properties of the two vocal folds (temporary, or permanent), and/or the subglottic air

column result in enough of a dissimilarity to produce a phase difference, but are insufficient for gross amplitude asymmetry under normal conditions. This may be thought of as physiologic asymmetry. Determining the threshold for the introduction of significant asymmetry (phase, amplitude, or period) by alteration of the physical characteristics of a single vocal fold relative to the other could have an enormous impact on the modeling of the phonatory system, and clinically, in determining how advanced a particular pathologic state must be to manifest as a pathologic asymmetry of phase, or amplitude.

It was further observed that one-third of all subjects exhibited the asymmetry when phonating in their upper register. Only one-third of these individuals redemonstrated the phase asymmetry in their comfortable chest voice. This has some interesting implications. It is postulated that at these higher frequencies bilaterally differential changes in the viscoelastic properties of the vocal folds introduces asymmetry into the phonatory system. The degree to which the subglottic air column contributes to the phenomena is unknown. As such, it may be that any phonation that extends the phonatory limits of an individual may lead to asymmetries. The 10.5% that exhibited consistent asymmetries in both registers are more likely to be noticed on routine stroboscopy, which might raise the suspicion of occult pathology. In contrast, the remainder of the 36.5% in whom asymmetry is present only during vocal extremes (eg, in their upper register alone), are less likely to be of practical clinical importance, although the information may be useful to the eventual modeling of this event.

Female laryngeal and glottal characteristics are not simply comparable to male characteristics transposed by one octave. Females, who typically phonate at frequencies >200 Hz might have been expected to have a higher incidence of asymmetry. No statistically significant gender difference existed

in this study. This is consistent with the findings of Miller et al¹³ regarding gender differences and lateral phase asymmetry. This has clinical implications, as the majority of non-smoking persons seeking care for vocal complaints are female.

Voice signals recorded at the mouth of a subject reflect the interaction of the acoustic characteristics of the vocal fold function with the filtering properties of the vocal tract.²¹ Acoustically, the voicing continuum ranges from the turbulence of voiceless airflow to the orderly arrangement of energy in the harmonic series of voiced tones.²² In the presence of mucosal lesions, even if the two vocal folds appear similar on the surface, they may be quite different from a mechanical point of view. Such differences in the mechanical properties of the folds (ie, elasticity, viscosity, tension, form) disturb the balance between the aerodynamic forces in the glottis. The normal vibratory pattern becomes asymmetrical, and the phonation is characterized by excessive nonharmonic energy (noise), subharmonics, or complete breakdown of the harmonic structure. Similar, but not pathological, spectrographic patterns may be observed in marginal phonatory behavior such as low-frequency phonation (ie, vocal fry), turbulent phonation characterized by excessive airflow, and some forms of harmonic signing.

In the absence of pathology, complex spatial vibratory patterns, which may be asymmetrical in phase and amplitude, are attributed to two or more normal vibratory modes superimposed on the vibration of the vocal folds. In other words, the presence of subharmonics presupposes that the two cords are vibrating asynchronously, or that a second mode of vibration coexists (along the horizontal axis of a vocal fold, for example). The presence of mucosal wave asymmetry in this study, does not necessarily indicate asynchrony, or a second mode of vibration. These phenomena appear to be independent.

In light of the findings presented here, one can conclude that phonations representing lateral phase asymmetries do not necessarily contain significant subharmonic components. For this reason, the female subjects did not undergo acoustic spectral analysis. Furthermore, the small number of asymmetrical phonations with strong subharmonics does not validate any conclusions with respect to this link.

A possible correlation between low magnitude subharmonics and phase asymmetries remains to be investigated. Nunez-Batalla, and colleagues,²³ studying subjects with known abnormal voices and documented pathological lesions of the vocal folds, indicate that the presence of subharmonics may correspond to a qualitative change in the vibratory system, even when the parameters of jitter and shimmer are within normal limits. Interestingly, the absence of a strong correlation between the presence of subharmonics and asymmetries in this study appears to support the normality of the phenomena investigated.

The human voice and the physical characteristics of the vocal folds may be affected by anything from serious pathologic conditions to breathing polluted city air. Various medications, which primarily or secondarily have effects on hydration status (diuretics, antihistamines), or hormonal status (oral contraceptives, corticosteroids), alter the physiology of the vocal tract to a certain degree. Similarly, acid reflux laryngitis and upper respiratory tract infections can have profound effects on phonatory function, with gross glottic manifestations. Most professional voice users are quite sensitive to these effects and are aware of the deterioration of vocal quality under these conditions. Although many of the primary and secondary laryngeal effects of these conditions and medications are known, or suspected, their association with asymmetries has not been reported. The medical questionnaire detected several individuals with conditions which may be effect modifiers for the presence of asymmetry. Even though no association was detected for individuals taking antihistamines, oral contraceptives, or having a history of URTI, or GE reflux, the sample size was insufficient to identify subtleties. The reader is referred to Sataloff¹ for a complete discourse of this subject.

Similarly, excessive talkativeness and voice abuse can have substantial consequences for the phonatory system. Despite the fact that it did not appear that either social or occupational talkativeness were related to the prevalence of asymmetry in this sample, a more thorough evaluation by a speech-language pathologist may uncover associations that were not found or considered here.

In spite of the tremendous strides having been made in the understanding of the complex physiology of voice production, the prevailing theories of

voice production by van den Berg,²⁴ augmented by the fundamental ultrastructural vocal fold analysis of Hirano,^{25,26} although essential to the understanding of voice production, do not adequately account for many non-pathological variations of the mucosal wave. Titze^{27,28} has begun to set the necessary theoretical framework for the study of vocal fold vibration, accounting for certain variations. However, the understanding of the physiology of vocal fold vibration is complicated by considerable uncertainty about the degree to which the normal system may be nonlinear, and about the degree to which the normal system may be affected by random influences.²⁹ Recently, the application of chaos theory to voice research has been made.³⁰⁻³² The application of nonlinear dynamics may also contribute to the understanding of common vocal events, for example pitch jumps between chest and head registers.³³

Interestingly, the degree to which these asymmetries evolve is also unclear. Perhaps with aging, improved vocal hygiene, or professional voice training one may affect the symmetry of their mucosal wave. It has been suggested that certain physiological parameters differ between trained and untrained singing and speaking voices.³⁴ Sataloff reports¹ (anecdotally) a lower incidence of mucosal wave asymmetries in trained singers. Surprisingly, Millet et al¹³ noted a higher incidence of lateral phase asymmetries in trained voice users (although the duration of training was significantly less than that of the typical professional). Regardless, these observations have enormous clinical implications and may influence outcome measures in patients presenting with voice disorders.

CONCLUSIONS

Clinically, no epidemiological studies have reported the prevalence of mucosal wave phase asymmetries in the general population. The 10.5% with lateral phase asymmetries that were discovered in this population may influence the way in which this phenomena is treated in the clinical laryngology practice. The 36.5% prevalence in the upper register, coupled with the notation that none of the lateral phase asymmetries existed in the modal voice alone may provide clues to nonlinear modeling of the phonatory system. Mucosal wave dissimilarities could

be far more common in the general population than previously recognized, representing a physiologic variance of normal. However, taking into account the small number of subjects participating in this study and the paucity of reported databases of normal parameters, interpretation of the results should be undertaken with a degree of caution. These results establish a starting point and justification for normative population studies for epidemiological purposes, which are required before the generalization of variations of the human mucosal wave. The physiologic and pathologic variability of the mucosal wave should be familiar to any otolaryngologist using videostroboscopy as part of a clinical practice.

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